



# Identification and Management of Attention-Deficit/Hyperactivity Disorder (ADHD) in Adults

Academic Detailing Clinician Guide

**VA**



**U.S. Department of Veterans Affairs**

Veterans Health Administration  
*PBM Academic Detailing Services*

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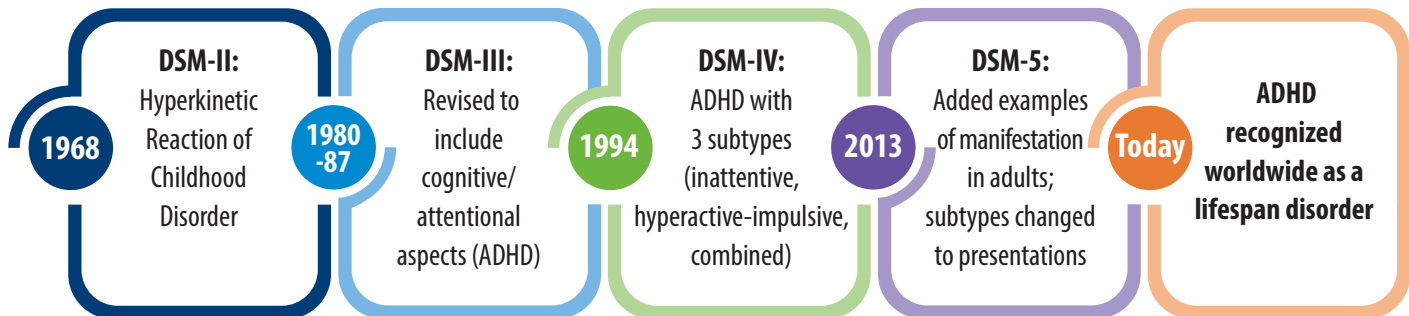
# Background

**Attention-Deficit/Hyperactivity Disorder (ADHD)** is typically a chronic, often lifelong, neurodevelopmental disorder.<sup>1</sup> The approach for diagnosing and treating Veterans with ADHD involves an individualized clinical assessment which should include consideration of risks and benefits for both treating and not treating the disorder.



- ➔ **Prescription stimulants are considered first-line treatment** for ADHD and have been shown to improve symptoms and outcomes.<sup>1</sup>
  - Untreated ADHD has been associated with increased morbidity and mortality as well as decreased social, educational, vocational, and self-care functioning.<sup>1</sup>
- ➔ **Treatment of ADHD with stimulants has not been associated with an increased risk of substance use disorder (SUD).**
  - A meta-analysis of 15 longitudinal studies of patients with a history of stimulant-treated ADHD vs. matched cohorts without treatment found no association between treatment and subsequent substance use, abuse, or dependence.<sup>2</sup>
  - In adolescents, treating ADHD with stimulants has been found to either lower the risk of SUD or have no impact on SUD risk.<sup>3-5</sup>
- ➔ **Stimulant overdose deaths are primarily driven by cocaine and methamphetamine, not prescription stimulants.**<sup>6</sup>

**Figure 1. The diagnostic criteria for the condition now known as ADHD have evolved as research has furthered our understanding of the characteristics of the disorder.**<sup>1,7-10</sup>



“Like many psychiatrists, we began our medical and psychiatric training in the last century. We were taught that patients with adult attention deficit/hyperactivity disorder (ADHD) had a dubious diagnosis and were probably seeking stimulants for nefarious purposes.”

— Dr. Josh Geffen<sup>11</sup>

## FAST FACTS

- **45-70% of childhood cases persist into adulthood.**<sup>1,13-15</sup>
  - More recent data suggest that > 90% of childhood cases have residual, sometimes fluctuating, symptoms and impairments through at least young adulthood.<sup>16</sup>
- **Estimated prevalence rate is about 4.4-5.2% in U.S. adults.**<sup>14,17</sup>
  - In military samples, estimated prevalence rates range between 5.8–9%.<sup>12,15</sup>
- **Highly heritable:** parents with ADHD have a > 50% chance of having a child with ADHD.<sup>1</sup>

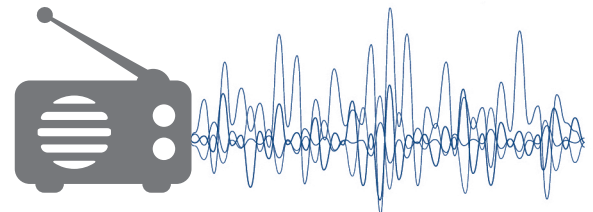
In nondeployed U.S. Army personnel, the estimated 30-day prevalence for ADHD was found to be 7.0%. Only 2 disorders were higher, intermittent explosive disorder (11.2%) and PTSD (8.6%).<sup>12</sup>



## Clinical manifestation 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.<sup>7,9,20,21</sup>

- Although onset occurs in childhood, ADHD is not necessarily diagnosed at that time.<sup>1</sup>
- The clinical manifestation is heterogeneous, with different levels of severity and prevalence of each core symptom.<sup>22-24</sup>
- Symptoms may wax and wane due to changing life circumstances, functional expectations, and/or comorbid conditions.<sup>25</sup>
- Some may experience a reduction or remission of symptoms, particularly hyperactivity, with age.<sup>20,24,26</sup>
- Approximately 30-70% of adults with ADHD have emotional dysregulation (e.g., mood lability, irritability, anger outbursts, low frustration tolerance, motivational deficits).<sup>7,20,27,28</sup>
- Dysfunctional strategies (e.g., drinking alcohol, smoking cannabis) may be used to cope with emotional turmoil, social isolation, and rejection.<sup>29</sup>
- 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.<sup>19</sup>



**Focus with ADHD** *“feels like a short wave radio that most of the time can’t find the right frequency.”*<sup>19</sup>



**People with ADHD are unable to distinguish important neuronal signals from unimportant ones. This results in challenges focusing on one thing more than another.**<sup>18</sup>

## Gender differences

- **ADHD is thought to be underrecognized and underdiagnosed in females** with implications for long-term social, educational, and health outcomes.<sup>29-31</sup>
- Females are more likely to be diagnosed with predominantly inattentive ADHD.<sup>29,32,33</sup>
  - Inattention in girls and women with ADHD may present as being easily distracted, disorganized, overwhelmed, and lacking in effort or motivation.<sup>29</sup>
- In females, symptoms are typically pervasive and impairing rather than transient or fluctuating.<sup>29</sup>
- 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).<sup>29</sup>
- Difficulties with emotional lability and emotional dysregulation may be more severe or common in girls and women with ADHD.<sup>29</sup>
- Social problems may be particularly impairing.<sup>29</sup>
- ADHD symptoms may become more obvious later in females, often during periods of social or educational transition.<sup>29</sup>
- Adult women may develop awareness of their difficulties leading them to seek services.<sup>29</sup>



Females with undiagnosed ADHD are more likely to receive a primary diagnosis of internalizing disorders (e.g., anxiety, depression) or personality disorders.

This delays diagnosing ADHD and accessing appropriate treatment.<sup>29</sup>



**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.**

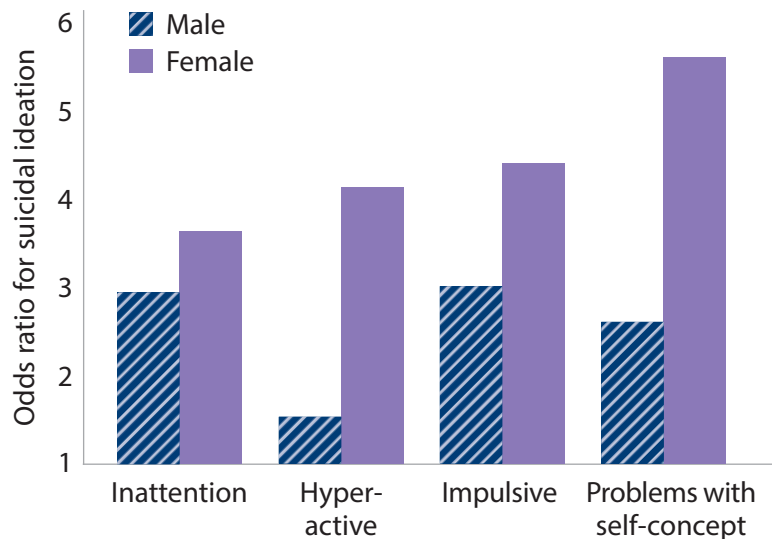
This was more than double the 1.27x (95% CI = 0.89-1.76) higher risk of death in boys and men.<sup>30</sup>

## 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).<sup>34</sup>



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



**ADHD is a chronic health problem with significant risk for mortality and long-term morbidity in adulthood.<sup>1</sup>**

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-lag of 17 years without treatment.<sup>22</sup>

**Almost every aspect of adult life can be impacted by ADHD,** particularly if the condition remains undiagnosed, untreated, or ineffectively treated.<sup>1,7,22-24,30,32,35-39</sup>

### Health problems

- Suicidality (completions, attempts, and ideation)
- Development of comorbidities (e.g., mood, sleep difficulty, anxiety, SUD)
- Obesity and overeating

### High-risk behavior consequences

- Delinquency and crime
- Motor vehicle accidents
- Risky driving, more speeding tickets
- Unplanned pregnancies
- Sexually transmitted infections

### Relationship and work challenges

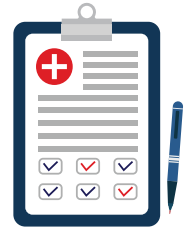
- Lower educational and occupational achievement
- Financial problems
- Diminished social functioning
- Divorce

## Screening tools: your tool to guard against missing a comorbidity




Adults with undiagnosed ADHD may seek treatment for what seems like a primary mood, anxiety, or other mental health disorder. Others may get medical attention for substance use or high-risk behavior consequences (e.g., motor vehicle accidents, unplanned pregnancies).<sup>1,19</sup>

### It is important to know when to screen for underlying ADHD.

Missing a diagnosis of ADHD can result in years of trials with antidepressants, mood stabilizers, and anxiolytics without adequate symptom response.<sup>1</sup>

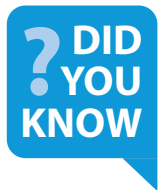


### Example screening opportunities<sup>1</sup>

-  **A patient seeking an assessment for ADHD with no prior diagnosis.** This may happen if:
  - Someone close to the patient learned about ADHD and recognized the traits.
  - The patient learned about ADHD and recognized the relevant symptoms.
  - A relative was diagnosed with ADHD, triggering an awareness of ADHD (e.g., child is diagnosed).
-  **The patient has symptoms attributed to another psychiatric diagnosis** (mania, depression, anxiety) but is not responding as expected to treatment.<sup>29</sup>
-  **There are functional difficulties** such as attention problems, academic issues, time management, driving, or marital problems and the clinician postulates ADHD as a possible explanation.



**ADHD screening tools can be used to help determine the probability that someone has the disorder.**<sup>41</sup> However, *“just as a thermometer records a fever but does not identify the many reasons it could be occurring, ADHD symptom scales do not tell you if ADHD is the specific reason the symptoms are occurring.”*<sup>1</sup> A mental health evaluation that includes a detailed developmental history should be performed on those who screen positive.<sup>41</sup>



### Transitioning from military to civilian life may disrupt behavioral support and coping mechanisms relied on by those with undiagnosed ADHD.

Studies suggest the discipline of a highly structured context (e.g., military) provides an environment for those with ADHD to develop organizational skills. Routine physical training, exercise, and use of substances (e.g., caffeine) are thought to reduce at least some ADHD symptoms.<sup>40</sup>

**Use ADHD screening tools to identify potential cases of ADHD in need of further evaluation.**

# Assessment and diagnosis

The clinical interview and evaluation continues to be the mainstay of ADHD diagnosis.<sup>1</sup>

Use the DSM-5-TR diagnostic criteria for ADHD to guide your clinical assessment of the patient.<sup>7,10,20,42</sup>

**Table 1. Linking diagnostic criteria with adult manifestations of ADHD<sup>7,20</sup>**

## INATTENTION (5 or more for adults)

| DSM-5-TR Criterion A for ADHD*  | Example behaviors**   | Possible signs (self-report or coping mechanisms) <sup>19</sup>   |
|---|---|---|
| <b>Often</b> fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities | Overlooks or misses details, work is inaccurate   | <ul style="list-style-type: none"> <li>• May use substances (e.g., caffeine, nicotine, alcohol) to mitigate symptoms<sup>40</sup></li> <li>• Fatigued from energy required to sustain tasks<sup>43</sup></li> </ul> |
| <b>Often</b> has difficulty sustaining attention in tasks or play activities  | Has difficulty remaining focused during lectures, conversations, or lengthy reading; has difficulty making decisions                          | <ul style="list-style-type: none"> <li>• Interpersonal problems</li> <li>• Forgetful</li> </ul>   |
| <b>Often</b> does not seem to listen when spoken to directly  | Mind seems elsewhere, even in the absence of any obvious distraction  | <ul style="list-style-type: none"> <li>• Poor or underdeveloped reading/verbal skills</li> </ul>  |
| <b>Often</b> does not follow through on instructions, does not finish schoolwork, chores, or duties                                 | Starts tasks but quickly loses focus and is easily sidetracked; procrastinates  | <ul style="list-style-type: none"> <li>• Problems learning new material<sup>43</sup></li> <li>• Relies on others to remind them of tasks</li> </ul>   |
| <b>Often</b> has difficulty organizing tasks and activities   | Difficulty managing sequential tasks, keeping materials/belongings in order; messy, disorganized work; poor time management; misses deadlines | <ul style="list-style-type: none"> <li>• Avoids reading books or activities that require sustained attention for leisure</li> </ul>   |
| <b>Often</b> avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort                              | Avoids, dislikes, or is reluctant when preparing reports, completing forms, or reviewing lengthy papers                                       | <ul style="list-style-type: none"> <li>• Has a hard time completing activities that require sustained attention</li> </ul>  |
| <b>Often</b> loses things necessary for tasks or activities   | Loses tools, wallet, keys, paperwork, eyeglasses, mobile telephones   | <ul style="list-style-type: none"> <li>• Works harder than others to perform</li> </ul>   |
| Is <b>often</b> easily distracted by extraneous stimuli   | Easily distracted; has unrelated thoughts   | <ul style="list-style-type: none"> <li>• Establishes structure/routines to increase capacity to complete tasks</li> </ul>   |
| Is <b>often</b> forgetful in daily activities   | Forgetful when doing chores/running errands; forgets to return calls, pay bills, attend appointments  |   |

\*5 or more symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities. \*\*Example behaviors should be “often.”

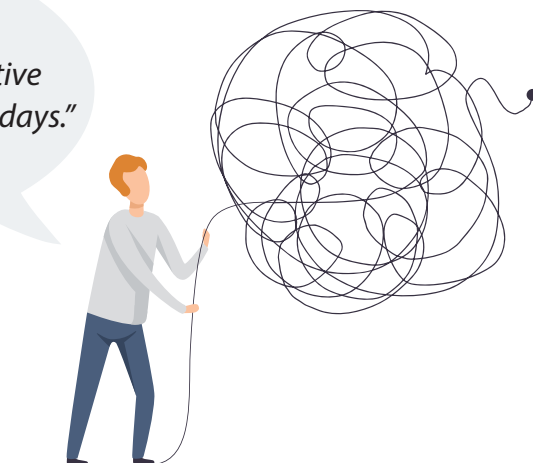


## HYPERACTIVITY AND IMPULSIVITY (5 or more for adults)

| DSM-5-TR Criterion A for ADHD*   | Example behaviors**   | Possible signs (self-report or coping mechanisms) <sup>19</sup>   |
|--|---|---|
| <b>Often</b> fidgets with or taps hands/feet or squirms in seat          | Restless, unable to sit still   | <ul style="list-style-type: none"> <li>• Reports frequent interpersonal conflict</li> </ul>   |
| <b>Often</b> leaves seat in situations when remaining seated is expected | May avoid situations/places that require remaining in place (e.g., movie theaters, standing in line)                            | <ul style="list-style-type: none"> <li>• Reports needing exercise or substances as a coping mechanism to manage symptoms<sup>43</sup></li> </ul>  |
| <b>Often</b> runs/climbs in situations where it is inappropriate         | Feeling restless; may tend to choose very active jobs   | <ul style="list-style-type: none"> <li>• Feels misinterpreted by others</li> </ul>  |
| <b>Often</b> unable to play or engage in leisure activities quietly      | Constant activity; avoids activities that require staying quiet or inactive (e.g., yoga, meditation)                            | <ul style="list-style-type: none"> <li>• Impulsively blurts out inappropriate comments</li> </ul>   |
| Is <b>often</b> “on the go,” acting as if “driven by a motor”            | Is unable/uncomfortable being still for extended time; may be experienced by others as being restless/difficult to keep up with | <ul style="list-style-type: none"> <li>• Feels less connected to others due to frequent conflict</li> <li>• Describes their actions/verbalizing thoughts as “ready, fire, aim”</li> </ul> |
| <b>Often</b> talks excessively   | Long-winded responses (may be perceived by others as talking too much or all the time)  | <ul style="list-style-type: none"> <li>• Reports difficulty keeping friends or meeting new people</li> </ul>  |
| <b>Often</b> blurts out an answer before a question has been completed   | Verbal impulsivity; completes people's sentences; cannot wait for turn in conversation  | <ul style="list-style-type: none"> <li>• Reports partner, friends, and/or family say they feel neglected or unimportant<sup>43</sup></li> </ul>   |
| <b>Often</b> has difficulty waiting his or her turn                      | Difficulty waiting in line/for others to finish, overreacting to frustrations   | <ul style="list-style-type: none"> <li>• Has difficulty following rules (e.g., criminal history, speeding tickets)</li> </ul>   |
| <b>Often</b> interrupts or intrudes on others                            | Interrupts conversations/activities; may intrude/take over things   | <ul style="list-style-type: none"> <li>• Reports difficulty with social cues</li> </ul>   |

\*5 or more symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities. \*\*Example behaviors should be “often.”

*“I guess everyone has ADHD because everyone is inattentive sometimes, especially these days.”*



While the symptoms of ADHD can occur in everyone occasionally (e.g., forgetting items), **people with ADHD experience significantly greater numbers of symptoms ( $\geq 5$  for adults) with greater frequency and more significant difficulties and impairment.<sup>1</sup>**

# Stepped diagnostic procedure for ADHD in adults<sup>7,10</sup>

An “ideal” or “gold standard” adult ADHD evaluation should include a clinical interview, a structured/semi-structured interview, informant reports/collateral information, assessment of impairment, and evaluation of alternative symptom sources.<sup>10</sup>

If malingering (intentionally feigning or exaggerating symptoms for personal gain) is suspected, consider providing or referring the Veteran for a psychological assessment that includes use of symptom and performance validity measures. Informant and objective records can be used to verify self-reports.



**Please see the ADHD Quick Reference Guide (QRG)** for more information on stepped diagnostic procedure.

## STEP

1

**Assess each of the eighteen DSM-5-TR ADHD symptoms to ensure 5 or more are present for at least 6 months.**<sup>10</sup> Combining self- and informant-reported symptoms is the most effective way to establish the A-criterion. Although rating scales alone are not sufficient to diagnose ADHD, using them as a part of the evaluation is widely recommended.<sup>1</sup>

## STEP

2

**Establish chronicity (several symptoms present prior to age 12) and contextual stability (several symptoms are present in 2 or more settings).**<sup>10</sup> A complete childhood developmental history is an important part of a comprehensive assessment.<sup>1</sup>  
Note: Diagnosis of ADHD does not require uninterrupted symptoms since childhood.<sup>9,10</sup>

## STEP

3

**Establish clinically significant impairment.**<sup>10</sup> The impact of ADHD is best judged by considering the level of impairment, pervasiveness, and familial and social context.<sup>31</sup> There should be clear evidence that the symptoms interfere with or reduce quality of functioning.

### CLINICAL PEARL

Assessing the effect of ADHD symptoms on impairment and quality of life should include an assessment of the broader range of problems linked to ADHD (e.g., executive function impairments, sleep problems, irritability, internal restlessness) in addition to functional impairments (e.g., traffic accidents, occupational underachievement).<sup>1</sup>

As with many mental health disorders, even minor levels of symptoms can cause considerable distress to individuals because of the chronic and persistent nature of symptoms.<sup>44</sup> **Focus on subjective accounts of mental state phenomena, as with someone who reports feeling depressed, experiencing a panic attack, or hearing a voice.**<sup>44</sup>

**STEP 4 Rule out other causes of symptoms: differential diagnosis.**<sup>10,20</sup> A thorough ADHD evaluation typically includes a physical examination, necessary tests, and review of medical history to rule out other causes of symptoms—e.g., post-traumatic stress disorder (PTSD), traumatic brain injury (TBI), SUD, sleep disorders, anxiety, and depression.<sup>45</sup>

- ADHD as a diagnosis may be eliminated if symptom onset is simultaneous with the onset of a separate physical or mental disorder, or if symptoms solely occur during substance use, medical problems, or other mental health disorders.<sup>10</sup>
- **One clear distinction of ADHD is the typical early onset and trait-like persistence of ADHD symptoms.**<sup>44</sup>

**STEP 5 Finalize diagnosis.**<sup>10</sup>

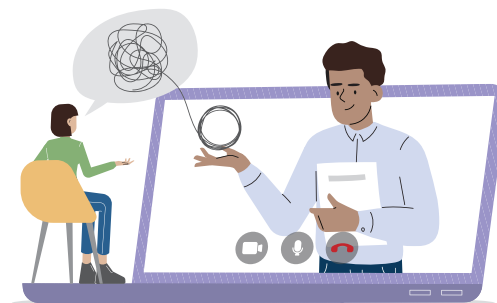
If the patient meets DSM-5-TR criteria for ADHD, determine presentation (e.g., predominantly inattentive) and severity (mild, moderate, severe) to finalize the diagnosis.

**Clinical pearl:**<sup>10</sup> When making a first-time ADHD diagnosis in adulthood, consider documenting factors that may have prevented childhood diagnosis.

## Support after diagnosis

Following a diagnosis of ADHD, have a structured discussion with the patient about ADHD and provide support (include families/caregivers as appropriate). This could include:<sup>24,31</sup>

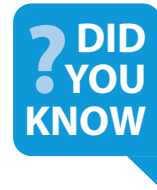
- ✓ Improving understanding of symptoms and how ADHD may affect relationships and functioning
- ✓ Identifying and building on individual strengths
- ✓ Facilitating access to services
- ✓ Modifying the environment to reduce the impact of ADHD symptoms; use of electronic devices to provide reminders, track to-do lists, etc.
- ✓ Understanding the importance of structure in daily activities
- ✓ Increasing understanding of how ADHD may impact career choices and rights to reasonable accommodations in the workplace and/or school
- ✓ Recognizing the increased risk of substance misuse/use disorder



**Adults who screen positive for ADHD should receive a mental health assessment to evaluate for ADHD.**<sup>1,31</sup>

# Treatment

ADHD requires a comprehensive, collaborative, and multimodal treatment approach tailored to meet the unique needs of the person with ADHD.<sup>1</sup> 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.<sup>1</sup>



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.<sup>17</sup>



**Pharmacotherapy** is first-line treatment for ADHD in adults to target core symptoms causing impairment.<sup>1,9,11,20,21,28,31,44,46-49</sup>

- 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.<sup>46,50,51</sup>

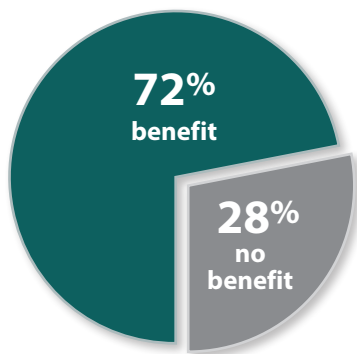
## Treatment outcomes

Patients with ADHD who receive treatment (by any modality) have better long-term outcomes than their non-treated counterparts across most studied domains.<sup>25,44,52-56</sup> Examples include:

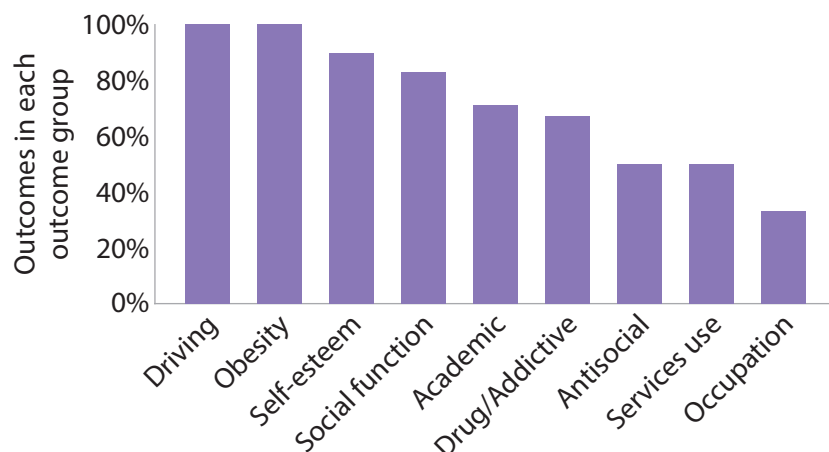
- Reduced suicidal ideation and attempts<sup>57</sup>
- Reduced likelihood of motor vehicle accidents<sup>54</sup>
- Reduced criminal behavior<sup>53</sup>
- Higher self-esteem and social functioning<sup>52</sup>

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

### Treated participants with ADHD

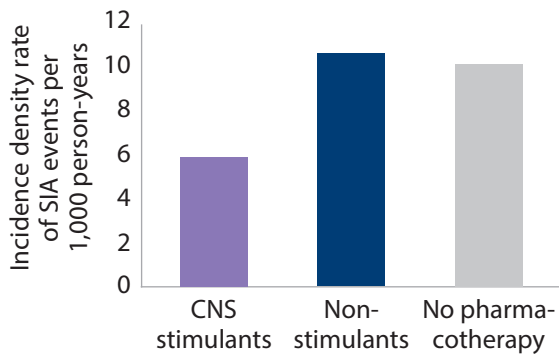


### Treatment benefit by outcome group



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).<sup>55</sup>

**Figure 5. ADHD pharmacotherapy reduces risk of suicidal ideation and attempts (SIA).**



According to a study in 797,189 patients with ADHD (aged  $\geq 6$  years), compared with no pharmacotherapy, central nervous system (CNS) stimulant treatment was significantly associated with a lower risk of SIA events in all age groups.

When subdivided by age, no significant differences were observed between adults treated with CNS stimulants and non-stimulants (atomoxetine, clonidine, guanfacine).<sup>57</sup>

In adults, adjusted hazard ratios (HR) for SIA were as follows: 18–24 years = 0.66 (0.57–0.75,  $p < 0.001$ ); 25–44 years = 0.56 (0.46–0.70,  $p < 0.001$ );  $\geq 45$  years = 0.74 (0.55–1.00,  $p < 0.05$ ).<sup>57</sup>

## Before starting ADHD treatment



As with all medications, risk versus benefit ratios need consideration before initiating any medication. Among the factors to be considered, the risks of morbidity and mortality associated with untreated ADHD makes it important to also weigh the risk of not treating ADHD.<sup>1</sup>

- The 2018 National Institute for Health and Care Excellence (NICE) ADHD Guidelines recommend medication treatment when symptoms are still causing a significant impairment in at least one domain of everyday life despite environmental modifications.<sup>31</sup>

### Before starting treatment, ensure the Veteran has an assessment that includes, but is not limited to:<sup>20,21,31</sup>

- Confirmation of ADHD diagnosis
- Evaluation of current medications and supplements
- Review of occupational, educational, caregiving/parenting, and relationship circumstances
- Identification of coexisting physical, mental health, and neurodevelopmental conditions
- Asking women of child-bearing age about pregnancy status, intention, and contraceptive use
- A review of physical health, including baseline pulse and blood pressure, medical history, and family medical history.<sup>58</sup> Cardiology consultation should be considered in patients with established or suspected heart disease (e.g., significant findings on physical exam or family history).<sup>1,31</sup>
- Assessment of care needs including risk assessment for substance misuse and drug diversion. Vigilance identifying potential misuse or abuse of medication requires judicious follow-through (e.g., urine drug testing [UDT] and Prescription Drug Monitoring Program [PDMP]).

#### Environmental modifications<sup>31</sup>

Changes to the physical environment to minimize the impact of the person's ADHD on day-to-day life.

**Examples:** changes to seating arrangements, reducing distractions, optimizing work to have shorter periods of focus with movement breaks



**See ADHD QRG for more information.**

**Figure 6. Possible “red flags” for stimulant misuse or diversion<sup>25,59</sup>**



- ❑ Symptoms of intoxication or symptoms associated with heavier use (e.g., agitation, psychosis, shortness of breath, and palpitations)
- ❑ A pattern of losing prescriptions or early re-ordering of prescriptions
- ❑ PDMP check identifies unexpected medication activity; discuss finding with the Veteran
- ❑ UDT contains unexpected result
  - **Please note:** UDT screening results for prescription stimulants should be interpreted with caution as they are subject to false negatives and false positives. Discuss unexpected findings with the Veteran and consider checking with your local laboratory and/or ordering confirmation testing.

## Pharmacotherapy for ADHD in adults

**For most adults with ADHD, psychostimulants (amphetamines or methylphenidate) should be considered first line.**<sup>1,31</sup> The 2020 Canadian ADHD Practice Guidelines recommend more specifically that longer acting psychostimulants be considered first.<sup>1</sup>

**Atomoxetine** is generally considered as the second-line treatment for ADHD in adults.<sup>60</sup> However, some sources recommend atomoxetine first-line when anxiety disorders, tic disorders, and/or SUD co-occur with ADHD.<sup>28,46,61</sup> In general, atomoxetine should also be considered when:<sup>1,31</sup>

- Patients experience significant side effects or have a suboptimal response with first-line medications
- Stimulant agents are contraindicated
- There is high risk of stimulant misuse



**See ADHD QRG for more information.**

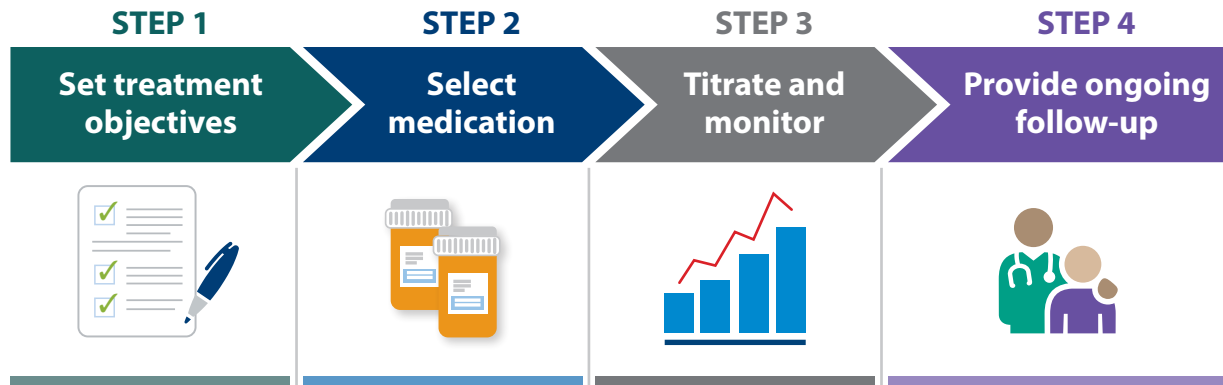
**Table 2. ADHD medication clinical pearls\***

|                              |  |
|------------------------------|--|
| <b>Amphetamine salts</b>     | <ul style="list-style-type: none"> <li>• The most efficacious compounds, as rated by clinicians and self-report, and as well tolerated as methylphenidate.<sup>62</sup></li> <li>• More potent than methylphenidate; recommendations generally suggest a dose that is roughly 1/2–2/3 the dose of methylphenidate.<sup>63</sup></li> </ul> |
| <b>Methylphenidate (MPH)</b> | <ul style="list-style-type: none"> <li>• Efficacy on ADHD core symptoms rated by clinicians as superior to placebo, comparable with that of atomoxetine.<sup>62</sup></li> <li>• Many products are not bioequivalent and not interchangeable on a mg/mg basis.<sup>64</sup></li> </ul>   |
| <b>Atomoxetine (ATX)</b>     | <ul style="list-style-type: none"> <li>• Observed effect size is generally smaller than that for psychostimulants.<sup>56</sup></li> <li>• Can take several weeks for therapeutic effect, can be a barrier to adherence.<sup>21,59</sup></li> </ul>  |
| <b>Viloxazine</b>            | <ul style="list-style-type: none"> <li>• Once-daily non-stimulant recently approved for ADHD</li> <li>• Similar to atomoxetine, appears to have a delayed therapeutic effect</li> </ul>  |

Other medications sometimes used for ADHD in adults (e.g., bupropion, tricyclic antidepressants [TCAs], clonidine) may have some benefit for treatment of ADHD but are generally reserved for treatment-resistant cases/specialized care.<sup>1,65</sup>

\*See QRG for more detailed information about medications.

Figure 7. Stepped approach to prescribing<sup>1</sup>



### Key points for a successful medication trial:

- Involve the patient (and their family/caregiver where clinically appropriate).
- Identify the specific ADHD symptoms that impair function to define treatment goals.
- Select treatment options and strategies to measure change.
- Start with first-line treatment options and titrate doses balancing clinical efficacy and side effects.
- Assess for use of substances (e.g., caffeine, alcohol, drugs) and provide recommendations, support, and/or treatment as clinically appropriate.
- Measure response at planned intervals. If response is unsatisfactory, explore why and try a different treatment option until symptom control is optimized.
- Follow up and reassess efficacy and need for treatment regularly.

### Psychiatric comorbid disorders and treatment selection

Many adults with ADHD present with co-occurring disorders.<sup>21</sup> Often these need to be addressed concomitantly; however, in some cases prioritization may need to be given to the most impairing illness first (e.g., psychosis, severe mood disorder, bipolar disorder, active SUD [see Table 3]).<sup>1,20,21,46</sup>

- Where mood symptoms are apparent but not pervasive, treat ADHD symptoms and monitor for improvement first, prior to considering or initiating treatment for mood disorders.<sup>29</sup>
- **The presence of suicidal/violent thoughts needs to be addressed as a priority.<sup>1</sup>**

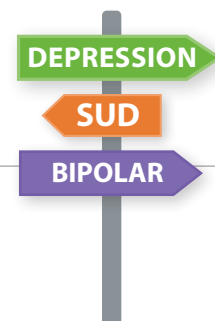


**Consider a slower dose titration and provide more frequent monitoring if any of the following are present:<sup>31</sup>**

- Other neurodevelopmental disorders (e.g., autism spectrum disorder, tic disorders, learning disability/intellectual disability)
- Mental health conditions (e.g., anxiety disorders, schizophrenia or bipolar disorder, depression, personality disorder, eating disorder, PTSD, substance misuse)
- Physical health conditions (e.g., cardiac disease, epilepsy, brain injury).

**Table 3. Co-occurring disorder considerations**

|   | <b>Medication recommendations</b>   | <b>Treatment considerations</b>   |
|---|---|---|
| <b>SUD</b>  | <ul style="list-style-type: none"> <li>Atomoxetine (has efficacy in adult ADHD; little to no abuse potential).<sup>21,31,59</sup></li> <li>Methylphenidate long-acting preparations (lower abuse potential than immediate release)</li> <li>Longer-acting prodrug formulations (e.g., lisdexamfetamine) may have lower abuse potential than other amphetamines.<sup>66,67</sup> According to the Canadian ADHD practice guidelines, “Since the bioavailability of the active ingredient is not influenced by route of administration (oral, intranasal, or intravenous), the abuse potential of this pro-drug delivery system is significantly reduced in comparison to short-acting medication due to the product formulation.”<sup>71</sup></li> <li>If stimulants are used, remain vigilant for any signs of misuse or diversion (see page 18).<sup>31,46,59,66</sup></li> </ul> | <ul style="list-style-type: none"> <li>Higher rate of SUD in adults with ADHD than in the general population; ADHD is a risk factor for SUD.<sup>1</sup></li> <li>Stimulant use in patients with SUD may increase risk for misuse.<sup>68</sup></li> <li>Consider co-management of ADHD and SUD with substance use disorder treatment team.</li> <li>In patients with an active, severe SUD, SUD treatment should be the priority.<sup>1,21,59</sup></li> <li>If active SUD is less severe or ADHD symptoms are severe and interfering with ability to engage in SUD treatment, treat ADHD and SUD concurrently.<sup>1,21,59</sup></li> </ul> |
| <b>Generalized / Social Anxiety Disorder +/- Depression</b> | Combination of a stimulant + selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI). <sup>21</sup> Monitor for serotonin syndrome. <sup>21</sup>   | To reduce risk of worsening anxiety, consider starting the SSRI/SNRI first, then adding the stimulant once anxiety symptoms have improved, or titrate the stimulant medication at a slower pace and monitor more frequently. <sup>1,21</sup>  |
| <b>Bipolar disorder</b>                                     | Stabilize the Veteran on a therapeutic dose of a mood stabilizing medication prior to treating ADHD with a stimulant to reduce the risk of triggering mania. <sup>21,28</sup> Monitor for serotonin syndrome. <sup>21</sup>   | <ul style="list-style-type: none"> <li>If mania is triggered, the stimulant should be reduced or discontinued, and treatment of bipolar disorder should be prioritized.<sup>1</sup></li> <li>Once mood is stabilized, stimulant may be cautiously restarted (start low, go slow).<sup>1</sup></li> </ul>  |
| <b>Emotional dysregulation</b>                              | <ul style="list-style-type: none"> <li>Several studies and meta-analyses have suggested that methylphenidate has benefit for emotional dysregulation.<sup>27,28</sup></li> <li>Atomoxetine may be considered after methylphenidate as it also appears to have some efficacy for emotional dysregulation.<sup>27,28</sup></li> <li>Mood stabilizers have yielded mixed results.<sup>27</sup></li> </ul>  | Treating core symptoms of ADHD with a stimulant is often linked to a beneficial effect on emotional dysregulation and should be considered the first line of treatment.   |





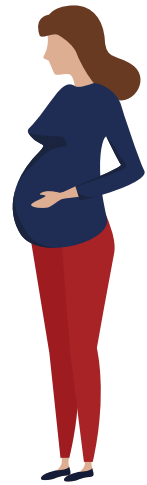
## Pregnancy considerations

### Decisions about stimulants for ADHD in pregnancy are especially challenging.

There is a paucity of high-quality studies of stimulants in pregnancy and the risks of untreated ADHD vary. That said, stimulants are not among the highest-risk medications during pregnancy. In many cases, the risks of untreated ADHD are substantial and exceed the risks of stimulants, especially amphetamine/dextroamphetamine.<sup>69-71</sup>

When clinically indicated, a detailed history and pregnancy test can be used to assess the intention of becoming pregnant and current pregnancy status of a woman of child-bearing potential.

- Having this conversation ahead of time allows for the development of a treatment plan compatible with pregnancy for anyone who might become pregnant, and to include perinatal consideration in the risk/benefit discussion.
- These discussions are important even for medications with favorable perinatal safety profiles. Without such discussions, a patient may abruptly discontinue a medication on learning of a pregnancy, even if the risks of the untreated symptoms outweigh the risks of the medication.



**The VA Reproductive Mental Health Consultation Program is available to help clinicians: [ReproMHConsult@va.gov](mailto:ReproMHConsult@va.gov).**

## Non-pharmacologic treatment<sup>11,20,21,24,31,44,46,47,49</sup>

When treating adults with ADHD, it is imperative to address not only core symptoms of ADHD but also the affected sleep behaviors, perceived stress, and maladaptive coping styles to maximize the potential for overall increases in well-being.<sup>47,72</sup>

Various non-pharmacologic interventions such as cognitive behavioral therapy, cognitive remediation and rehabilitation, and mindfulness-based therapies have shown efficacy for ADHD core behavioral symptoms and/or associated dysfunction and are generally well tolerated.<sup>50</sup> Benefits of psychosocial treatments are more apparent for executive functioning and functional impairment, rather than on ADHD symptom checklists.<sup>24,47</sup>

- Other psychotherapeutic principles and techniques can be useful under specific circumstances (e.g., couples therapy can be used to increase communication skills and conflict resolution).<sup>47</sup>
- Consider referral to Occupational Therapy for daily life management skills (e.g., paying bills on time; using electronic devices for reminders; improved efficiency at home, work, or school).



For adults with ADHD with prominent deficits in executive functioning, consider combined treatment (pharmacotherapy + non-pharmacologic treatment).<sup>21,48</sup>

***Provide evidence-based treatment to Veterans with ADHD.***

# Monitoring, follow-up, and continued care

## Assessing treatment response

In general, stimulant effects are likely to be stable at a given dose after 1-3 weeks (for atomoxetine, after 4-6 weeks).<sup>1</sup> A 6-week trial at an optimal, tolerated dose is recommended before switching to or adding on another ADHD treatment. Use subjective impressions of response along with objective measures to guide dosage adjustments, treatment switch, or add-on therapy.<sup>31</sup>



An excessive dose of a stimulant medication can induce an inflexible pattern of responding (e.g., as would be seen following uncontrollable stress), restricted affect, and/or cognitive inflexibility.<sup>1,18</sup>

While treatment success could be defined as remission of all ADHD symptoms, improvement should be clinically significant and represent observable change from baseline.<sup>21</sup>



See ADHD QRG for more information on use of rating scales to measure change.



### ADHD symptom control

- Use validated rating scales to monitor response and assess changes in ADHD symptoms.<sup>21,56</sup> This increases positive clinical outcomes and chance of remission.<sup>21,56</sup>



### Changes in functioning/quality of life

- Assess functional benefits from symptom control at each visit (e.g., functional impairment, quality of life, executive function).<sup>56</sup>
  - Consider getting input from other sources (e.g., family members, coworkers) to assess impact of ADHD treatment.<sup>21,56</sup>



### Tolerability of medication

- Ask the Veteran about the positive and negative effects of the medication and duration of these effects at each visit and following each dose adjustment.<sup>21</sup>
- Ask about adverse effects in a “review of systems” manner focusing on the most likely adverse effects of each medication.<sup>56</sup> See ADHD QRG for common adverse effect information.

**Table 4. Monitoring and follow-up considerations**

|  |   |
|--|---|
| <p><b>Robust response<sup>21</sup></b></p>         | <p>Continue medication. <b>Note:</b> timing of the stimulant dose(s) may still need to be adjusted despite overall robust response.</p>   |
| <p><b>Partial response<sup>21,31</sup></b></p>     | <ul style="list-style-type: none"> <li>• Consider dose adjustment to account for total versus peak dose effects (e.g., the Veteran may need an additional dose later in the day instead of morning)</li> <li>• Consider increasing to the maximum recommended therapeutic dose.</li> <li>• Consider augmentation with non-pharmacologic treatment for Veterans who are tolerating the medication but only having a partial response.</li> <li>• Consider switching medications. No washout or tapering is necessary in switching from one stimulant medication to another.</li> </ul> |
| <p><b>Unable to tolerate<sup>1,21,31</sup></b></p> | <p>Consider a different medication or formulation if the Veteran is unable to tolerate a therapeutic dose.</p> <ul style="list-style-type: none"> <li>• When adverse effects are not mild or pose risk, consider changing to a different class of medication or managing an underlying vulnerability.<sup>1</sup></li> <li>• When adverse effects are mild or seem related to the delivery system, consider a product with a different pattern of release of the same active ingredient.<sup>1</sup></li> </ul>   |

**Please note:** If negative symptoms are experienced at the time when medications would be expected to be wearing off, or with sudden cessation of pharmacotherapy, the symptoms may be from the medication wearing off too quickly.<sup>1</sup>



**If the initial stimulant fails to deliver an optimal response,** evidence supports the need for sequential trials of both stimulants (amphetamines, methylphenidate) before deeming stimulants unsuccessful.<sup>63</sup>

**For Veterans with partial or no response to treatment, review both the diagnosis (including comorbidities) and treatment plan** to ensure compliance to treatment as well as to check if there are external factors that could complicate the clinical picture.<sup>1</sup> Consider obtaining a second opinion or referring to a mental health provider if ADHD symptoms are unresponsive to one or more stimulants and one non-stimulant.<sup>31</sup>

## Maintenance treatment

Long-term benefit of ADHD treatment is a controversial area and recommendations typically suggest to individualize treatment plans and consider risks versus benefits of long-term treatment.<sup>56</sup>

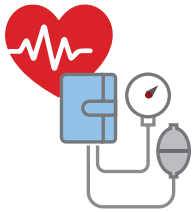


## Monitoring recommendations

After stabilization of symptoms, reassess treatment response and adherence, vital signs, and side effects/adverse effects at least once a year.<sup>56</sup> ADHD patients can benefit from having access to mental health care when needed during their life-course with ADHD.



**Monitor Veterans on stimulants + SSRI/SNRI/tricyclic antidepressants (TCA) for serotonin syndrome.** Other medications and over-the-counter agents can also precipitate serotonin syndrome when combined with stimulants (e.g., MAO-Is, lithium, linezolid, triptans, St John's Wort, etc.); refer to medication package insert for more about drug interactions.



**Measure heart rate and blood pressure regularly during treatment.**<sup>21,31,73</sup>

- To assess the effects of medications on vital signs, it may be useful to take measures before a dose is taken and compare to measures while the dose is active.<sup>1</sup>
- If a person taking ADHD medication has sustained resting tachycardia (> 120 beats per minute), arrhythmia or significant increase in blood pressure measured on two occasions, consider reducing the dose by half and refer for assessment. Ask about caffeine use and recommend to reduce or avoid use as needed.



**Monitor for the appearance of, or worsening of, aggressive or anxious behavior and sleep disturbances.**<sup>31</sup>



**Remain vigilant and assess risk for substance misuse and drug diversion** (e.g., PDMP checks, UDT as clinically appropriate).<sup>74</sup>



**Consider monitoring body mass index (BMI)** in adults with ADHD if there has been weight change as a result of their treatment, and changing the medication if weight change persists.<sup>31</sup>



Continue to assess, support, and oversee treatment of **mental health care needs.**

## Treatment considerations for older adults

As patients with ADHD age, several factors may impact the risk versus benefit assessment.<sup>75,76</sup>

- Possible reduction or remission of ADHD symptoms, particularly hyperactivity<sup>20,24,26</sup>
- Age-related decline of liver and kidney function may impact drug metabolism
- Increased number of comorbidities (e.g., cardiovascular disease, glaucoma)
- Increased number of medications and subsequently the risk of drug-drug interactions
- Greater risks from side effects (e.g., appetite reduction, insomnia, dry mouth, tremors)



## What you can do:

- ✓ Understand how ADHD symptoms have affected the Veteran's health, quality of life, and function when weighing the benefits versus risks of continuing pharmacotherapy.<sup>76</sup>
- ✓ Assess for use of drugs, alcohol, and other substances (e.g., caffeine) and encourage the Veteran to minimize use. Offer evidence-based treatment when clinically applicable.
- ✓ Individualize treatment plans to minimize risk and maximize benefits. Consider:
  - Adjusting the dose, formulation, or switching to a different medication to minimize risks
  - Tapering and discontinuing the medication if risks outweigh benefits
  - Using non-pharmacologic treatments either alone or in addition to pharmacotherapy
- ✓ Follow up with Veterans after treatment plan changes to ensure benefits are outweighing the risks and provide follow-up care as needed.

## Supporting people with ADHD<sup>31</sup>

Studies highlight the need for long-term psychiatric and psychosocial support in patients with ADHD, regardless of pharmacologic or non-pharmacologic treatment.<sup>24</sup> Patients diagnosed with ADHD will often go through a three-step process:<sup>19</sup>



- 1** **The initial sense of relief stems from validation of the experience,** and its sequelae, and optimism for treatment.
- 2** **Frustration often ensues as patients realize they have a chronic condition** and recall their past experiences and life decisions that may have been different if the condition was recognized and treated sooner.
- 3** **Self-acceptance occurs when a patient embraces ADHD as a life-long condition** that is not singularly defining yet may help explain prior self-defeating behavior and decision-making.

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**This reference guide was created to be used as a tool for VA providers and is available from the Academic Detailing SharePoint.**

**These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.**

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