

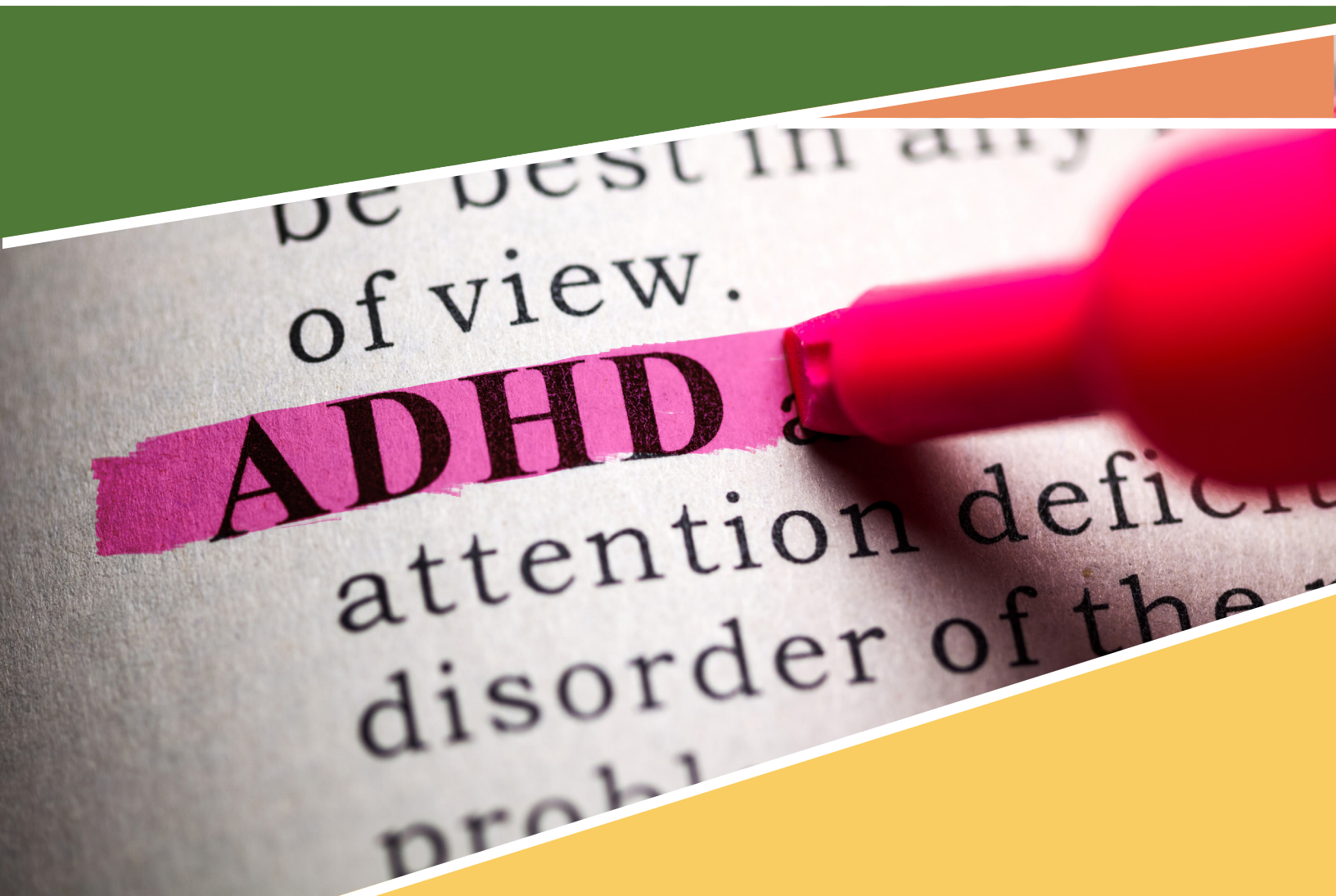
**VA**



U.S. Department  
of Veterans Affairs

## Prescription Stimulants

A VA Clinician's Guide to Re-evaluating  
Use of Prescription Stimulants for Adult  
Attention-Deficit / Hyperactivity Disorder  
(2017)



**Attention Healthcare Provider:**

These recommendations are intended for re-evaluating prescription stimulant use in patients with attention-deficit / hyperactivity disorder.

Individual patient-specific characteristics should be considered when determining appropriate therapy.



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These materials were developed by:

**VA PBM Academic Detailing Service**

*Your Partner in Enhancing Veteran Health Outcomes*

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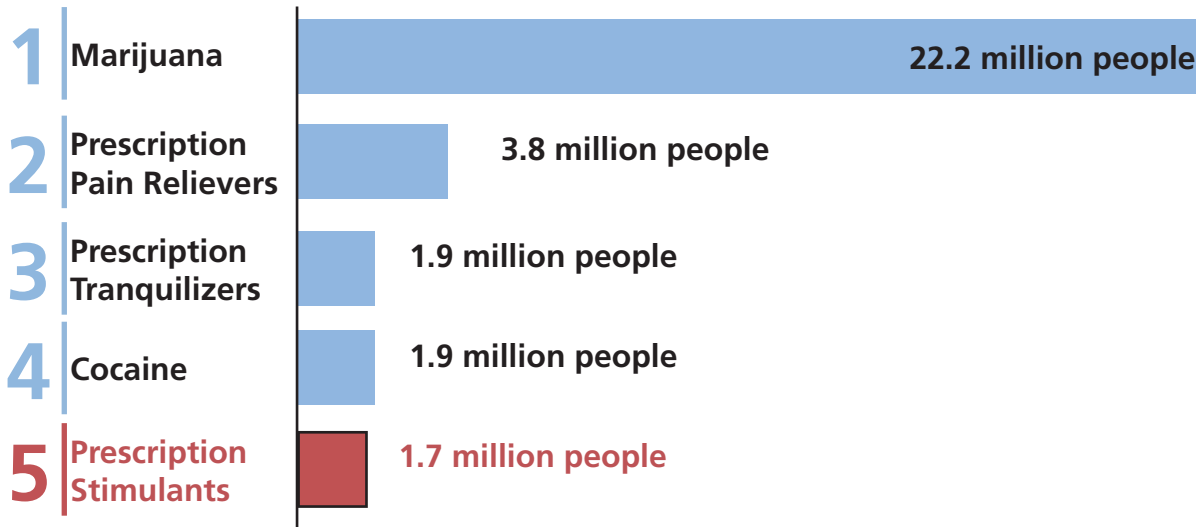
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# Stimulant Use: Importance of Prescribing Appropriately

## The misuse of prescription stimulants is one of the top 5 contributors to illicit drug use in this country <sup>(1)</sup>

Stimulants are considered 1<sup>st</sup> line medications for managing Attention-Deficit/Hyperactivity Disorder (ADHD) and reduce symptom severity with response rates of approximately 70%. However, it is important that we prescribe stimulants only when indicated as misuse of **prescription stimulants** is one of the top 5 contributors to **illicit drug use** in this country.<sup>1</sup>

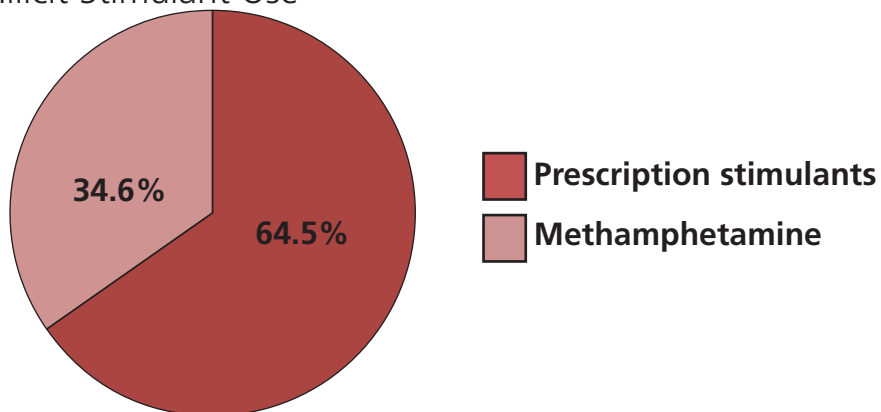
**Figure 1.** Illicit Drugs Used in the United States



Data presented based on a 2015 National Survey on Drug Use and Health in people 12 and older in the civilian, non-institutionalized population in the United States.

A majority of the illicit stimulant use is due to **misuse of prescription stimulants**.<sup>1</sup>

**Figure 2.** Illicit Stimulant Use<sup>1</sup>



## Understanding when stimulants are indicated, and when they aren't

It's important to understand evidence-based treatment options for common disorders and recommend evidence-based management strategies for our Veterans.

**Table 1.** Summary of common disorders and treatment recommendations<sup>2-12</sup>

	1st line recommendation	Place for stimulants	FDA approved?	Evidence about stimulant use
<b>Attention-Deficit Hyperactivity Disorder (ADHD)</b>	Medication and/or behavioral and organizational techniques (depending on medical stability, severity of symptoms, and environmental demands)	1st line medication	Yes	Stimulants are efficacious for reducing ADHD symptom severity with response rates ~70%
<b>Narcolepsy</b>	Pharmacotherapy**: <ul style="list-style-type: none"> <li>Excessive daytime sleepiness (EDS): modafinil, armodafinil or sodium oxybate</li> <li>Cataplexy: sodium oxybate, SNRI</li> </ul> Non-pharm considerations: <ul style="list-style-type: none"> <li>Patient education regarding: dangerous situations due to EDS, sleep hygiene, smoking cessation etc.</li> </ul>	Methylphenidate and amphetamines considered 2nd or 3rd line options for EDS but do not have an established role for cataplexy	Yes	<ul style="list-style-type: none"> <li>Sympathomimetic side effects may be problematic</li> <li>Evidence for efficacy not as strong as with other agents</li> </ul>
<b>Depression</b>	Psychotherapy* Pharmacotherapy* <ul style="list-style-type: none"> <li>SSRI</li> <li>SNRI</li> <li>Bupropion</li> <li>Mirtazapine</li> </ul>	May have a role as augmentation agents, although the evidence is stronger in support of other agents	No	<ul style="list-style-type: none"> <li>Stimulants are not recommended for routine use in patients with depression</li> <li>Stimulants are more effective as a facilitating agent (short term use with an antidepressant; increases rate of improvement) than an augmenting agent or monotherapy</li> <li>May have a place in treatment for elderly patients and/or terminally ill patients with depression</li> </ul>
<b>Post Traumatic Stress Disorder (PTSD)</b>	Psychotherapy: <ul style="list-style-type: none"> <li>Trauma-focused psychotherapy (e.g. PE, CPT, EMDR)</li> <li>Stress inoculation training</li> </ul> Pharmacotherapy: <ul style="list-style-type: none"> <li>SSRI</li> <li>SNRI</li> <li>Prazosin (if trauma nightmares present)</li> </ul>	No established role for treatment of PTSD at this time	No	Stimulants have not been shown to be effective for treatment of PTSD symptoms
<b>Concussion - Mild Traumatic Brain Injury (mTBI)</b>	<ul style="list-style-type: none"> <li>Psychoeducation, supportive stress management and/or cognitive behavioral interventions to enhance recovery, in concert with optimizing the individual's overall comorbid health and psychiatric conditions</li> <li>Psychological/behavioral symptoms should be evaluated and managed according to evidence-based clinical practice guidelines for the respective disorder/symptoms</li> <li>Pharmacotherapy not recommended</li> </ul>	VA/DoD Clinical Practice Guidelines (2016) suggest against offering medication, supplements, nutraceuticals or herbal medicines for neurocognitive effects attributed to mTBI	No	Evidence for efficacy is limited; studies have been small and some have significant methodological flaws; however, emerging evidence suggests there may be a role for stimulants (e.g. cognitive function)

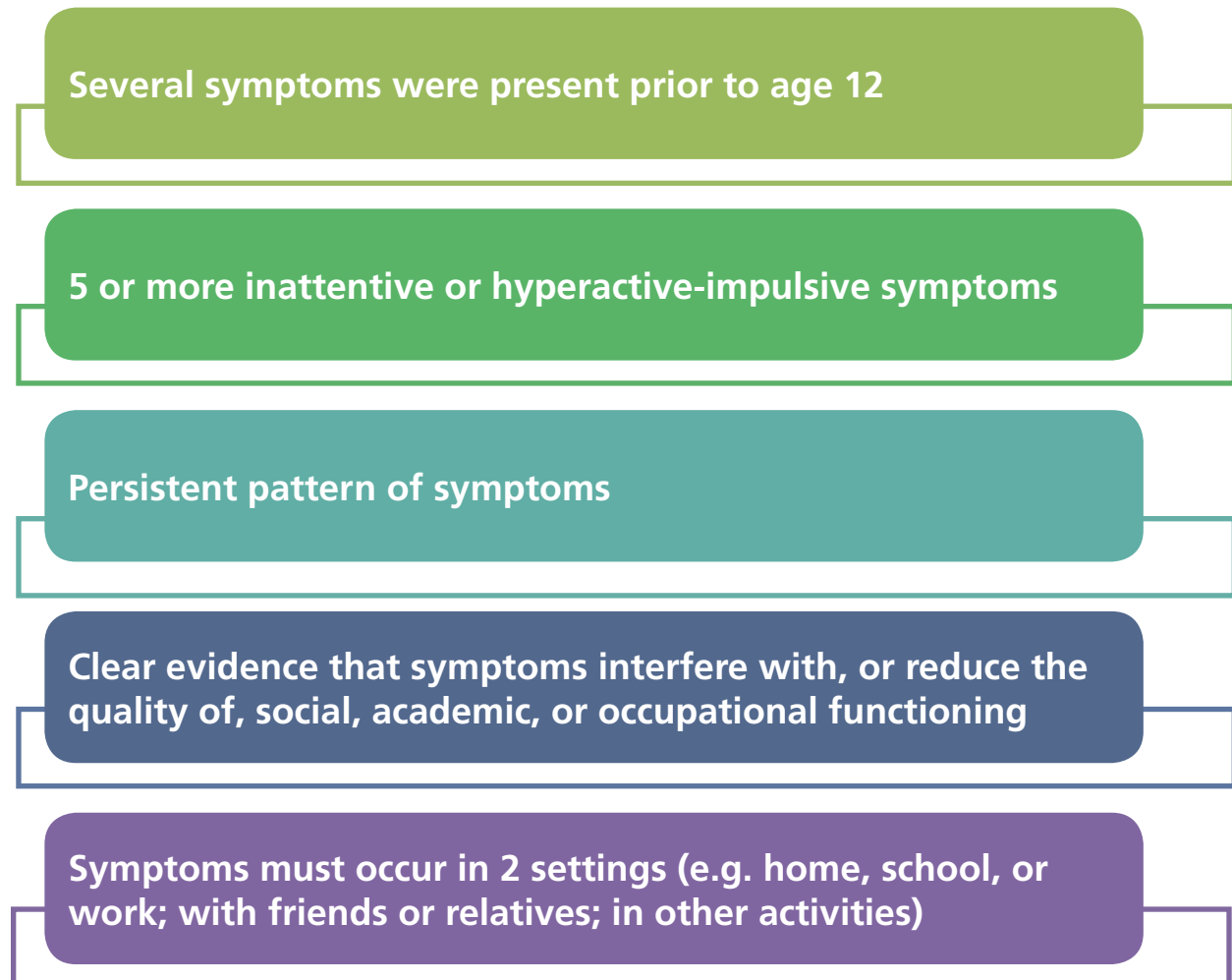
\*Evidence does not support a specific evidence-based psychotherapy or pharmacotherapy over another (e.g. acceptance and commitment therapy (ACT), behavioral therapy/behavioral activation (BT/BA), cognitive behavioral therapy (CBT), interpersonal therapy (IPT); mindfulness-based cognitive therapy (MBCT), problem-solving therapy (PST); offer a combination of pharmacotherapy and psychotherapy for patients with severe, chronic, and/or recurrent major depressive disorder; Electroconvulsive therapy (ECT) may be considered for patients with severe major depressive disorder (MDD) and certain conditions (e.g. catatonia, psychotic depression, severe suicidality, pregnancy); PE= Prolonged exposure; CPT= Cognitive processing therapy; EMDR= Eye movement desensitization and reprocessing; SSRI= selective serotonin reuptake inhibitor; SNRI= selective norepinephrine reuptake inhibitor;

\*\* Please see VA National Formulary for current list of formulary medications (<https://www.pbm.va.gov/PBM/NationalFormulary.asp>)

## Directing our Focus to ADHD

ADHD is a neurodevelopmental disorder defined by symptoms of inattention and/or hyperactivity and impulsivity with resultant impairments of social, academic and occupational functioning.

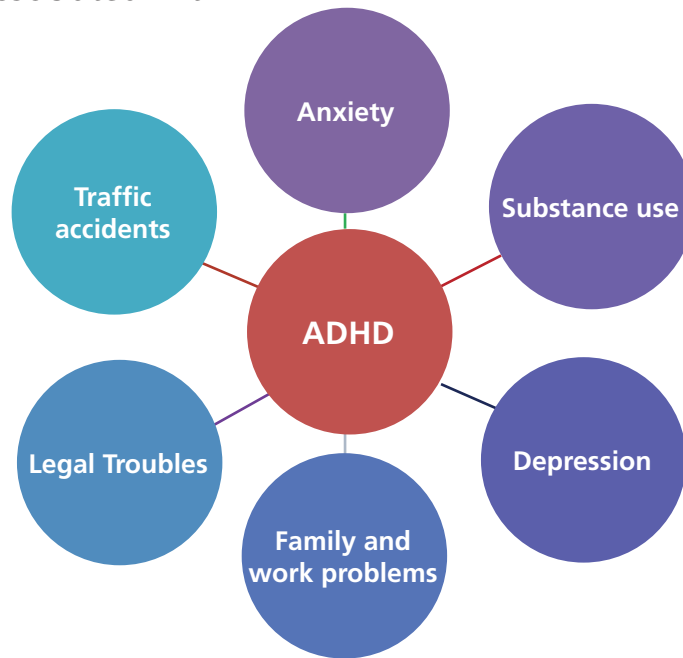
**Figure 2.** Highlights from DSM-5 criteria for ADHD\*



\*See quick reference guide for full criteria

Approximately 1/3 to 1/2 of childhood ADHD persists into adulthood.<sup>8,13-17</sup> Patients with ADHD are at risk for impaired mental health (anxiety, substance use, depression, suicide), impaired psychosocial functioning (academic underachievement, work and relationship difficulties, underemployment, legal troubles) and traffic accidents.

**Figure 3.** Risks associated with ADHD<sup>13,18,19</sup>

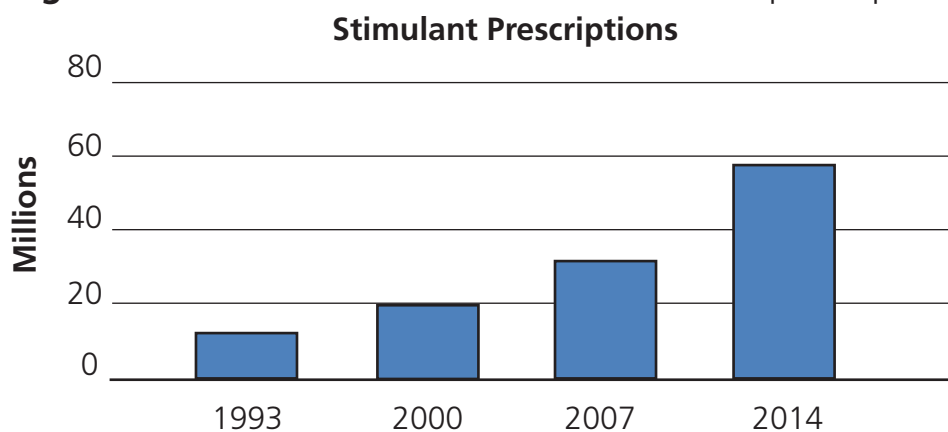


## The Good News: Efficacy

- Stimulants are efficacious for reducing ADHD symptom severity with response rates ~70%.<sup>15, 20</sup>
- Augmenting medication with cognitive behavioral therapy and/or psychosocial interventions such as skill-building may produce better treatment outcomes.<sup>21-23</sup>

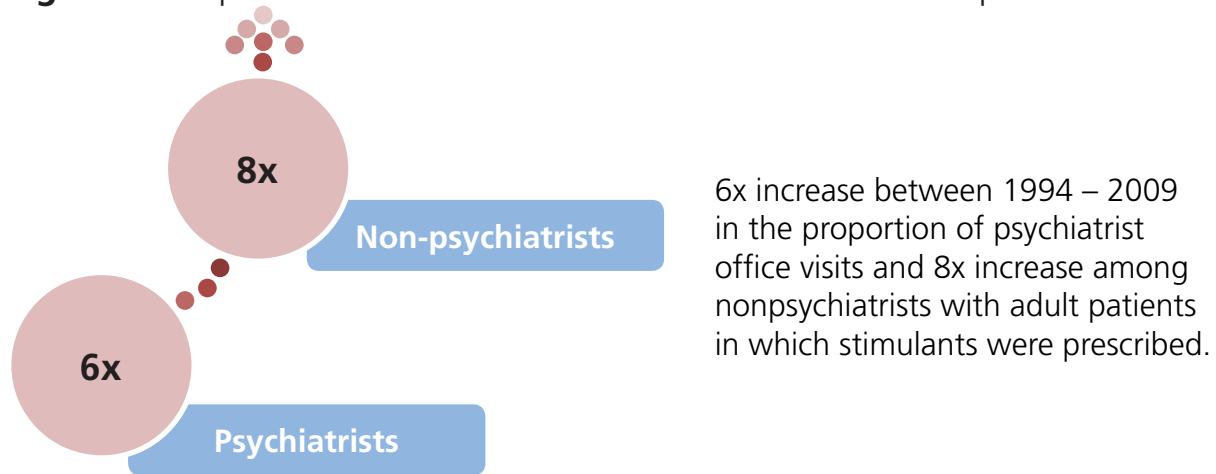
## Too much of a good thing?

**Figure 4.** Increase in total number of stimulant prescriptions<sup>24</sup>



In the U.S., the total number of stimulant prescriptions has increased significantly over the years. The number of prescriptions has leveled off for children but is continuing to increase for adolescents and adults.

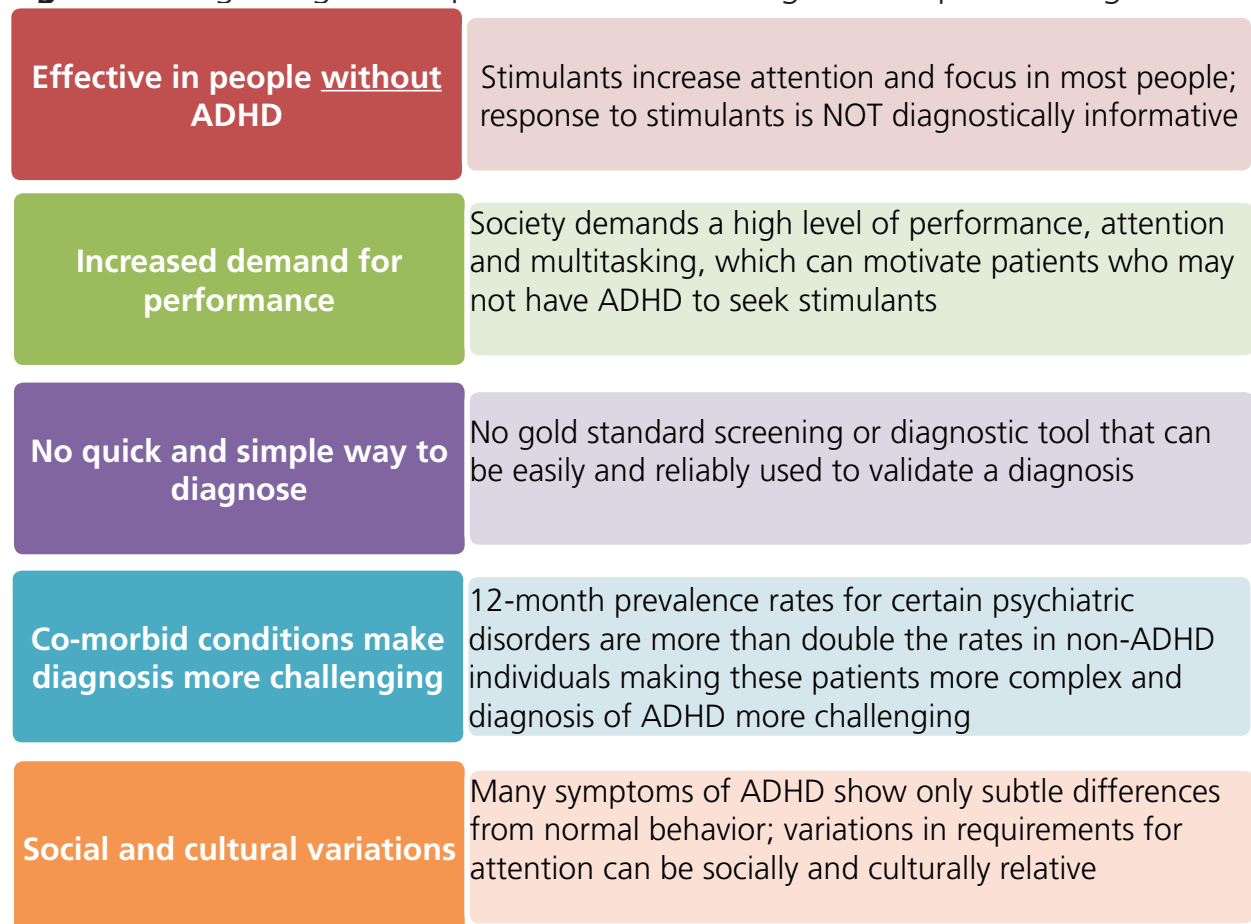
**Figure 5.** Proportion of office visits in which stimulants were prescribed<sup>14</sup>



**Is the increasing frequency of diagnosis a result of **increased recognition** or a **diagnostic epidemic**?**<sup>14, 25</sup>

Various factors can make diagnosis of ADHD challenging.

**Figure 6.** Diagnosing ADHD: potential factors leading to a complicated diagnosis<sup>14,26</sup>



## What can you do?

### 1. Assess for co-morbidities

Determine if there are untreated or undertreated psychiatric conditions that may be producing symptoms that mimic ADHD then manage or refer the patient for treatment of that disorder.<sup>19,26</sup>

**Timing of the ADHD symptoms is extremely important.**

E.g. Did inattentiveness begin after the depressive episode or before?

**Table 2.** Common diseases and disorders that may contribute to or mimic ADHD-like symptoms<sup>14,27-29</sup>

<b>Cognitive disorders</b>	<ul style="list-style-type: none"> <li>Mild cognitive impairment</li> <li>Traumatic brain injury</li> <li>Dementia</li> </ul>
<b>Toxic / metabolic / infectious</b>	<ul style="list-style-type: none"> <li>Nutritional deficiency (e.g. thiamine)</li> <li>Heavy metal toxicity</li> <li>Infection (e.g. urinary tract infection)</li> </ul>
<b>Psychiatric conditions</b>	<ul style="list-style-type: none"> <li>Depression</li> <li>Anxiety</li> <li>Post-traumatic stress disorder (PTSD)</li> <li>Substance use disorder (SUD)</li> <li>Bipolar disorder</li> </ul>
<b>Other</b>	<ul style="list-style-type: none"> <li>Parkinson's disease</li> <li>Developmental disorder</li> <li>Sleep apnea</li> <li>Thyroid disease</li> <li>Hepatic disease</li> </ul>
<b>Medications</b>	<ul style="list-style-type: none"> <li>Steroids</li> <li>Caffeine and nutritional supplements</li> <li>Nicotine</li> <li>Central nervous system (CNS) sedating medications (e.g. opioids, benzodiazepines, antipsychotics, anticholinergics)</li> <li>Anticonvulsants</li> </ul>

**Table 3.** Differentiating ADHD symptoms from those of other common comorbidities<sup>13,19</sup>

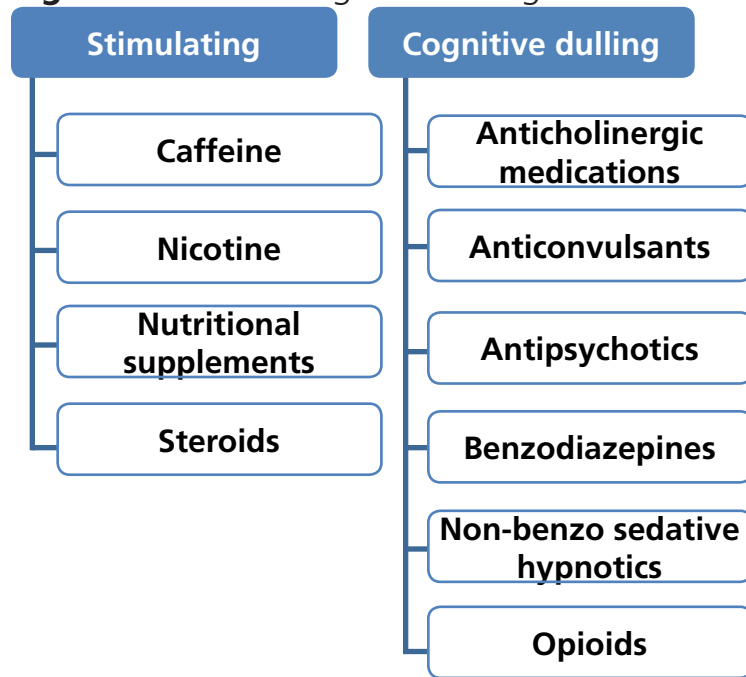
	<b>ADHD</b>	<b>Depressive Disorders</b>	<b>Bipolar Disorder</b>	<b>Anxiety Disorders</b>	<b>Substance Use Disorders</b>	<b>PTSD</b>
<b>Hyperactivity / impulsivity</b>	Persistent pattern of hyperactivity/impulsivity					Symptoms begin after traumatic event and are present along with intrusive symptom(s), avoidance, negative alterations in cognitions and mood
<b>Inattention</b>	Persistent pattern of inattention	Impaired concentration occurring during depressive episode; episodic	Cyclical/episodic; occurring for days at time	Inattention due to worry and rumination	Symptoms first started after onset of use or frequent use	

***Before diagnosing ADHD, assess for and manage other co-morbidities that may be mimicking or causing ADHD-like symptoms.***



## 2. Evaluate medications currently being taken by the patient<sup>23</sup>

**Figure 7.** Stimulating and dulling medications



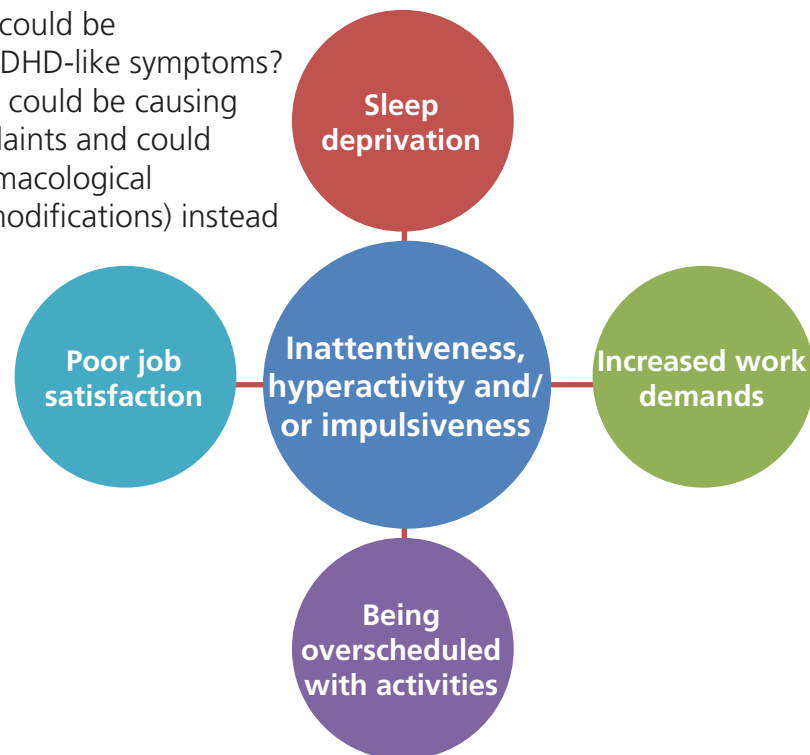
Some medications have adverse effects that can mimic ADHD symptoms (hyperactivity / impulsivity) while others are sedating and may contribute to the patient's concerns of cognitive dulling, concentration or attention difficulties.

- **It's important to evaluate a patient's medications and consider whether a dose reduction, a change of formulation or timing of dose, discontinuation, or medication switch is indicated rather than adding another medication to treat a side effect.**

## 3. Consider social history<sup>15,26</sup>

**Figure 8.** Social factors to consider

Are there other factors that could be contributing to or causing ADHD-like symptoms? Assess for social factors that could be causing similar symptoms and complaints and could be managed with non-pharmacological interventions (e.g. lifestyle modifications) instead of medications.



***Rule out medication and social factors as causes of ADHD-like symptoms***

#### 4. Assess for childhood diagnosis of ADHD<sup>30</sup>

✓ **No childhood diagnosis reported** → Refer to mental health specialist if:

- Patient reports symptoms began during childhood and have persisted throughout life
- Symptoms are not explained by other medical or psychiatric issues (see below)
- Symptoms have resulted in or are associated with moderate or severe psychological, social, and/or educational or occupational impairment

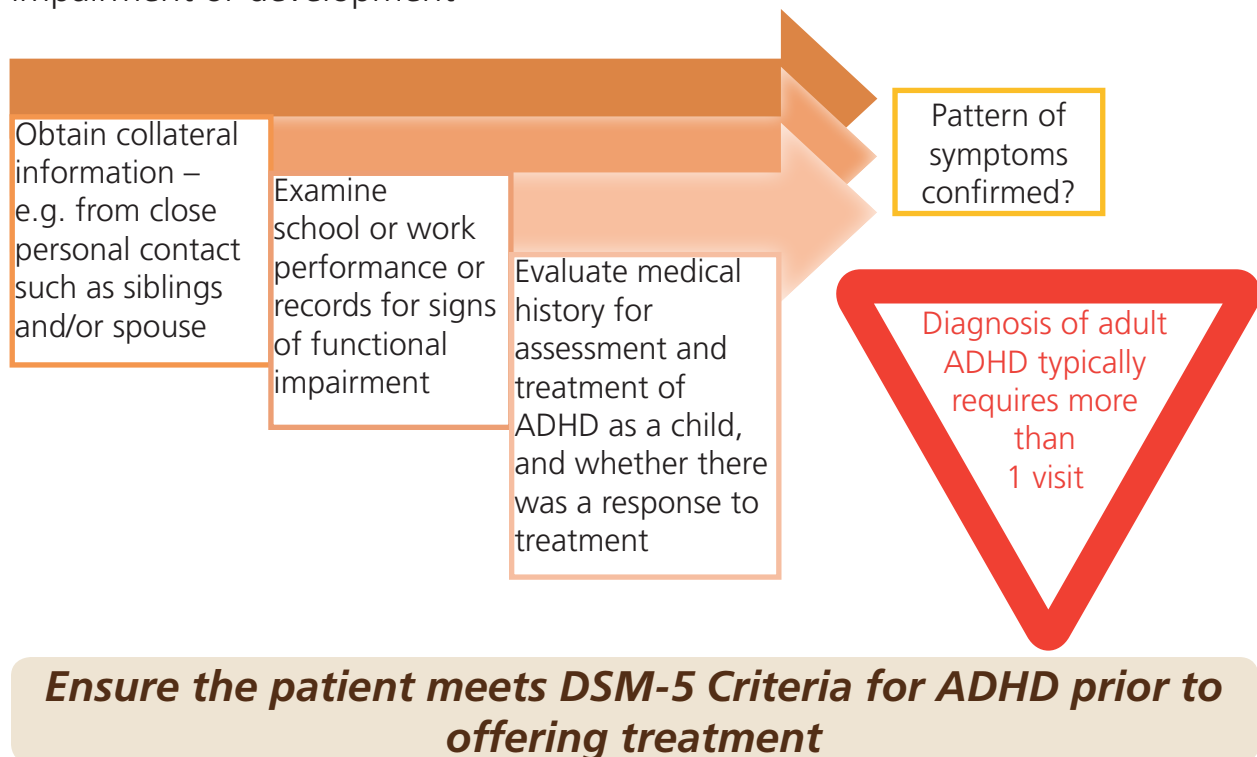
✓ **Childhood diagnosis reported** → Use multiple methods to confirm childhood impairment<sup>31</sup>

#### 5. Evaluate the impact of symptoms on functioning

**It is important to assess the impact of symptoms on the patient's functioning and quality of life (ability to perform activities of daily living, learning, socialization and work)**<sup>21</sup>

- ✓ Rating scales can be useful for assessment and should be used in combination with a clinical interview<sup>32</sup>
- ✓ Various screening, assessment and diagnostic tools are available (e.g. Conners' Adult ADHD Rating scale, Wender Utah Rating Scale, ADHD Self-Report Scale (ASRS)) and are based on diagnostic criteria for ADHD<sup>33</sup>

**Figure 9.** Methods to confirm pattern of symptoms interfering with functional impairment or development



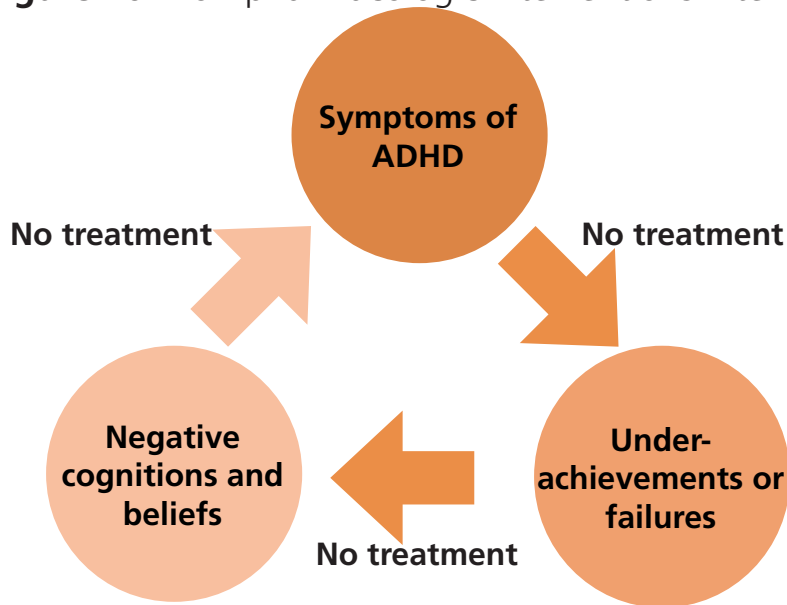
## Treatment of adult ADHD

Non-pharmacologic interventions <sup>23,29,34,35</sup>

Psychosocial treatments such as psychoeducation, cognitive behavior therapy, support groups, and skills training are thought to provide additional benefits when used in combination with medication management.

- Medication alone does not provide patients with strategies and skills for coping with associated functional impairment, negative cognitions and beliefs

**Figure 10.** Non-pharmacologic interventions interrupt a negative cycle



- Psychosocial treatments interrupt the cycle by addressing the negative cognitions and beliefs.
- Skills-based training assists with developing and practicing compensatory strategies.

Pharmacotherapy:

Psychostimulants are considered 1st line treatment for adults with **moderate or severe levels of impairment**.<sup>30</sup>

- Non-stimulant medications (such as atomoxetine) may be considered 2nd line or in patients with substance use disorders.<sup>20,36-38</sup>

Before starting pharmacotherapy, complete a full assesment including:



- Mental health assessment
- Social assessment
- History and physical examination\*
- Assessment for substance use and drug diversion (e.g. urine drug screen, prescription drug monitoring program)

\*Cardiac evaluation: per package labeling, patients being considered for treatment with stimulant medications should have a history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram).<sup>39</sup>

**Start low...  
Go slow**



Medications should be started at the lowest possible dose, and increased slowly, as individual patient response to these drugs is known to vary widely.<sup>40</sup>

**Figure 11.** Treatment of Adult ADHD<sup>+8,21,30,41-43</sup>

<b>First line</b>	<ul style="list-style-type: none"> <li>• Psychoeducation and long-acting or extended release formulation of psychostimulant* (methylphenidate, lisdexamfetamine, amphetamine salts)</li> </ul>
<b>Second line</b>	<ul style="list-style-type: none"> <li>• Adjunctive short and intermediate formulation of psychostimulant (amphetamine salts, methylphenidate)</li> <li>• Atomoxetine (non-stimulant medication)</li> </ul>
<b>In the presence of active alcohol or drug use disorder (SUD)**</b>	<ul style="list-style-type: none"> <li>• 1st line = atomoxetine</li> <li>• 2nd line = extended release methylphenidate or lisdexamfetamine unless the risk of stimulant abuse is high, then bupropion is recommended</li> </ul>

\* Longer-acting formulations preferred: improved compliance (fewer doses) and longer-lasting, smoother improvement of symptoms

\*\* The treatment needs of individuals with SUD and ADHD need to be considered simultaneously but if possible, the SUD should be addressed initially; if SUD is active, immediate attention needs to be paid to the stabilization of the addiction.

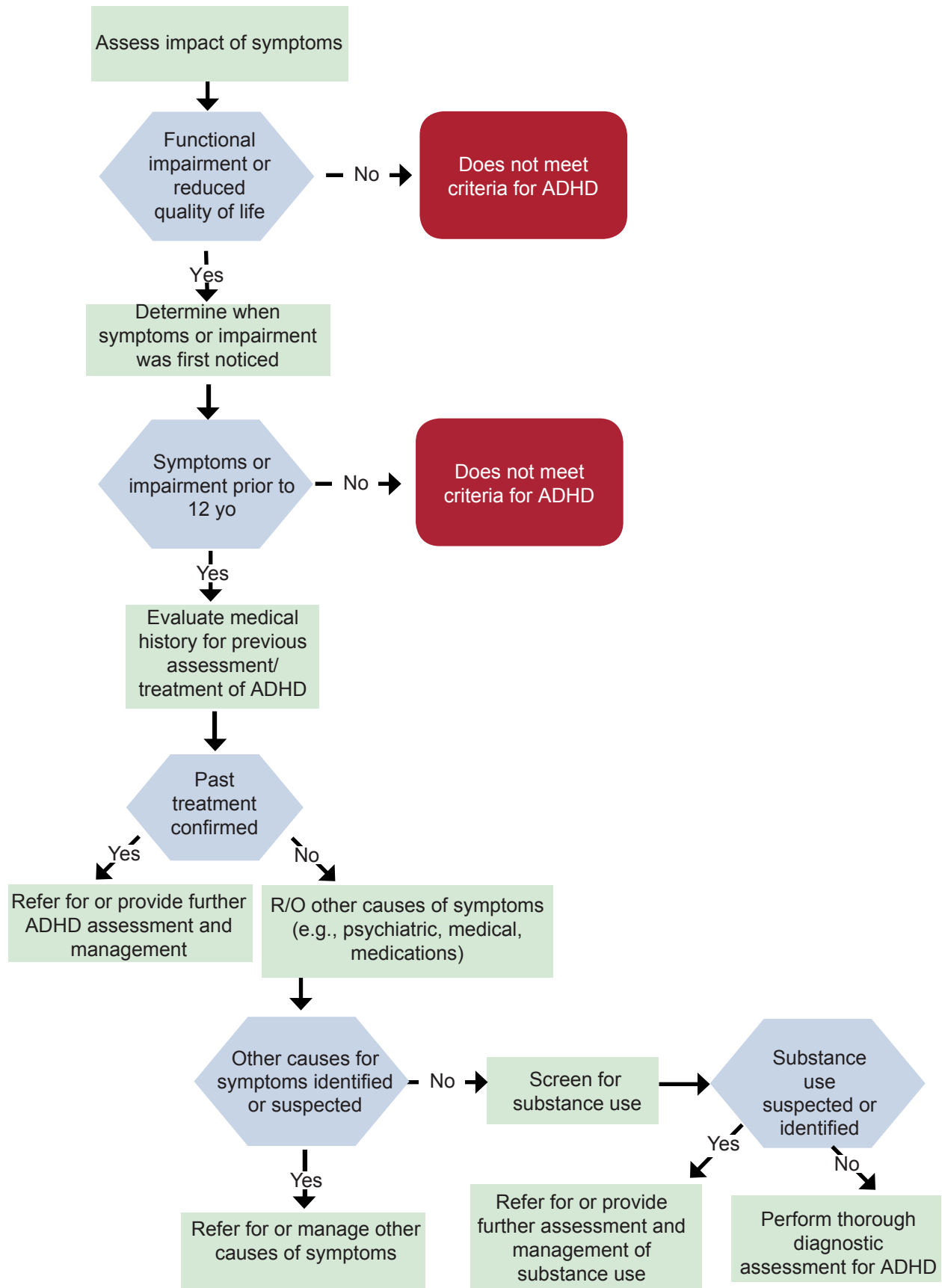
+ Please see VA National Formulary for current list of formulary medications (<https://www.pbm.va.gov/PBM/NationalFormulary.asp>)

**Table 4.** Medication considerations<sup>23,39,44-47</sup>

<b>Efficacy</b>	Establish an objective measure or goal of treatment <ul style="list-style-type: none"> <li>• For example: a specific target that needs to change, like hourly work production; rating scales can help to quantify specific medication changes</li> </ul>	
<b>Risks</b>	Misuse/abuse	<ul style="list-style-type: none"> <li>• Perform random urine drug screens</li> <li>• Check prescription drug monitoring program reports (frequency as required by state or at least yearly)</li> <li>• Schedule periodic visits to assess medication effectiveness, behaviors, fill dates, side effects</li> </ul>
	Cardiac Risks	<ul style="list-style-type: none"> <li>• More recent studies show no increased risk of serious CV events from stimulant medications, however monitoring for cardiac symptoms is still recommended</li> <li>• Blood pressure and pulse should be evaluated during follow-up within 1-3 months and at follow-up every 6-12 months</li> </ul>
	Side effects	<ul style="list-style-type: none"> <li>• Dry mouth, insomnia, irritability, dysphoria, diminished appetite, weight loss, headaches</li> </ul>

***Assess Veterans who are currently on stimulants to assure that the benefits of the medication outweigh the risks***

**Figure 12.** Evaluating a patient with ADHD-like symptoms<sup>13,14</sup>



# Prescription Stimulants

## Key Messages:

1. Before diagnosing ADHD, assess for and manage other co-morbidities that may be mimicking or causing ADHD-like symptoms
2. Rule out medication and social factors as causes of ADHD-like symptoms
3. Ensure the patient meets DSM-5 Criteria for ADHD prior to offering Treatment
4. Assess Veterans who are currently on stimulants to assure that the benefits of the medication outweigh the risks

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