









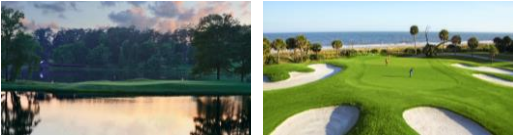


Agenda

-  ADHD
-  Anxiety
-  Sleep
-  Chronic Pain

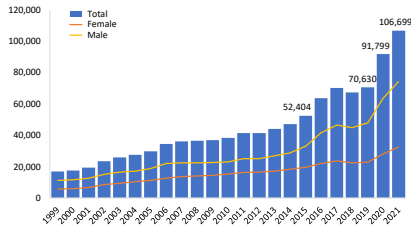
Introduction

Mental illness is common.
 Treatment is effective, especially in terms of Recovery.
 Addiction is a risk of some commonly used psychotropics.



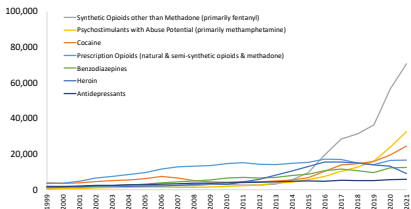
Source

Figure 1. National Drug-Involved Overdose Deaths*, Number Among All Ages, by Gender, 1999-2021



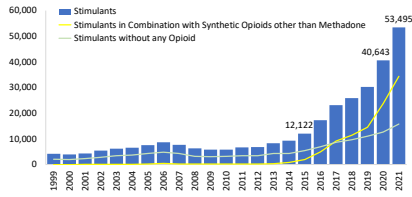
*Includes deaths with underlying causes of unintentional drug poisoning (9A0-9A4), suicide drug poisoning (9B0-9B4), homicide drug poisoning (9E5), or drug poisoning of undetermined intent (Y10-Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2021



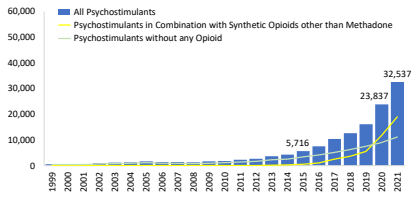
*Includes deaths with underlying causes of unintentional drug poisoning (9A0-9A4), suicide drug poisoning (9B0-9B4), homicide drug poisoning (9E5), or drug poisoning of undetermined intent (Y10-Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021



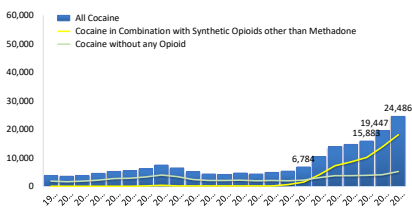
*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the ICD-10 multiple cause-of-death code. Abbreviated to psychostimulants in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Figure 7. National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement, Number Among All Ages, 1999-2021

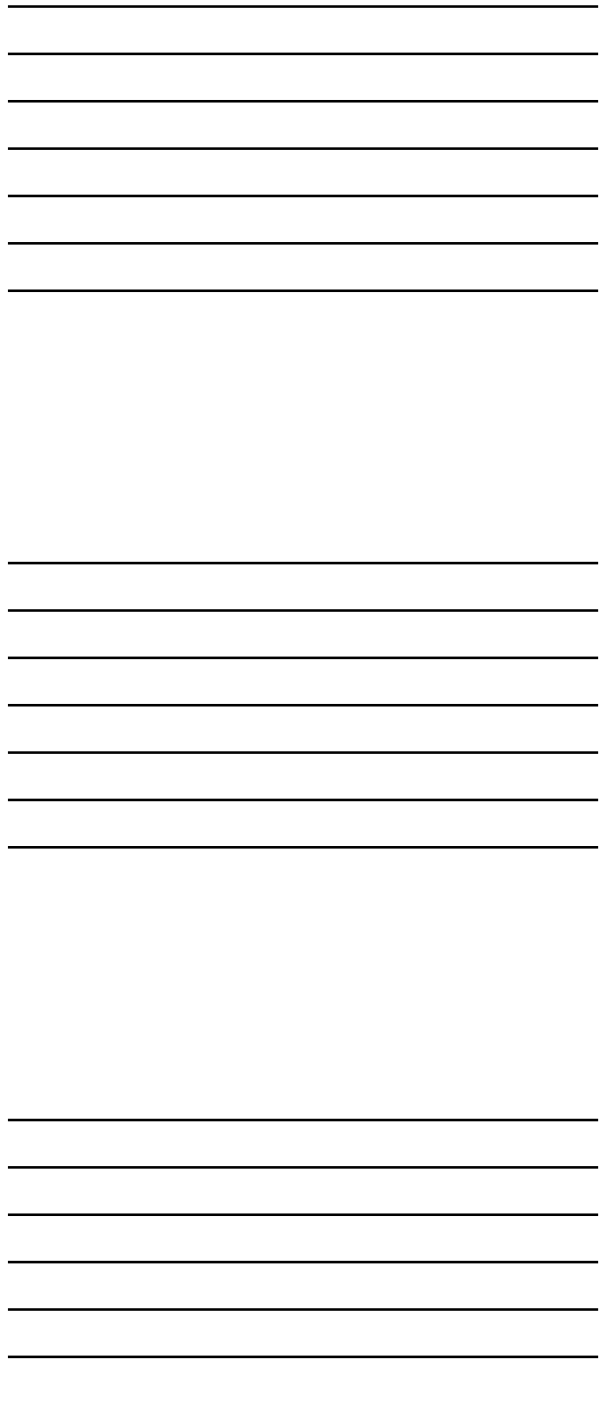


*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the ICD-10 multiple cause-of-death code. Abbreviated to psychostimulants in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Figure 8. National Drug Overdose Deaths Involving Cocaine*, by Opioid Involvement, Number Among All Ages, 1999-2021



*Among deaths with drug overdose as the underlying cause, the cocaine category was determined by the ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.



Awareness

Raising awareness

- Drug overdose is the leading cause of accidental death in the United States.¹
- Drug overdose deaths in the United States were up 30% in 2021.²
- Amphetamine-related hospital costs totaled \$436 million in 2003 and increased to \$2.17 billion in 2015.³

>80 people died every day in the United States due to stimulants in 2019.⁴

Stimulant overdose deaths are rising primarily due to the co-involvement of synthetic opioids, increased availability, higher potency, and lower cost.

While synthetic opioids still account for most overdose deaths, from 2009 through 2019 there have been:

10-fold increase in deaths involving psychostimulants.⁵

10-fold increase

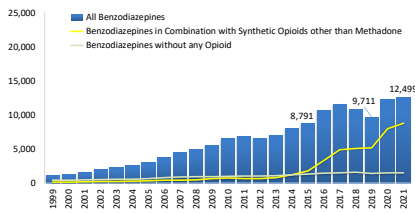
5.5-fold increase in deaths involving cocaine and opioids; after 2012, **9-fold increase** in deaths involving psychostimulants and opioids.⁶

In 2019, **3 out of every 4** cocaine related deaths involved opioids and **1 out of every 2** psychostimulant related deaths involved opioids.⁷

*Psychostimulants are primarily methylamphetamines.

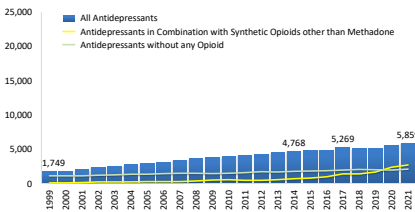
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Figure 9. National Drug Overdose Deaths Involving Benzodiazepines*, by Opioid Involvement, Number Among All Ages, 1999-2021



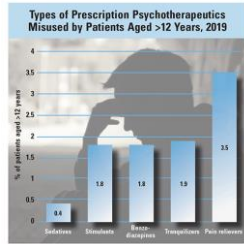
*Among deaths with drug overdose as the underlying cause, the benzodiazepine category was determined by the T42.4 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2/23.

Figure 10. National Drug Overdose Deaths Involving Antidepressants*, by Opioid Involvement, Number Among All Ages, 1999-2021



*Among deaths with drug overdose as the underlying cause, the antidepressant subcategory was determined by the following ICD-10 multiple cause-of-death codes: Tricyclic and tetracyclic antidepressants (T43.0), monoamine oxidase inhibitor antidepressants (T43.1), and other unspecified antidepressants (T43.2). Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2/23.

Misuse of Psychotropics

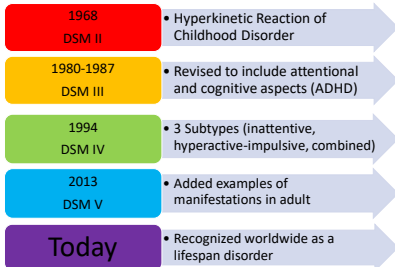


Misuse of Prescription Psychotropic Drugs (uspharmacist.com)

ADHD

1. Definition
2. Prevalence
3. Diagnosis
4. Treatment





DSM-5-TR

DSM-5-TR



- A. Inclusion criteria (for adults)
 1. Inattention: need 5 or more of 9
 2. Hyperactivity/impulsivity: need 5 or more of 9
- B. **Some** symptoms present since before age 12 [neurodevelopmental]
- C. Several symptoms present in 2 or more settings
- D. **Interfere with or reduce quality of** social, academic, or occupational **functioning**
- E. Not better explained by other disorders

"[cognitive] tests are not sufficiently sensitive or specific to serve as diagnostic indices," (APA, 2022).

Clinical Manifestations in Adults

ADHD is characterized by a persistent pattern of attention deficit, hyperactivity, and/or impulsivity that pervades across a variety of settings and results in functional impairment.^{18,19,21}

- Although onset occurs in childhood, ADHD is not necessarily diagnosed at that time.
- The clinical manifestation is heterogeneous, with different levels of severity and prevalence of each core symptom.^{22,23}
- Symptoms may wax and wane due to changing life circumstances, functional expectations, and/or comorbid conditions.²⁴
- Some may experience a reduction or remission of symptoms, particularly hyperactivity, with age.^{25,26}
- Approximately 30-70% of adults with ADHD have emotional dysregulation (e.g., mood lability, irritability, anger outbursts, low frustration tolerance, motivational deficits).^{27,28}
- Dysfunctional strategies (e.g., drinking alcohol, smoking cannabis) may be used to cope with emotional turmoil, social isolation, and rejection.²⁹
- People with ADHD often identify positive aspects such as creativity, enthusiasm, awareness of the multiplicity of things, and the ability to hyper focus and multitask when interested in a topic.³⁰



Focus with ADHD "feels like a short wave radio that most of the time can't find the right frequency."³¹

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Hyperactivity and Impulsiveness

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HYPERACTIVITY AND IMPULSIVITY (3 or more for adults)

| What to Watch for When? | Group Behavior? | People who self-report as being hyperactive? |
|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| When there is too much restlessness or fidgeting? | Restless, restless or still | • Excessive movement • Inattention • Impulsivity • Disruptive behavior |
| When there is too much restlessness or fidgeting when talking or when others are talking? | • Too much restlessness or fidgeting when talking or when others are talking • Too much restlessness or fidgeting when talking or when others are talking | • Excessive movement • Inattention • Impulsivity • Disruptive behavior |
| When there is too much restlessness or fidgeting when talking or when others are talking? | • Too much restlessness or fidgeting when talking or when others are talking • Too much restlessness or fidgeting when talking or when others are talking | • Excessive movement • Inattention • Impulsivity • Disruptive behavior |
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18. The term "persistent" does not mean that symptoms must be present every day. It means that symptoms must be present on a regular basis. For example, symptoms must be present on most days of the week for at least 6 months.

19. The term "pervasive" does not mean that symptoms must be present in every setting. It means that symptoms must be present in two or more settings. For example, symptoms must be present in at least two of the following settings: home, school, work, or other important areas of functioning.

20. The term "interferes with or reduces the quality of" means that symptoms must cause significant problems in social, academic, or occupational functioning. For example, symptoms must cause significant problems in at least one of the following areas: social relationships, academic performance, or occupational performance.

21. The term "not better explained by another disorder" means that the symptoms must not be better explained by another mental disorder. For example, symptoms must not be better explained by anxiety disorder, depression, or bipolar disorder.

22. The term "heterogeneous" means that symptoms can vary in severity and prevalence. For example, some people may have only a few symptoms, while others may have many symptoms.

23. The term "wax and wane" means that symptoms can change in severity over time. For example, symptoms may be more severe during certain periods of a person's life.

24. The term "life circumstances, functional expectations, and/or comorbid conditions" means that symptoms can be influenced by these factors. For example, symptoms may be more severe during periods of stress or when there are other mental health conditions present.

25. The term "reduction or remission of symptoms" means that symptoms may become less severe or stop altogether. For example, symptoms may be less severe in adulthood compared to childhood.

26. The term "approximately 30-70%" means that the majority of people with ADHD experience emotional dysregulation, but not all.

27. The term "emotional dysregulation" means that people with ADHD may experience difficulties with mood, irritability, anger, and frustration tolerance.

28. The term "dysfunctional strategies" means that people with ADHD may use unhealthy coping mechanisms to deal with their symptoms.

29. The term "creativity, enthusiasm, awareness of the multiplicity of things, and the ability to hyper focus and multitask" means that people with ADHD may have strengths in these areas.

The clinical interview and evaluation continues to be the mainstay of ADHD diagnosis.^{1,11,12}
 Use the DSM-5-TR diagnostic criteria for ADHD to guide your clinical assessment of the patient.^{1,11,12}

Table 1. Linking diagnostic criteria with adult manifestations of ADHD^{11,12}

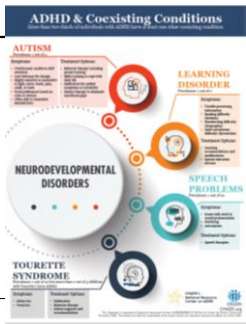
| DSM-5 TR Criterion for ADHD | Typical behaviors ^{11,12} | Provider signs (self-report or coding manifestations) ^{11,12} |
|-------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities | Distractions or errors in detail, work & household | <ul style="list-style-type: none"> • May be careless (e.g., careless, careless, careless, careless) • Fatigued from energy required to control "inattention" problems • Forgetful • May be underdeveloped metacognitive skills • Problems learning new material • May be unable to record them of tasks |
| Often has difficulty sustaining attention in tasks or play activities | No difficulty sustaining focused during lectures, conversations, or lengthy reading, but difficulty reading fiction | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Often does not seem to listen when spoken to directly | Does not seem to listen, even in the absence of any obvious distraction | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Often has trouble organizing tasks and activities | Does not seem to organize, even in the absence of any obvious distraction | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort | Usually, dislikes or is reluctant when preparing reports, completing forms, or reviewing lengthy projects | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Often loses things necessary for tasks or activities | Loses books, notes, keys, appointment, calendar, mobile telephone | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Is often easily distracted by extraneous stimuli | Easily distracted by unrelated thoughts | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |
| Is often forgetful in daily activities | Forgetful when doing household chores, forgetful to return calls, pay bills, attend appointments | <ul style="list-style-type: none"> • Avoids reading books or activities that require sustained attention for leisure • May have unengaging activities that require sustained attention • Work harder than others to get things • Engages in distractions to increase ability to complete tasks |

¹¹ If no more symptoms have persisted for at least 6 months for a clinician that is inconsistent with developmental level and that regularly impacts directly or indirectly on social and academic/occupational activities. ¹² "Average behavior" does not refer to "normal."

Inattention

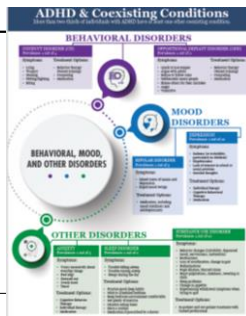
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Comorbidity



ADHD-Coexisting-Conditions-2023.pdf (d393uh8gb46i22.cloudfront.net)

Comorbidity



ADHD-Coexisting-Conditions-2023.pdf (d393uh8gb46i22.cloudfront.net)

Differential

Overview of Possible Causes for Presenting Symptoms Similar to ADHD

| Psychiatric Disorders | Non-Psychiatric Disorders | Other |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> Mood disorders (depression, bipolar) Personality disorders (antisocial and borderline) Generalized anxiety disorder Substance abuse disorders, dependence, intoxication or withdrawal Dementia Asperger's and Autism spectrum disorders | <ul style="list-style-type: none"> Medication interactions and adverse effects Hearing difficulties Hepatic diseases Lead toxicity Obstructive sleep apnea Head injury Seizure disorders Thyroid disorders Vitamin B12 deficiency | <ul style="list-style-type: none"> Transient stress, loss or grief Malingering |

[adhd19-assessment-table2.pdf \(aafp.org\)](#)

Millions of US children have been diagnosed with ADHD

- The estimated number of children aged 3–17 years ever diagnosed with ADHD, according to a national survey of parents,¹ is 6 million (9.8%) using data from 2016-2019. This number includes
 - 3–5 years: 265,000 (2%)
 - 6–11 years: 2.4 million (10%)
 - 12–17 years: 3.3 million (13%).
- Boys (13%) are more likely to be diagnosed with ADHD than girls (6%).¹
- Black, non-Hispanic children and White, non-Hispanic children are more often diagnosed with ADHD (12% and 10%, respectively), than Hispanic children (8%) or Asian, non-Hispanic children (3%).¹

[Data and Statistics About ADHD | CDC](#)

Prevalence

45-70% of childhood cases persist into adulthood.

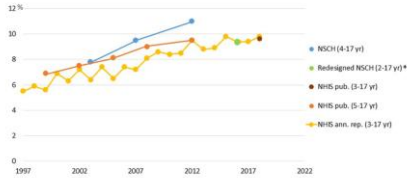
Estimated prevalence rate is 4.4-5.2% in U.S. adults.

Highly heritable: parents with ADHD have a > 50% chance of having a child with ADHD.

National Academic Detailing Services - ADHD Clinician Guide - GroupbyCampaign (sharepoint.com)

Clinical Manifestations

(Percent of children with a parent-reported ADHD diagnosis)



ADHD Throughout the Years | CDC

Impact

| | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Health problems</p> <ul style="list-style-type: none"> • Suicidality (completions, attempts, and ideation) • Development of comorbidities (e.g., mood, sleep difficulty, anxiety, SUD) • Obesity and overeating | <p>High-risk behavior consequences</p> <ul style="list-style-type: none"> • Delinquency and crime • Motor vehicle accidents • Risky driving, more speeding tickets • Unplanned pregnancies • Sexually transmitted infections | <p>Relationship and work challenges</p> <ul style="list-style-type: none"> • Lower educational and occupational achievement • Financial problems • Diminished social functioning • Divorce |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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AAFP

ADHD Risk Reduction Checklist

Diagnosis:

- Confirm symptoms and impairment meet DSM-5 criteria for ADHD diagnosis
- Confirm symptoms are not explained by other conditions
- Treat any co-existing mental health conditions first
- Confirm patient understands their condition and their role in ADHD management

Treatment considerations:

- Consider non-pharmacological management
- Address risk related to driving and other lifestyle risks
- Determine the importance of pharmacological and non-pharmacological treatment options and patient's readiness to participate in their care
- Confirm patient has no contraindications to suggested treatment
- Confirm patient has no suicidal ideations before initiation medication treatment
- If suicidality detected, address it first
- Do not prescribe short acting stimulants to patients with active substance use, including alcohol and cannabis

adhd19-risk-safety-checklist.pdf (aafp.org)

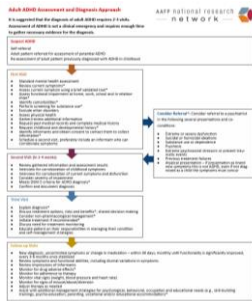
AAFP

Treatment with stimulants:

- Confirm patient understands risks associated with stimulant treatment (treatment effects, side effects, legal considerations)
- Measure baseline symptom severity, weight, blood pressure, heart rate and sleeping patterns before initiating stimulant medications
- Confirm patient has no history of seizures and tics
- Remember that stimulants are addictive and that they are controlled substance
- Prescribe stimulants according with the requirements for a Schedule II controlled substance
- Consider dose titration using the smallest available dose increment over intervals to maximum effective tolerated dose
- Continually monitor for treatment effects, side effects and outcomes
- Conduct regular vital signs monitoring (blood pressure, weight, heart rate)
- Monitor for stimulant misuse including treatment non-adherence and signs of abuse
- Assess regularly for signs of use of other substances
- Assess symptom severity and treatment effects at least annually

[adhd19-risk-safety-checklist.pdf \(aafp.org\)](#)

AAFP ADHD Algorithm



[adhd19-algorithm.pdf \(aafp.org\)](#)

Psychological Testing for ADHD

1. IQ Testing (WISC or WAIS)
2. Digit Span, Number-Letter Sequencing
3. Working memory and Processing Speed
4. Rating Scales (Vanderbilt or Brown)
5. Continuous Performance Test (Conners, Integrated Visual and Auditory, Auditory, Tests of Variables of Attend, Gordon Diagnostic)

[ADHD: Is Objective Diagnosis Possible? - PMC \(nih.gov\)](#)

Gender

Gender differences

- ADHD is thought to be underrecognized and underdiagnosed in females with implications for long-term social, educational, and health outcomes.¹⁴
- Females are more likely to be diagnosed with predominantly inattentive ADHD.¹⁵⁻¹⁶
 - Inattentive in girls and women with ADHD may present as being easily distracted, disorganized, overwhelmed, and lacking in effort or motivation.¹⁶
- In females, symptoms are typically pervasive and impairing rather than transient or fluctuating.¹⁶
- Hyperactive-impulsive symptom severity may be lower in females than in males and/or may be more verbal (e.g., interrupting others, talking excessively, frequently changing topics).¹⁶
- Difficulties with emotional lability and emotional dysregulation may be more severe or common in girls and women with ADHD.¹⁶
- Social problems may be particularly impairing.¹⁶
- ADHD symptoms may become more obvious later in females, often during periods of social or educational transition.¹⁶
- Adult women may develop awareness of their difficulties leading them to seek services.¹⁶

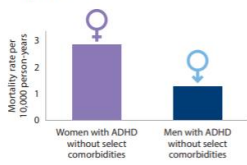
Females with undiagnosed ADHD are more likely to receive a primary diagnosis of internalizing disorder (e.g., anxiety, depressive, personality disorder). The delay diagnosing ADHD and seeking appropriate treatment.¹⁶



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Mortality

Figure 2. ADHD is associated with increased mortality, and mortality is higher for women compared to men.



A Danish nationwide cohort study estimated Mortality Rate Ratios (MRRs) in 1.92 million individuals, including 32,061 with ADHD, for 24.9 million person-years. Girls and women with ADHD without oppositional defiant disorder, conduct disorder, or substance use disorder had a **2.85x (95% CI = 1.56-4.71) higher risk of death than women without the 4 disorders.** This was more than double the 1.27x (95% CI = 0.89-1.76) higher risk of death in boys and men.¹⁶

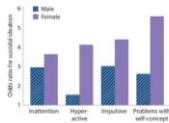
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Suicidal Thoughts

Gender and symptom severity have been shown to influence suicidal thoughts.

According to one study, the likelihood of suicidal ideation was significantly higher in women with ADHD compared to controls. There was also a statistically significant positive association between the likelihood of suicidal ideation and symptom severity (4 of 4 Conners Adult ADHD Rating Scale (CAARS) subscales in females).¹⁷

Figure 3. Odds ratios for suicidal ideation for a one-point increase in severity on each item on the four CAARS subscales



1 ADHD is a chronic health problem with significant risk for mortality and long-term morbidity in adulthood. People with ADHD may live with unrecognized symptoms from childhood (median age of 6) to adulthood (up to the median age of 25) for a median time (up of 17 years) without treatment.¹⁸

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Diagnosis of ADHD

1. 5 of 18 symptoms present for 6 months
2. Establish chronicity (several symptoms before age 12) and contextual stability (2 settings)
3. Clinically significant impairment in functioning
4. Differential diagnosis
5. Finalize diagnosis (document what prevented childhood diagnosis)

Treatment

Treatment

ADHD requires a comprehensive, collaborative, and multimodal treatment approach tailored to meet the unique needs of the person with ADHD.¹ It is important to clearly identify all areas of impairment due to ADHD at the onset of treatment and regularly re-evaluate the impact of the condition.¹



Pharmacotherapy is first-line treatment for ADHD in adults to target core symptoms causing impairment.^{1,5,11,20,21,28,31,41,46-49}

- Psychostimulants: amphetamines, methylphenidate
- Non-stimulants: atomoxetine

Non-pharmacological interventions for adult ADHD can play an important role in helping adults manage and understand their condition.^{46,50,51}



According to a study in a nationally representative sample of adults in the U.S., only 10.9% of respondents with adult ADHD received treatment for ADHD in the 12 months before interview.¹⁷

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Behavioral Therapy

Psychotherapy may help you:

- Improve your time management and organizational skills
- Learn how to reduce your impulsive behavior
- Develop better problem-solving skills
- Cope with past academic, work or social failures
- Improve your self-esteem
- Learn ways to improve relationships with your family, co-workers and friends
- Develop strategies for controlling your temper

Conundrums

Clinical Conundrums for the Experienced Clinician

Difficulty determining whether stimulant treatment is yielding a benefit in a patient with co-occurring ADHD and SUD

- Carry out structured assessments of ADHD symptoms.
Determine the severity of the SUD. Often in severe cases, don't see improvement in ADHD symptoms unless SUD severity is reduced/alcohol-drug use diminishes.
It is critical to target treatment of both ADHD symptoms and drug use.
If don't see an effect on ADHD symptoms, may need to use higher doses. If you are afraid to use medications in active substance users, under-dosing may increase risks without benefit.
Look for functional improvements. If there is no improvement in social, occupational, academic settings and still actively using drugs, then no reason to keep prescribing.

PDSI Lecture Frances R. Levin

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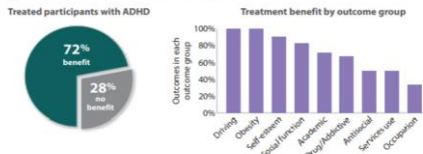
Treatment Outcomes

Four colored boxes containing text: Reduced suicidal ideation and attempts (red), Reduced likelihood of MVA (blue), Reduced criminal behavior (green), Higher self-esteem and social functioning (purple).

Horizontal lines for notes.

Outcomes

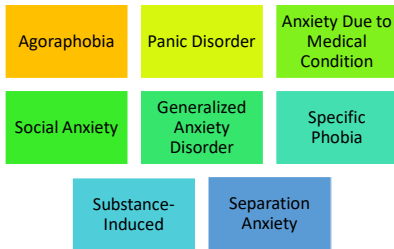
Figure 4. ADHD treatment improves outcomes, compared with untreated ADHD.



According to one systematic review of over 300 studies, without treatment, people with ADHD had poorer long-term outcomes in all categories compared with people without ADHD. Treatment of ADHD (versus untreated) resulted in favorable outcomes for 72% of outcomes reported (55 of 76 outcome results from 48 studies) (shown on left). Treatment benefits varied by outcome group (shown on right).¹¹

Horizontal lines for notes.





Prevalence of Anxiety

*Based on diagnostic interview data from the National Comorbidity Study Replication (NCS-R), Figure 1 shows past year prevalence of any anxiety disorder among U.S. adults aged 18 or older.¹



- An estimated **19.1%** of U.S. adults had any anxiety disorder in the past year.
- Past year prevalence of any anxiety disorder was higher for **females (23.4%)** than for **males (14.3%)**.

*An estimated **31.1%** of U.S. adults experience any anxiety disorder at some time in their lives.²

[Any Anxiety Disorder - National Institute of Mental Health \(NIMH\) \(nih.gov\)](https://www.nimh.nih.gov)

Treatment

Evidence-based treatment options for anxiety and insomnia

| Anxiety ²⁸ | Insomnia ²⁹ |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Medications:</p> <ul style="list-style-type: none"> Selective serotonin reuptake inhibitors (SSRIs) or serotonin/norepinephrine reuptake inhibitors (SNRIs) Bupropion Hydroxyzine Pregabalin <p>Behavioral therapies:</p> <ul style="list-style-type: none"> Cognitive behavioral therapy Exposure therapy  | <p>Behavioral therapies:</p> <ul style="list-style-type: none"> Cognitive behavioral therapy for insomnia (CBT-I) Brief behavioral therapy (BBT-I) <p>Medications:</p> <ul style="list-style-type: none"> Low-dose doxepin Non-benzodiazepine receptor agonist (e.g., zolpidem)  |

National Academic Detailing Services - 10-1527_Benzos_Provider_QRG_P97047-GroupbyCampaign (sharepoint.com)

Prevalence of Benzodiazepine Use

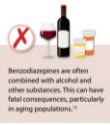
Prevalence of benzodiazepine use

Millions of people are prescribed benzodiazepines for the treatment of anxiety, insomnia, depression, muscle spasms, and neurologic conditions.³⁰ Best practice guidance recommends short-term use,³¹ but the reality is a large number of patients receive these drugs on a long-term basis.³²



Older adults will have the highest prevalence of benzodiazepine use compared to younger adults.³³ Veterans between 50-64 years old have the highest prescribed use of benzodiazepines.³⁴

Higher rates of alcohol and other substance use are also found in this aging population.³⁵ The combination of advanced age, benzodiazepine use combined with alcohol and other substances, and high-risk medical comorbidities can potentially put them at an increased risk of a fatal overdose.³⁶



Benzodiazepines are often combined with alcohol and other substances. This can have fatal consequences, particularly in aging populations.³⁷

Re-evaluating the Use of Benzodiazepines. A VA Clinician's Guide (B 10-1528)

Outcomes On Benzodiazepines

Serious outcomes associated with benzodiazepines



Overdose (OD) death^{38,39}

Benzodiazepines are the second most common medication class involved in intentional and unintentional pharmaceutical OD deaths.⁴⁰ The OD death rate involving benzodiazepines rose 8-fold from 2000-2018, with opioids involved in 85% of these deaths in 2018.^{41,42} **CAUTION:** Overdose risk is not just with opioids! While this combination is well-known, much less attention is given to alcohol and benzodiazepines which also has a risk of overdose when combined.⁴³



All-cause mortality

- Increases 60% in patients on benzodiazepines.⁴⁴
- No studies (N=23) show a protective effect on mortality from benzodiazepines.⁴⁴

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Outcomes On Benzodiazepines



Motor vehicle accident
Risk increases by 60%.¹⁹



Dependence and withdrawal
Dependence occurs in nearly all patients taking chronic benzodiazepines within as little as 4-6 weeks of continued therapy. In some, it can cause addiction.^{20,21}

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Outcomes on Benzodiazepines



Cognitive impairment
• Short- and long-term use of benzodiazepines may lead to impairment across many cognitive domains.²²⁻²⁶
• Long-term use impacts the spectrum of domains of cognitive function, especially verbal memory.²⁷



Falls risk
The risk of falls increases in older adults who use benzodiazepines and can double in those age 80 and over.²⁸ The risk of hip fractures also rises with benzodiazepine use.²⁹

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Outcomes on Benzodiazepines



Respiratory outcomes with benzodiazepine use
• **General population:** Use has been associated with a 50% risk of community acquired pneumonia.³⁰
• **Patients with COPD:** Use increases the risk of outpatient respiratory exacerbations, emergency room visits, and mortality.³¹⁻³²
• **Patients with sleep apnea:** Use worsens respiratory outcomes and oxygen levels overnight.^{33,34}



Pregnancy related outcomes
• A 2-fold increased risk of preterm birth in women using benzodiazepines during pregnancy.³⁵
• Advanced levels of care may be required when benzodiazepines are prescribed, such as cesarean delivery and neonatal intensive care admission.^{36,37}

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Misperceptions



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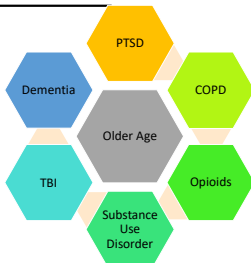
Taper

Clinical indications for tapering a benzodiazepine^{4,12,13}

| | INDICATIONS | TAPER METHOD |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SHORTER TAPER | <ul style="list-style-type: none"> Patients who have been on low doses of benzodiazepines for a relatively short time (less than a year)⁷ Medication adverse effects indicate risks are greater than benefit Comorbidities increase risk of complication | <ul style="list-style-type: none"> Gradually reduce total dose by 50% over the first 4 weeks (e.g., 10-15% decrease weekly) Maintain on that dose (50% original dose) 1-2 months, then Reduce dose by 25% every 2 weeks |
| LONGER TAPER | <ul style="list-style-type: none"> Patients on high doses of benzodiazepines or those who have been taking the medication consistently for many years¹¹ Function is not improved with benzodiazepine use Tolerance has developed with long-term prescription Comorbidities increase risk of complication | <ul style="list-style-type: none"> No faster than 10% every 2-4 weeks |

[National Academic Detailing Services - 10-1527_Benzos_Provider_ORG_P97047-GroupbyCampaign \(sharepoint.com\)](#)

Benzodiazepine High Risk Groups





Sleep History

CC:
HPI: (location, quality, quantity timing, setting, aggravating/relief, associated)
OSA (snoring, witnessed, morning headache, daytime sleepiness, awoken choked, diaphoresis)
 Epworth Sleepiness Scale
 Stanford Sleepiness Scale
PLMs (leg cramps, crawly/achy feeling in legs, bedcovers in disarray)
Parasomnias (nightmares, fight in sleep, sleepwalk, seizures, uncontrolled urination)
Insomnia (unable to fall asleep less than 15 minutes, wake up and can't get back to sleep, wake up 1-2 hours early, watch clock, anxiety about sleep, muscle tension)
Bruxism
Shift work
Caffeine/Alcohol/Smoking

[ScreeningQuestions-SleepHistoryandExam.qxd \(aasm.org\)](#)

STOP BANG for OSA

| STOP | | | |
|----------|----------------------------------------------------------------------------------------------|-----|----|
| S | So you snore loudly (louder enough to be heard through closed doors or louder than talking)? | Yes | No |
| T | Do you often feel tired, fatigued or sleepy during the daytime? | Yes | No |
| O | Has anyone observed you stop breathing or choking or gasping during your sleep? | Yes | No |
| P | Do you have or are you being treated for high blood pressure? | Yes | No |

| Bang | | | |
|----------|-------------------------------------------------------------------------------------------|-----|----|
| B | BMI more than 35? | Yes | No |
| a | Age - over 50 years old? | Yes | No |
| n | Neck circumference - is it greater than 17" if you are a male or 16" if you are a female? | Yes | No |
| g | Gender - are you a male? | Yes | No |

Insomnia Differential

1. Insomnia associated with other sleep disorders most commonly includes sleep related breathing disorders (e.g., obstructive sleep apnea), movement disorders (e.g., restless legs or periodic limb movements during sleep) or circadian rhythm sleep disorders
2. Insomnia due to medical or psychiatric disorders or to drug/substance (comorbid insomnia)
3. Primary insomnias including psychophysiological, idiopathic, and paradoxical insomnias

[040515.pdf \(aasm.org\)](#)

Behavioral Techniques for Insomnia

1. Stimulus Control (20 minutes)
2. Relaxation Training (muscle, breathing, guided imagery)
3. CBT-I
4. Sleep Restriction (limit time in bed to sleep time)
5. Paradoxical Intention (confront fear of staying awake)
6. Biofeedback
7. Sleep Hygiene

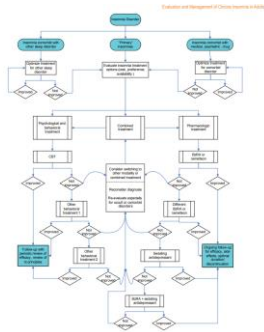
| Component | Intended Effect | Specific Directions for Patients |
|--------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sleep restriction | Increase sleep drive and stabilize circadian rhythm | Reduce time in bed to perceived total sleep time (not less than 5-6 hours), choose specific hours on the basis of personal preference and circadian timing. Increase time in bed gradually as sleep efficiency improves |
| Stimulus control | Reduce arousal in sleep environment and promote the association of bed and sleep | Attempt to sleep when sleepy; get out of bed when awake and anxious at night; use the bed only for sleep or sexual activity (e.g., no watching TV in bed) |
| Cognitive therapy | Restructure maladaptive beliefs regarding daytime and health consequences of insomnia | Maintain reasonable expectations about sleep; review previous insomnia experiences, challenging perceived catastrophic consequences |
| Relaxation therapy | Reduce physical and psychological arousal in sleep environment | Practice progressive muscle relaxation, breathing exercises, or meditation |
| Sleep hygiene | Reduce behaviors that interfere with sleep drive or increase arousal | Limit caffeine and alcohol, keep bedroom dark and quiet, avoid daytime or evening napping, increase exercise (not close to bedtime), remove bedroom clock from sight |

Benzodiazepine Commentary Rosenbaum

This commentary is not meant to be a call for a **benzodiazepine renaissance** but rather an attempt to offer a perspective. Beyond their established efficacy in anxiety distress and insomnia and fueling the debate between "pharmacological Calvinism and psychotropic hedonism" (8), these medications can also offer transient relief and comfort from stress; in a world replete with distress, it may be difficult for people to refrain from seeking a comforting remedy.

[Benzodiazepines: A Perspective | American Journal of Psychiatry \(pschiatryonline.org\)](#)

Algorithm



[040515.pdf \(aasm.org\)](#)

Management Plan

Start with offering evidence-based behavioral therapies

- Cognitive behavioral therapy for insomnia (CBT-I) is recommended as first-line treatment for chronic insomnia.
- Brief behavioral therapy for insomnia (BBT-I) can also be encouraged but is not as effective as CBT-I.

If patient still suffers from insomnia, or if CBT-I is not a good option

Consider medication for chronic insomnia

- Intermittent (e.g., 3 or 5 days/week) dosing for a period of < 2 weeks may help.
- Preferred options include low-dose doxepin (3 or 6 mg) and non-benzodiazepine receptor agonist (e.g., zolpidem).
- Continue to offer CBT-I, if not already completed.

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Management Plan

Avoid benzodiazepines

- In most cases the harm of benzodiazepines (e.g., triazolam, temazepam) outweigh the benefits.
- Benzodiazepines may negatively affect sleep architecture, and have significant interactions with alcohol and other medications (e.g., opioids).
- Tolerance quickly develops to the ability to induce and prolong sleep. Rebound insomnia can occur 1-2 weeks after treatment discontinuation.

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Benzodiazepine Discontinuation Strategy

Strategies for successful benzodiazepine discontinuation

Minimal educational interventions are effective strategies to assist patients with decreasing or stopping benzodiazepines, such as:⁴¹⁻⁴³

- **Brief educational intervention:** medication review, consultation (risk/benefits), assessment of patient readiness, provision of a withdrawal schedule, and education about benzodiazepine use
- **Direct to consumer education:** letters designed to promote cognitive dissonance (e.g., EMPOWER trial), which increased success of discontinuation by 8-fold
- **Augmentation:** psychotherapy and/or pharmacotherapy aimed at addressing underlying condition

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Benzodiazepine Discontinuation Strategy

Framework of a brief educational intervention⁴⁴

Provide information on benzodiazepine dependence, abstinence, and withdrawal symptoms; risks of long-term use, memory and cognitive impairment, accidents, falls, and reassurance about reducing medication.



Patients receiving a brief intervention were 3 times more likely to discontinue benzodiazepine use after 12 months vs. controls.⁴⁵

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Success



30% more patients discontinued benzodiazepines at 12 months.



70% of patients remained benzodiazepine free at 36 months.

75 general practitioners were randomized to provide usual care or a brief educational and a self-help leaflet to improve sleep. Benzodiazepine withdrawal effects (i.e., anxiety, irritability, insomnia) worsened in the intervention group at 6 months but was not different by 12 months. There was no increase in anxiety, depression, insomnia, or alcohol consumption.²²

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Taper

- Go slow!
- Provide written instructions for the taper schedule.
- Document taper schedule in electronic medical record.
- Schedule follow-up with the Veteran to assess tolerability of the taper. This can be done by various health care team members (e.g., nurse, clinical pharmacy practitioner) and provided via clinic visit, telehealth, and/or telephone.
- Be flexible! Adjust schedule to accommodate issues that may arise.
- If withdrawal is experienced, hold or slow down the taper schedule.
- Substitute a longer-acting benzodiazepine if the patient is on a short-acting form and experiencing withdrawal.



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Summary

Summary of strategies to discontinue benzodiazepines

- 1 Determine benefit vs. harm of benzodiazepine therapy.**
 - Is there still an indication for the benzodiazepine?
 - What specific risk factors does the Veteran have?
 - Does the benefit of the benzodiazepine outweigh the risk?
- 2 Employ strategies that help with long-term benzodiazepine discontinuation.²³**
 - Recommend gradual dose reduction and discontinuation.
 - Use educational interventions to achieve better discontinuation outcomes.
 - Offer psychotherapy interventions (e.g., cognitive behavioral therapy for insomnia).
- 3 Perform slow taper over months.**
 - Provide written instructions and document taper recommendations in the medical record.
 - Educate patient on signs and symptoms of withdrawal.

Re-evaluating the Use of Benzodiazepines. A VA Clinician's Guide (18-10-1528)



Chronic Pain

1. Antidepressants
2. Suboxone

Myths
About
Suboxone

1. You aren't really in recovery if you're on Suboxone (medical model)
2. People frequently misuse Suboxone (partial agonist of mu receptor, self-treatment)
3. It's as easy to overdose on Suboxone as it is to overdose on other opiates. (partial agonist with ceiling effect, problems probably combining with other sedatives)
4. Suboxone isn't treatment for addiction if you aren't getting therapy along with it. (combination with therapy is great but Suboxone alone effective)
5. Suboxone should only be taken for a short period of time (chronic medical illness, patient preference)

[5 myths about using Suboxone to treat opiate addiction - Harvard Health](#)



| Pharmacological Agent | Pharmacological Target(s) | FDA-Approved for Insomnia | Pharmacological Agent | Pharmacological Target(s) | FDA-Approved for Insomnia |
|----------------------------------------------|---------------------------|---------------------------|-------------------------------------------|---------------------------|---------------------------|
| Benzodiazepine Hypnotics (Benzos) | | | Hypnotic/Opioid Antagonist (DORAs) | | |
| Eszopiclone | GABA _A | ✓ | Suvorexant | orexin 1/2 | ✓ |
| Flurazepam | GABA _A | ✓ | Lamotrexant | orexin 1/2 | ✓ |
| Quazepam | GABA _A | ✓ | Darborexant | orexin 1/2 | ✓ |
| Temazepam | GABA _A | ✓ | Melatonin Receptor Agonists | | |
| Triazolam | GABA _A | ✓ | Melatonin | melatonin 1/2 | |
| Nonbenzodiazepine Hypnotics (Z drugs) | | | Ramelteon | melatonin 1/2 | ✓ |
| Eszopiclone | GABA _A | ✓ | Tasimelteon | melatonin 1/2 | |
| Zaleplon | GABA _A | ✓ | Anticoagulants | | |
| Zolpidem | GABA _A | ✓ | Clonazepam | GABA _A | |
| Zopiclone | GABA _A | | Gabapentin | α ₂ ligands | |
| Antidepressants | | | Progabalin | α ₂ ligands | |
| Doxepin | 5HT _{2A/3} /H1 | ✓ | Targemine | GABA receptor inhibitor | |
| Trazodone | 5HT _{2A/3} /H1 | | Antihistamines | | |
| Analgesics | | | Diphenhydramine | H1 | |
| Quetiapine | H1/5HT _{2B} | | Hydroxyzine | H1 | |
| Olanzapine | H1/5HT _{2A} | | Antihypertensives | | |
| | | | Clonidine | Alpha 2 antagonist | |
| | | | Clonidine | Alpha 2 antagonist | |
