ADHD and Substance Use Disorders

Adolescent Substance Abuse Program
Center for Adolescent Substance Abuse Research
Children's Hospital, Boston

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Supplemental Materials

This module is a part of a curriculum designed to introduce clinicians to adolescent Screening, Brief Intervention and Referral to Treatment (SBIRT), and provide them with tools and knowledge to efficiently and effectively address adolescent substance use in the primary-care setting. The curriculum is intended to build upon the core SBIRT Overview module, and includes:

- SBIRT Overview
- Brief Motivational Interviewing
- Confidentiality
- Parent Guidance
- ADHD and Substance Use Disorders
- Pain and Addiction
- Drug Testing

- Buprenorphine Treatment of Opioid Dependence
- Club Drugs
- Infectious Diseases
- Neurobiology of Alcohol and Marijuana Addiction
- Smoking Cessation

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Learning Objectives

• To review the basis of the increased risk of substance use disorders in adolescents with ADHD
• To review pharmacological treatment of ADHD
• To define prescription medication misuse, abuse and dependence
• To review epidemiology of prescription medication misuse
• To present suggestions for safe prescribing practices
Taylor

Taylor is a 14 year old girl with ADHD who you have followed since infancy. She started taking stimulant medication in 2nd grade and has been doing well in school. She presents for a routine physical and medication refill. She reports past-year marijuana use and screens into the “lower risk” category.

Teens with ADHD are more likely to try alcohol and other drugs earlier than their peers, and they are also more likely to develop a substance addiction. Screening and brief interventions are particularly important for this group.
Brief Advice for Taylor

As your physician, I recommend that you quit using marijuana. Smoking marijuana can make it harder for you to concentrate at school and remember things. Unfortunately, kids with ADHD also are more likely to become addicted to drugs than their friends who don’t have ADHD. You have been doing so well in school, I would hate to see anything interfere with your future.

As with all teens, we recommend brief, medically-based advice for kids with “lower risk” substance use. In this case the physician discusses both the potential for marijuana to make ADHD symptoms worse as well as the risk of developing a substance use disorder.
Individuals with ADHD are more likely to develop a substance use disorder than their peers.

Predictors of Drug Use in Teens with ADHD

Teens with ADHD are more likely to try tobacco, alcohol, and illicit substance use by age 14.

- Inattention symptoms at age 14 increase likelihood of early alcohol use initiation.
- Symptoms on the hyperactivity/impulsivity spectrum at age 14 increase likelihood of tobacco/illicit drug use, and nicotine and marijuana abuse/dependence by age 18.
- Co-occurring disruptive behavior disorders strongly predict early initiation of all substance use, and substance abuse/dependence diagnoses by age 18.

Understanding the link between ADHD and SUD

Three theories:

1. “Impulsivity” – impulsivity associated with ADHD leads to poor decisions, including trying drugs
2. “Dopamine” – drug use may increase extracellular dopamine which is deficient in individuals with ADHD
3. “Common gene” – genes associated with ADHD-risk are inherited together with genes for SUD-risk

The links between ADHD and SUD are poorly understood. Evidence for each of the three theories described above will be reviewed on the following slides. It is likely that they each play a role as do other, yet to be described mechanisms.
Impulsivity

• Impulsivity is associated with an increased substance use (a prerequisite for developing a substance use disorder (SUD)).

• Earlier onset of substance use is associated with increased risk of SUD and may contribute to the association between ADHD and SUD.

• Executive functioning deficits and poor decisions may also contribute to the development of substance use disorders—i.e. kids with ADHD may have more problems associated with substance use than their peers.

While poor decisions and early experimentation both contribute to the association between ADHD and SUD this is not the entire story. (ref 20) Individuals with ADHD may also be more vulnerable to develop the neurologic disorder of addiction than peers, probably due to biologic differences in brain structure.


Dopamine

• Individuals with ADHD have greater dopamine transporter density resulting in rapid clearance and low levels of synaptic dopamine.

• Cocaine, amphetamine, methamphetamine, Ecstasy, nicotine, alcohol, opiates and marijuana all increase synaptic dopamine levels in the brain (stimulant medications treat ADHD symptoms by increasing synaptic dopamine levels in the striatum via pre-synaptic transporters).

• Some individuals with ADHD may use substances to increase synaptic dopamine levels as a form of self-medication.


Some evidence suggests that a common genetic factor underlies both ADHD and risk for SUD.

- Individuals with drug dependence, with or without co-morbid ADHD are more likely to have first-degree relatives with ADHD.
- Individuals with ADHD are also more likely to have first-degree relatives with alcohol or drug dependence.
- There is a likely genetic link between hyperactivity/inattention spectrum behaviors and risk of developing alcohol dependence in adulthood.

Stimulant Treatment Reduces the Risk of SUD in ADHD patients

- Majority of studies (4/7) indicate **reduced risk** for SUD in treated vs. untreated ADHD individuals
- Meta-analysis suggests treatment of ADHD associated with a 2-fold reduction in the risk for SUD
- Evidence suggests that the abuse potential of **stimulant** medication is **lower** for individuals with ADHD than their peers and the risk of abusing prescription medication is relatively low.

Kollins SH. Abuse liability of medications used to treat attention-deficit/hyperactivity disorder (ADHD). The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions. 2007;16 Suppl 1:35-42; quiz 43-34.
# Pharmacotherapy for ADHD

<table>
<thead>
<tr>
<th>ADHD Stimulants</th>
<th>Non-Stimulant Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextroamphetamine</td>
<td>Dextedrine Spansules DextroStatXR</td>
</tr>
<tr>
<td>Mixed amphetamine salts</td>
<td>Adderall/Adderall XR Vyvanse (prodrug)</td>
</tr>
<tr>
<td>Dexmethylphenidate</td>
<td>Focalin/Focalin XR</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Concerta Metadate CD Methylin/Methylin ER Ritalin/ Ritalin SR/Ritalin LA Daytrana (patch)</td>
</tr>
</tbody>
</table>

The AAP recommends expanding patient history to include specific cardiac symptoms, Wolf-Parkinson-White syndrome, sudden death in the family, hypertrophic cardiomyopathy, and long QT syndrome when considering stimulant medications in treatment of ADHD.


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Abuse Potential

Amphetamine > Methylphenidate > extended release/long acting > non-stimulant medications
Non-pharmacologic treatment

The Multimodal Treatment Study of Children with ADHD (MTA) found that behavioral interventions were protective against SUD.

Co-occurring mental health disorders are common in individuals with ADHD and are associated with increased substance use disorder risk. Treating depression, anxiety and low self-esteem may reduce the risk of SUD.

Intensive behavioral interventions such as clinical behavior therapy, parent training, school intervention, and summer treatment programs are more protective against SUD than medication alone.


Parental Involvement Reduces Drug Use

Teens that did not use drugs reported:

- Parents often checked homework
- Parents praised frequently
- Teens perceived strong disapproval of drug use by parents

Bill

Bill is a 16 year old boy who presents for an initial primary care appointment. He recently moved from another state and his medical records are not available. He says he was diagnosed with ADHD several years ago and needs an Adderall refill.

Making or even confirming a diagnosis of ADHD in a teenager can be difficult, but it is important before prescribing a medication with potential for misuse or diversion. If it is impossible to get the medical record, we recommend getting more history from a parent.
You call Bill’s mother at work and she confirms that he was diagnosed with ADHD at age 6. After a trial of behavioral management alone, he was put on stimulants in 3rd grade and has done well on them. He now manages his medication on his own though she picks up his medication from the pharmacy and she knows that it is time for a refill.

This history from Bill’s mother is very reassuring. Since Bill is a new patient and managing medications on his own, screening for medication misuse and medication instructions are warranted.
On routine SBIRT screening, Bill reports past year alcohol use and falls into the “lower risk” category. You give him brief advice to stop drinking.

To date, no screen has been validated for identifying misuse of prescription medications. For patients who are prescribed long-term medications with potential for misuse, we recommend adding specific questions about how medication is being taken.
Suggested Questions for Identifying Medication Misuse

• Have you ever taken your medication more often than prescribed?
• Have you ever taken a larger dose than prescribed?
• Have you ever shared or sold your medication?

These questions may help to identify medication misuse or diversion. If the answer to any of the questions is yes, explore further. Find out why the patient is reporting taking more frequent or larger doses. Perhaps the dose needs to be adjusted, or perhaps the teen is using the medication “recreationally”.
Bill says he takes an extra tablet to study longer before big exams and once he gave a pill to his girlfriend to help her study for a final.

“Non-prescribed” use of stimulant use has become increasingly common and many teens (and adults) do not see this type of use as problematic. However, use of stimulants by individuals who do not have ADHD is NOT recommended. Stimulant use in these cases has been compared to corrective lenses for a student who does not have a vision problem. The lenses will make everything appear larger, but will not improve reading. Stimulants also have a significant abuse potential and should not be used without medical supervision. See the next slide for suggested advice to all patients prescribed stimulant medication.
Definitions

- **Diversion** - transfer of medication to a person for whom it is not prescribed.
- **Misuse** - use of medications not prescribed to the individual or use of medications in ways other than prescribed (taking more than prescribed or by an alternative route of administration).
- **Abuse** - use associated with risk or problems that interfere with functioning.
- **Dependence** (addiction) - loss of control or compulsive use of a substance

The term “substance use disorder” includes both “abuse” and “dependence”, which were defined by formal diagnostic criteria in DSM-IV. DSM-V will change the categories to substance use disorder “moderate” and “severe” and the criteria will change slightly. However, the essence of the terms will remain the same, and the words “abuse” and “dependence” are likely to be in the lexicon for some time to come.
Epidemiology

• As a group, prescription medications are misused by adolescents more than any other illicit drug except marijuana.
• For any class of prescription medications, misuse increases with age and grade.

The data on the next two slides comes from the Monitoring the Future Survey, which is a nationally representative, anonymous annual survey of 46,000 8th, 10th and 12th graders administered in public and private schools. Data from a web-based survey of 1086 students in grades 7 to 12 conducted in May 2005 found that as students get older the rate of prescription medication misuse increases.

Rates of misuse of Rx stimulants by 12th graders in 2011

<table>
<thead>
<tr>
<th>Substance</th>
<th>Lifetime</th>
<th>Past year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>12.2</td>
<td>8.2</td>
</tr>
<tr>
<td>Adderall®</td>
<td>NA</td>
<td>6.5</td>
</tr>
<tr>
<td>Ritalin®</td>
<td>NA</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Approximately 1 in 12 high school seniors reported past year amphetamine misuse in 2011; the vast majority of amphetamine misuse involved prescription stimulants.


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Misuse of stimulants among 12th graders

Note the recent resurgence in misuse of amphetamine after a period of decline from 2002-2010. Also note that rates of methylphenidate (Ritalin) misuse are less than the rate of amphetamine (Adderall) misuse.


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Perceived harm

Which drug do high school students perceive as most harmful?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>21%</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>15%</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>14%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>9%</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>4%</td>
</tr>
</tbody>
</table>

This survey was conducted by the Partnership for a drug-free America and consisted of a nationwide sample of 7,216 students in grades 7 to 12. Questionnaires were administered in school and at home under the supervision of trained interviewers. Perhaps not surprisingly, most students rated illicit drugs as more physically harmful than prescription medications. In general, teens perceive prescription medications to be safe.
Sharing Medications

• Nearly a quarter (23%) of students prescribed stimulant medications have been asked to sell, trade, or give away their medications.

• 20% girls and 13% boys aged 9 -18 have borrowed and/or shared prescription medications in their lifetime.

This study was conducted in the Detroit school system and included over 1500 students in grades 6-11. Note that girls were more likely to share their medications than boys.


Another study found that the rate of stimulant misuse by students is directly related to the number of prescription users in the class.

## Misuse of Stimulants Among College Students

<table>
<thead>
<tr>
<th>Ranks of Colleges</th>
<th>% students who report stimulant misuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most competitive</td>
<td>5.9%</td>
</tr>
<tr>
<td>Competitive</td>
<td>4.5%</td>
</tr>
<tr>
<td>Less competitive</td>
<td>1.3%</td>
</tr>
<tr>
<td>All colleges</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

In this study 10,904 students from 119 colleges responded a self-administered mail survey with questions about stimulant (Ritalin, Dexedrine or Adderall) use. Note that the rates of stimulant misuse among college students is directly proportional to the “competitiveness” rank of the college.

# Sources of Misused Stimulants

<table>
<thead>
<tr>
<th>Teens aged 12-17</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Free: friend or relative</td>
<td>50%</td>
</tr>
<tr>
<td>Purchased</td>
<td>21%</td>
</tr>
<tr>
<td>From MD</td>
<td>12%</td>
</tr>
<tr>
<td>Theft/Fake Rx</td>
<td>12%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>College students</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Peers</td>
<td>68%</td>
</tr>
<tr>
<td>Family</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>29%</td>
</tr>
</tbody>
</table>


See previous slide for description.

Regardless of age, the primary source of misused medications is peers. It is critical to discuss diversion with all patients who receive prescriptions.
Proper Administration

At each clinic visit, review with the patient how he/she is taking his/her stimulant medication.

- Only take the amount of medicine prescribed. Do not take extra medication.
- Take your stimulant medication exactly as prescribed. Do not change the dose or timing. Speak to your doctor if you do not think your medication is working as it should or if you are experiencing side effects.
- Do not use alcohol, tobacco, marijuana or other illicit substances. Drug use worsens problems with attention, leads to medication non-compliance and can interact with stimulant medication.
- If stimulant medication is administered at school, it should be dispensed at school nurse’s office or other safe location with adult supervision.

Risk for misuse, diversion and abuse

- Explain that some people who do not have ADHD may take stimulant medications inappropriately.
- Inform patient and parent that children and adolescents may be asked to give away or sell their stimulant medications, but should never do so. Parents may role play appropriate responses so that the child will be prepared if asked. Have the patient and parents keep medication in a safe location – either at home or in a locked office at school. Medications should never be carried in a backpack or purse.
Jacob

Jacob is a 17 year old boy who has been followed on and off by your practice. He is a healthy boy who has had difficulty with impulsivity since childhood. At his last visit 5 years ago his parents questioned whether he had ADHD. You requested information from his teachers but his parents did not follow through. In 8th grade the school psychologist formally diagnosed him with ADHD and the school provided learning accommodations, but he has never tried medication.

Jacob was caught with marijuana in his locker and the school has requested “medical clearance” in order for him to return.

Teens with ADHD are more likely both to try substances and develop a substance use disorder. Screening, brief intervention and early referral to treatment are critical.
In private, Jacob tells you that he has been smoking marijuana every day for the past 2 years, and he screens into the “high risk” category. He does not see marijuana use as dangerous. He is confident that he can quit at any time; he has never tried because he has not seen the point. However, his parents were very upset about the incident in school and have grounded him and taken away his driving privileges.

You do a brief motivational intervention Jacob agrees to quit marijuana, at least until the end of the school year. He will monitor with drug testing and you will recommend restoring driving privileges once he has 3 consecutive negative drug tests. You recommend an individual counselor but he is not interested. You agree to write him a note to return to school on the condition that he agrees to counseling if he is not able to remain abstinent.
Jacob invites his mother in to discuss the plan and she is satisfied. She then asks you whether you think Jacob should start a stimulant medication to treat his ADHD.

Teens with ADHD have reduced risk of developing a substance use disorder if they are treated with stimulant medication. On the other hand, teens with a history of tobacco, alcohol, marijuana or other drug use are more likely to divert or misuse medications.

In this case because Jacob agrees to abstinence and monitoring, we think a trial of stimulant medication is reasonable and can be done safely. In fact the evidence suggests that patients with ADHD are unlikely to abuse stimulant medications.

The next slides present suggestions for monitoring medications in “higher risk” teens.
# Tips for Prescribing to High Risk Teens

<table>
<thead>
<tr>
<th><strong>Use formulations with lower abuse potential</strong></th>
<th><strong>Keep careful medication records</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Avoid immediate release preparations</td>
<td>• Single prescriber</td>
</tr>
<tr>
<td></td>
<td>• Frequent office visits</td>
</tr>
<tr>
<td></td>
<td>• Avoid early refills</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Monitor with drug testing</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Urine specimen should be positive for amphetamine and negative for other substances</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Have parents supervise meds</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dispense dose daily</td>
</tr>
<tr>
<td>• Keep the bottle locked</td>
</tr>
</tbody>
</table>
Red Flags for Medication Abuse or Dependence

- Using stimulants for a “high”
- Requests for early refills or escalating dose
- Demands for immediate release compounds
- Buying or stealing meds or forging prescriptions
- “Sniffing” or “snorting” oral formulations
- Symptoms of stimulant toxicity (palpitations, syncope, shortness of breath, “panic attacks”)

All adolescents who are prescribed stimulants should be monitored frequently. If any of the “red flags” above occur, we recommend evaluation by a mental health or addiction specialist before continuing stimulant medication.
Summary

• Individuals with ADHD are at risk of trying substances and developing SUD. Screening, Brief Intervention and early referral are critical for this population.
• Stimulant treatment appears to reduce the risk of substance use disorders in teens with ADHD. Behavioral treatments and treating co-occurring disorders likely also reduces risk.
• Stimulants have significant misuse, abuse and diversion potential. Anticipatory guidance and careful monitoring are imperative.
Acknowledgements

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