UTAH SOCIETY OF
HEALTH–SYSTEM PHARMACISTS

Resident CE Series
November 3, 2018

Adult ADHD and Stimulant Use: the Emerging, Overshadowed Epidemic

Keaton Crockett, PharmD
PGY2 Ambulatory Care Resident

Resident CE Series
November 3, 2018

Disclosure

Relevant Financial Conflicts of Interest
- Keaton Crockett: No conflicts of interest
- Alisyn May: No conflicts of interest

Off-Label Uses of Medications
- Bupropion
- Clonidine
- Guanfacine

Technician Learning Objectives

At the conclusion of this activity, participants should be able to successfully:
- Identify common stimulants used to treat attention-deficit/hyperactivity disorder (ADHD)
- Discuss appropriate simulant use in adults diagnosed with ADHD
- Differentiate elements of legitimate vs. illegitimate stimulant prescriptions

Pharmacist Learning Objectives

At the conclusion of this activity, participants should be able to successfully:
- Discuss appropriate stimulant use in adults diagnosed with ADHD
- Examine diagnostic criteria for adult ADHD
- Identify stimulant adverse effects and the impact of stimulant use on comorbid conditions
- Investigate elements of appropriate stimulant prescribing and use

USHP

Prevalence

ADHD at Sugarhouse Clinic

- 550 patients seen in a 1 week period
  - 42 patients with current stimulant Rx
    - 13 visits for stimulant refills
  - 10 visits were new patients requesting ADHD medications or existing patients requesting new ADHD medication/diagnosis

7

ADHD Epidemiology Children[1]

- 6.1 million U.S. children (9.4%) diagnosed with ADHD
  - 62% were taking medication
  - 64% diagnosed with another behavioral, emotional, or mental health disorder

USHP

https://pixabay.com/en/children-win-success-video-game-593313/

8

ADHD Epidemiology Adults[2,3]

- Over 60% of children with ADHD continue to have symptoms into adulthood
- 4.4% to 5.2% of adults in the U.S. have ADHD

USHP

https://pixabay.com/en/magnifying-glass-human-head-faces-1607208/

9

Diagnosis

10

ADHD[4]

Attention Deficit Hyperactivity Disorder (ADHD) core patterns/symptoms:

- Inattention – "wanders off task"
- Hyperactivity – "moving constantly"
- Impulsivity – "hasty actions or socially intrusive"

ADHD

USHP

11

ADHD History[5,6]

- DSM II (1968) "Hyperkinetic Reaction of Childhood"
- DSM III (1980) "Attention Deficit Disorder with and without Hyperactivity"
- DSM III-R "Attention Deficit/Hyperactivity Disorder" (eliminated ADD without hyperactivity)
- DSM IV (1994) retained ADHD and introduced three subtypes
  - Predominantly Inattentive
  - Predominantly Hyperactive-Impulsive
  - Combined

12

DSM V Criteria

- A – Persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development
  - Gives examples how symptoms may manifest in adolescents and adults
  - Reduced required number of symptoms from 6 to 5 for "older" adolescents and adults (**17 years and older**)
- B – Several symptoms present prior to age 12
  - Changed age of symptom onset from before age 7 to before age 12

DSM V Criteria[7]

- C – Several symptoms present in 2 or more settings (home, school, work, social, other)
- D – Clear evidence that symptoms interfere with social, academic, or occupational functioning
- E – Symptoms are not better explained by another mental disorder

DSM V Criteria[7] Inattention – 5 or more required:

- Overlooks or misses details; work is inaccurate
- Difficulty remaining focused (during lectures, conversations, lengthy reading)
- Often does not seem to listen when spoken to directly (mind seems elsewhere)
- Does not follow through (starts tasks but quickly loses focus)
- Difficulty organizing tasks (messy, poor time management, misses deadlines)
- Avoid tasks requiring sustained mental effort (preparing reports, completing forms)
- Often loses things (books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones)
- Easily distracted (has unrelated thoughts)
- Often forgetful (returning calls, paying bills, keeping appointments)

DSM V Criteria[7] Hyperactivity/Impulsivity – 5 or more required:

- Often fidgets with or taps hands/feet or squirms in seat
- Often leaves seat in situations when remaining seated is expected (classroom, office)
- Often runs about or climbs in situations where it is inappropriate (feeling restless)
- Often unable to play or engage in leisure activities quietly
- Acts as if "driven by a motor" (hard time being still for a long periods – restaurants, meetings)
- Often talks excessively
- Often blurts out answers before questions are completed (can't wait for turn in conversations)
- Often has difficulty waiting his or her turn (while waiting in line)
- Often interrupts or intrudes others (butts into conversations, take over what others are doing)

Diagnosis and Treatment Gaps[8]

- Often goes undiagnosed or untreated
- Affects several aspects of daily life:
  - Set priorities
  - Relationships
  - Productivity at work
  - Manage home finances
  - Help children with homework
  - Criminal activity
  - Increase in traffic accidents
  - Self-esteem
  - Sleep

USHP

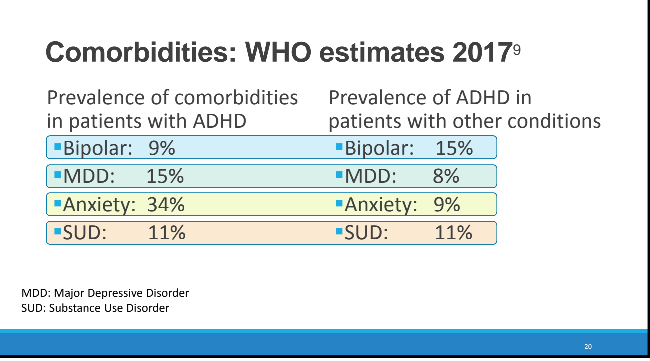
Question (Pharmacists)

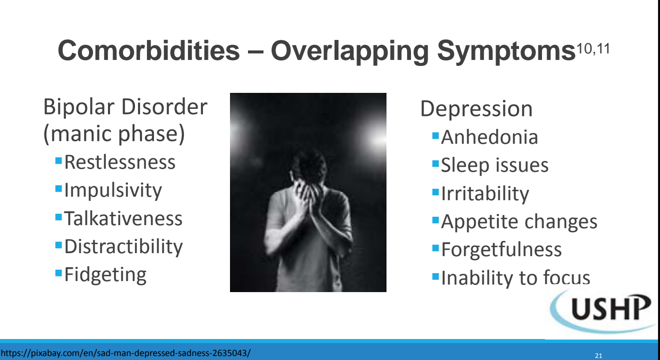
Examine whether the following patient's symptoms meet the required number of symptoms according to Criterion A in DSM V

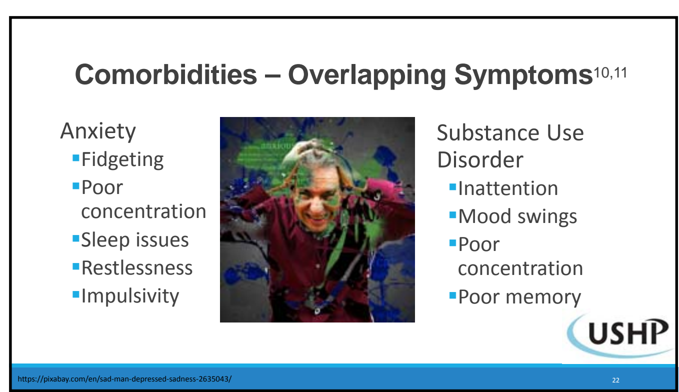
- Worries excessively about personal health
- Has started several projects at work that he has started, but been unable to finish
- Spends too much time playing Fortnite
- Wife complains that he doesn't seem to listen to her when they are having a conversation
- Frequently loses his keys or wallet
- Coworkers have complained that he is frequently tapping or fidgeting with his pen
- Has difficulty waking up in the morning
- Has forgot about and missed two recent PCP appointments and dental appointment
- Has a hard time remaining focused during weekly work meetings
- Has difficulty being patient with his 3-year-old daughter

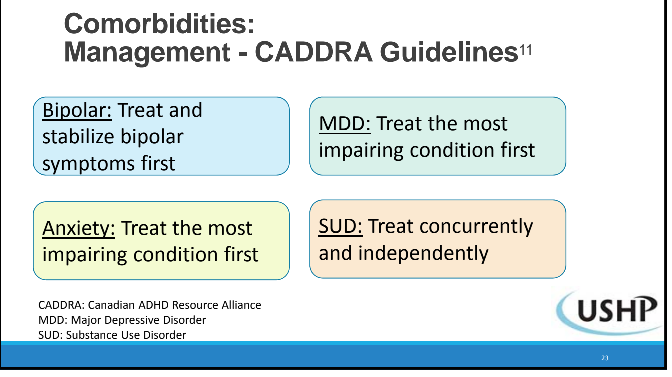
A – meets required number of symptoms
B – does not meet required number of symptoms

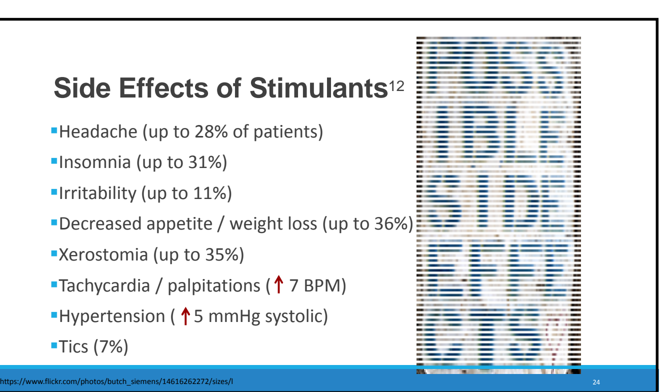
Comorbidities











Boxed Warnings[12]

- Abuse and Dependence:
  - "CNS stimulants, including methylphenidate-containing products and amphetamines, have a high potential for abuse and dependence…"
  - "Long-term abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behavior…"
- Cardiovascular events:
  - "Use has been associated with serious cardiovascular events including sudden death in patients with preexisting structural cardiac abnormalities or other serious heart problems…patients should be carefully evaluated for cardiac diseases prior to initiation of therapy…Use with caution in patients with cardiovascular conditions that may be exacerbated by increases in blood pressure or heart rate (eg, hypertension, heart failure, recent MI, ventricular arrhythmia)."

Question (Pharmacists)

A 46 year old female has recently been diagnosed with ADHD and is starting dextroamphetamine/amphetamine. Based on her medication profile, what comorbid conditions could be adversely affected with the initiation of dextroamphetamine/amphetamine?

- Metformin 500 mg twice daily [Diabetes]
- Losartan 100 mg daily [Hypertension]
- Simvastatin 20 mg daily [Hyperlipidemia]
- Sumatriptan 50 mg PRN [Migraines/Headache]
- Zolpidem 5 mg at night PRN [Insomnia]
- Buspirone 10 mg twice daily [Anxiety]

A – Yes
B – No

Stimulant Use in ADHD

Products[12]

- Stimulants
  - Methylphenidate (Ritalin®)
  - Amphetamine salts (Adderall®)
- Non-stimulants
  - Atomoxetine (Stratterra®) FDA approved
  - Clonidine (extended release) FDA approved in children only
  - Guanfacine (Intuniv®) FDA approved in children only
  - Bupropion Not FDA approved

USHP

Stimulant Products[12]

- Methylphenidate
  - Ritalin®
  - Ritalin LA®
  - Ritalin SR®
  - Aptensio XR®
  - Concerta®
  - Cotempla XR-ODT®
  - Daytrana®
  - Metadate CD®
  - Metadate ER®
  - Methylin®
  - Quillichew ER®
  - Quillivant XR®
  - Relexxii®
  - Jornay PM®
- Dexmethylphenidate
  - Focalin®
  - Focalin XR®
- Dextroamphetamine/amphetamine
  - Adderall®
  - Adderall XR®
  - Mydayis®
- Lisdexamfetamine
  - Vyvanse®
- Amphetamine
  - Adzenys® ER, XR ODT
  - Dyanavel XR®
  - Evekeo®

https://www.flickr.com/photos/buddah/2404182173/in/photolist-4Es4AM-4q6iBd-8pXRPz-4a2uM6-hRe5Nz-ABFyW-ydatq-oZTp6a-dQ7Mx4-4HFHwF-4HL3Fw-8ofgTb-4HKWTL-6ZqszQ-hRe46r-2Cdp1F-hX5Chs-de4WYQ-r2AQtq-5KdCCd-6nZgSS-7Lji15-7Ljwvf-6ZsofW-6zv8JW-XmufdU-5HxEss-oGsSjh-7Ljwvh-95joFB-7LJxiU-9N2DcZ-4thZws-nq9s9-54ftCH-7LjwuC-7LfoMn-7zoP6X-cURuLy-7LJxiE-7zoRSa-9CryJ-bUEbs-3gGFTY-G1b6Na-4MTfkx-5JUmT5-3eTmHh-9QrAGB-oaXDA6

Question (Technician)

Identify the following as either a stimulant for ADHD, non-stimulant for ADHD, or other:

- Guanfacine
- Vyvanse®
- Fluoxetine
- Atomoxetine
- Metadate®
- Amitriptyline

A – Stimulant for ADHD
B – Non-stimulant for ADHD
C – Other

Increase in Use Among Women[13]

Prescription claims among privately insured women aged 15-44 years, United States 2003-2015

- 344% increase overall
- 450% increase in women age 20-24
- 700% increase in women age 25-29
- 560% increase in women age 30-34

Increase in Use Among Women[13]

Prescription claims among privately insured women aged 15-44 years, United States 2003-2015

- Most commonly dispensed products
  - Mixed amphetamine salts: 60.8%
  - Lisdexamfetamine: 26.7%
  - Methylphenidate: 18.1%
  - Dexmethylphenidate: 3.1%

Prevalence of Prescription Stimulants[14]

2015-2016 National Surveys on Drug Use and Health

- Adult prescription stimulants have surpassed youth prescriptions
- Adults >18 years from 2015-2016
- Approximately 16 million adults (6.6%) used prescription stimulants
  - 11 million reported use without misuse
  - 5 million reported misuse at least once – **31.2% of stimulant users**
  - 0.4 million had prescription stimulant use disorders

Prevalence of Prescription Stimulants[14]

2015-2016 National Surveys on Drug Use and Health

- Definition of Misuse – in any way that a doctor did not direct you to use them, including:

  1 – Use without a prescription of your own

  2 – Greater amounts, more often or longer that you were told to take them

  3 – Use in any other way a doctor did not direct you to use them

Prevalence of Prescription Stimulants[14]

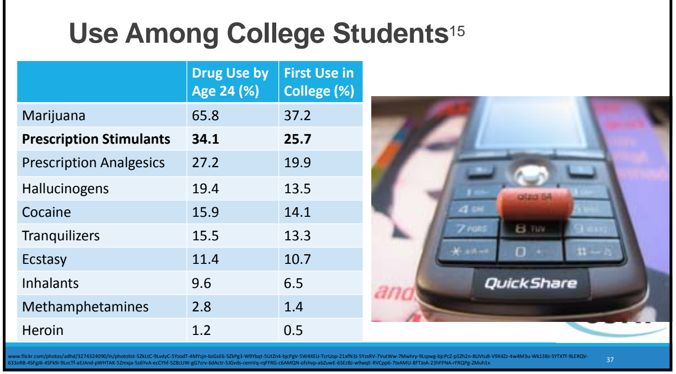
2015-2016 National Surveys on Drug Use and Health

- Main motivations for misuse
  - Help be alert of concentrate (56.34%)
  - Help Study (21.88%)
  - Get high or experiment (15.53%)
  - Lose weight (4.07%)
  - Other (2.17%)

Prevalence of Prescription Stimulants[14]

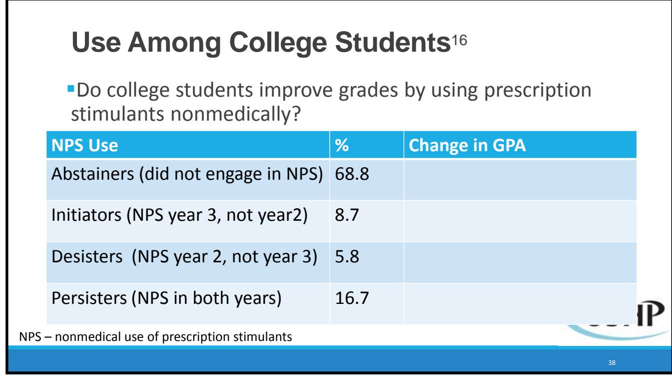
2015-2016 National Surveys on Drug Use and Health

- Source of misused prescription stimulants
  - Free from friend or relative (56.87%)
  - Bought or stole from friend or relative (21.77%)
  - One or more physicians (11.09%)
  - Drug dealer or stranger (4.33%)
  - Other (5.94%)



Use Among College Students[15]

	Drug Use by Age 24 (%)	First Use in College (%)
Marijuana	65.8	37.2
Prescription Stimulants	**34.1**	**25.7**
Prescription Analgesics	27.2	19.9
Hallucinogens	19.4	13.5
Cocaine	15.9	14.1
Tranquilizers	15.5	13.3
Ecstasy	11.4	10.7
Inhalants	9.6	6.5
Methamphetamines	2.8	1.4
Heroin	1.2	0.5

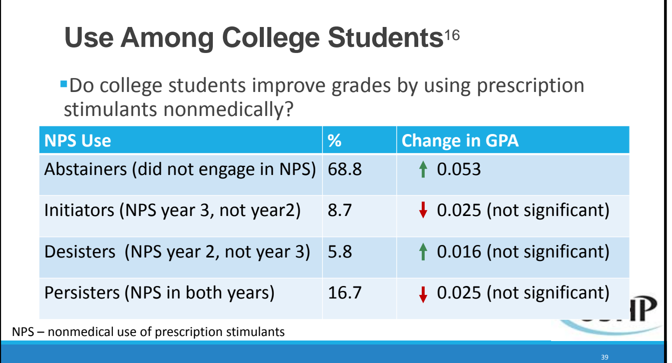


Use Among College Students[16]

- Do college students improve grades by using prescription stimulants nonmedically?

NPS Use	%	Change in GPA
Abstainers (did not engage in NPS)	68.8	
Initiators (NPS year 3, not year2)	8.7	
Desisters (NPS year 2, not year 3)	5.8	
Persisters (NPS in both years)	16.7	

NPS – nonmedical use of prescription stimulants



Use Among College Students[16]

- Do college students improve grades by using prescription stimulants nonmedically?

NPS Use	%	Change in GPA
Abstainers (did not engage in NPS)	68.8	↑ 0.053
Initiators (NPS year 3, not year2)	8.7	↓ 0.025 (not significant)
Desisters (NPS year 2, not year 3)	5.8	↑ 0.016 (not significant)
Persisters (NPS in both years)	16.7	↓ 0.025 (not significant)

NPS – nonmedical use of prescription stimulants

Stimulant Overdose[17]

- US poison centers reported 17,000 human exposures to ADHD medications in 2010 (20% in adults)
- Primary: neurologic and cardiovascular effects
  - Mydriasis
  - Tremor
  - Agitation
  - Hyperreflexia
  - Combative behavior
  - Confusion
  - hallucinations
  - Delirium
  - Anxiety
  - Paranoia
  - Tachycardia
  - Hypertension
  - Dysrhythmias

USHP

Legal Elements

Dispensing Requirements[18]

- Required Information for Schedule II Medications:
  - Date of issue
  - Patient's name and address
  - Practitioner's name, address, and DEA registration number
  - Drug name
  - Drug strength
  - Dosage form
  - Quantity prescribed
  - Directions for use
  - Signature of prescriber

Dispensing Requirements[19,20]

- May not exceed one-month's supply
- Must be dispensed within 30 days of issue or dispensing date
- Refills are not allowed
- Up to three prescriptions for the same CII may be issued at the same time
- Facsimile prescriptions require that the hard copy be presented at time of dispensing (exceptions for LTCFs and hospice)
- CII prescriptions "may be partially dispensed if the pharmacist is unable to supply the full quantity" – the remaining must be dispensed with in 72 hours, or a new prescription is required
- Must be issued for legitimate medical purpose – some occasions may require ICD-10 codes

43

Question (Technician)

Differentiate the legitimate and illegitimate elements of this prescription

General Health Center

Name: Addy Scatter DOB: 7/12/1982
Patient Address:
Date: 10/04/2018
Rx:

Focalin XR 20 mg tablet #60
take 1 tablet by mouth once daily

Refills: 2

Prescriber: Dr. Focus DEA: BS751385

44

Opioid legislation that could potentially translate to stimulants[21,22]

- HB127 – Prescribers shall check the controlled substance database when prescribing a CII or CIII opioid to a patient for the first time [Effective date 5/8/18]
- HB399 – Pharmacists shall apply warning labels to opiates and display pamphlets created by the Department of Health [Effective date 5/8/18]

45

Reporting[23,24]

- Controlled Substance Database
  - All pharmacies required to submit on a daily basis (real-time or batch)
- Theft or Loss
  - DEA form 106
  - For "theft of significant loss of any controlled substance"
  - Must be done within one business day of discovery
  - Encouraged to submit online
- Falsified Prescriptions
  - Notify prescriber
  - Notify law enforcement

46

Question (Pharmacist)

A new patient presents to your pharmacy for a prescription of Adderall XR 20 mg which was e-prescribed from Dr. Energizer. You run a DOPL report and find that 7 days ago the patient filled Concerta 27 mg at a different pharmacy, prescribed by Dr. Suspicion. Discuss with your neighbor how you would further investigate or handle the scenario.

47

Transitions of Care Pearls

- Do inpatients need to be continued on prescription stimulants? – Not typically
- Withdrawal is unlikely in patients taking prescribed therapeutic doses
- How soon are stimulants effective after resuming therapy? – "Immediately" (20-180 minutes)[12]

48

Question (Pharmacist and Technician)

Discuss in groups of 2 or 3 ways you have seen in your practice the appropriate use or misuse of stimulants in adults diagnosed with ADHD

49

Conclusions

- Historically a disease of children, ADHD increasingly being diagnosed and treated in adults
- Diagnostic criteria in DSM-V are recognizing adult ADHD
- Comorbid conditions make ADHD hard to diagnose and manage
- Stimulants are the mainstay of ADHD treatment
- Pharmacists and technicians play a vital role in the appropriate use and dispensing of Schedule II stimulant medications for ADHD

50

Final Thoughts and Questions

51

References

1. Melissa L. Danielson, Rebecca H. Bitsko, Reem M. Ghandour, Joseph R. Holbrook, Michael D. Kogan & Stephen J. Blumberg (2018) Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016, Journal of Clinical Child & Adolescent Psychology, 47:2, 199-212, DOI: 10.1080/15374416.2017.1417860
2. Sibley, M.H., Pelham Jr, W.E., Molina, B.S.G., Coxe, S., Kipp, H., Gnagy, E.M., & Lahey, B.B. (2014). The role of early childhood ADHD and subsequent CD in the initiation and escalation of adolescent cigarette, alcohol, and marijuana use. *Journal of Abnormal Psychology*, **123**, 362–374
3. Fayyad J., Sampson N. A., Hwang I., Adamowski T., Aguilar-Gaxiola S., Al-Hamzawi A., et al. . (2016). The descriptive epidemiology of DSM-IV Adult ADHD in the world health organization world mental health surveys. Atten. Defic. Hyperact. Disord. 9, 47–65. 10.1007/s12402-016-0208-3
4. Attention Deficit Hyperactivity Disorder. Overview. Last revised March, 2016. https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml. Accessed on 9/1/18.
5. Attention Deficit Hyperactivity Disorder. Overview. Last revised March, 2016. https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml. Accessed on 9/1/18.
6. Epstein JN, Loren REA. Changes in the definition of ADHD in DSM-5: subtle but important. Neuropsychiatry. 2013;3(5):455–458American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
7. American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
8. Jain R., Jain S., Montana B. (2017). Addressing Diagnosis and Treatment Gaps in Adults With Attention-Deficit/Hyperactivity Disorder. Prim Care Companion CNS Disord. 19(5):17nr02153
9. Katzman MA, Bilkey TS, Chokka PR, Fallu A, Klassen L. Adult ADHD and comorbid disorders: clinical implications of a dimensional approach. BMC Psychiatry (2017) 17:302. 10.1186/s12888-017-1463-3
10. Searight HR, Burke JM, Rottnek F. Adult ADHD: evaluation and treatment in family medicine. Am Fam Physician. 2000;62:2077–2086. 2091–2072.
11. Canadian ADHD Resource Alliance (CADDRA): Canadian ADHD Practice Guidelines, Fourth Edition, Toronto ON; CADDRA, 2018.
12. Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc.; 2018; September 5, 2018.

52

References

13. Anderson, K. N., Ailes, E. C., Danielson, M., Lind, J. N., Farr, S. L., Broussard, C. S., & Tinker, S. C. (2018). Attention-deficit/ hyperactivity disorder medication prescription claims among privately insured women aged 15–44 years—United States, 2003–2015. MMWR Morbidity and Mortality Weekly Report, 67, 66-70.
14. Compton WM, Han B, Blanco C, et al.: Prevalence and correlates of prescription stimulant use, misuse, use disorders, and motivations for misuse among adults in the United States. Am J Psychiatry 2018; 175:741–755
15. Arria AM, Caldeira KM, Allen HK, et al.: Prevalence and incidence of drug use among college students: an 8-year longitudinal analysis. Am J Drug Alcohol Abuse 2017; 43:711–718
16. Arria AM, Caldeira KM, Vincent KB, et al.: Do college students improve their grades by using prescription stimulants nonmedically? Addict Behav 2017; 65:245–249
17. Spiller HA, Hays HL, Aleguas A Jr. Overdose of drugs for attention-deficit hyperactivity disorder: Clinical presentation, mechanisms of toxicity, and management. CNS Drugs.2013;27:531–543
18. DEA Diversion Control Division. Prescriptions. https://www.deadiversion.usdoj.gov/faq/prescriptions.htm#rx-6. Accessed 9/8/18
19. DEA Diversion Control Division. Pharmacist's Manual Section IX-XIV. https://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/pharm_content.htm. Accessed 9/8/18
20. Utah Controlled Substances Act. https://le.utah.gov/xcode/Title58/Chapter37/C58-37_1800010118000101.pdf. Accessed 9/8/18
21. H.B. 127 Controlled Substance Database Act Amendments. https://le.utah.gov/~2018/bills/static/HB0127.html. Accessed 9/8/18
22. H.B. 399 Opioid Abuse Prevention and Treatment Amendments. https://le.utah.gov/~2018/bills/static/HB0399.html. Accessed 9/8/18
23. Utah Controlled Substances Database. https://dopl.utah.gov/programs/csdb/index.html. Accessed 9/8/18
24. DEA Diversion Control Division. Theft of Loss of Controlled Substances – DEA Form 106. https://www.deadiversion.usdoj.gov/21cfr_reports/theft/index.html. Accessed 9/8/18

53