ATTENTION TO STIMULANT MISUSE, ABUSE, AND DIVERSION:

Current Trends and Practice Strategies

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Objectives:

After the presentation, the participant will be able to…

- Participants will be able to describe current trends in misuse, abuse and diversion of ADHD stimulant medications
- Participants will be able to identify at least two reasons why stimulant medication is prone to abuse/diversion
- Participants will be able to determine at least two changes within their current practice that may be implemented to address abuse/diversion of stimulant medications

ADHD Diagnosis and Prevalence

Criteria

- Childhood/Developmental
- Symptoms are across domains
- Types
  - Inattention
  - Hyperactive
  - Combined
  - SUT
- Prevalence
  - 4-7% of the pediatric population
  - 60% of those diagnosed with persisting symptoms into adulthood
  - 42% increase in diagnoses of ADHD from 2003-2011

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Washington D.C.: 2013.
Mucci F, Carpita B, Pagni G, Vecchia AD, Bjedov S, Pozza A, Marazziti D. Lifetime evolution of ADHD treatment. J Neural Transm (Vienna). 2021 Jul;128(7):1085-1098. doi: 10.1007/s00702-021-02336-w. Epub 2021 May 15. PMID: 33993352.
Manos MJ, Giuliano K, Geyer E. ADHD: Overdiagnosed and overtreated, or misdiagnosed and mistreated? Cleve Clin J Med. 2017 Nov;84(11):873-880. doi: 10.3949/ccjm.84a.15051. PMID: 29173249.

Performance Enhancement

Greely H, Sahkaian B, Harris J, Kessler RC, Gazzaniga M, Campbell P, Farah MJ. Towards responsible use of cognitive-enhancing drugs by the healthy. Nature (2008) Vol 456; 702-705.

Definitions and Current Statistics

Misuse

- Use without a prescription or for other purposes than prescribed
- 43% College Age students reported misuse*
  - Taking more
  - Taking without a prescription
- Reason
  - 56% alert
  - 21.9% study
  - 15% get high or experiment
  - 4.1% Weight loss
- Adderall more prevalent in misuse

Abuse

- Using medications with the intent to become intoxicated or high
- 16 million users: .4 million had stimulant use disorders MPH is more likely to be abused—snorting and injecting
- Meta-analyses are consistent: ADHD was associated 50% likelihood to develop ETOH or drug use disorder than those without ADHD

Diversion

- 62% of college age students shared or sold stimulant medications at least once (higher percentage than that of pain, sleep other prescription substances)
- 14.7% of adolescents gave away medication (grades 7, 9, 10, 12)

*Benson K, Flory K, Humphreys KL, Lee SS. Misuse of stimulant medication among college students: a comprehensive review and meta-analysis. Clin Child Fam Psychol Rev. 2015 Mar;18(1):50-76. doi: 10.1007/s10567-014-0177-z. PMID: 25575768.

Faraone SV, et al. The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. Neurosci Biobehav Rev. 2021 Sep;128:789-818. doi: 10.1016/j.neubiorev.2021.01.022. Epub 2021 Feb 4. PMID: 33549739; PMCID: PMC8328933.

Clemow, D.B., & Walker, D.J. (2014). The Potential for Misuse and Abuse of Medications in ADHD: A Review. *Postgraduate Medicine, 126*, 64 - 81.

Malingering

- 20% of nonmedical users misrepresented symptoms to gain prescription
- 50% of those referred for medical evaluation exaggerated symptoms
  - More hyperactivity
  - Poor performances on cognitive tests and symptom validity measures

Demographic Data:

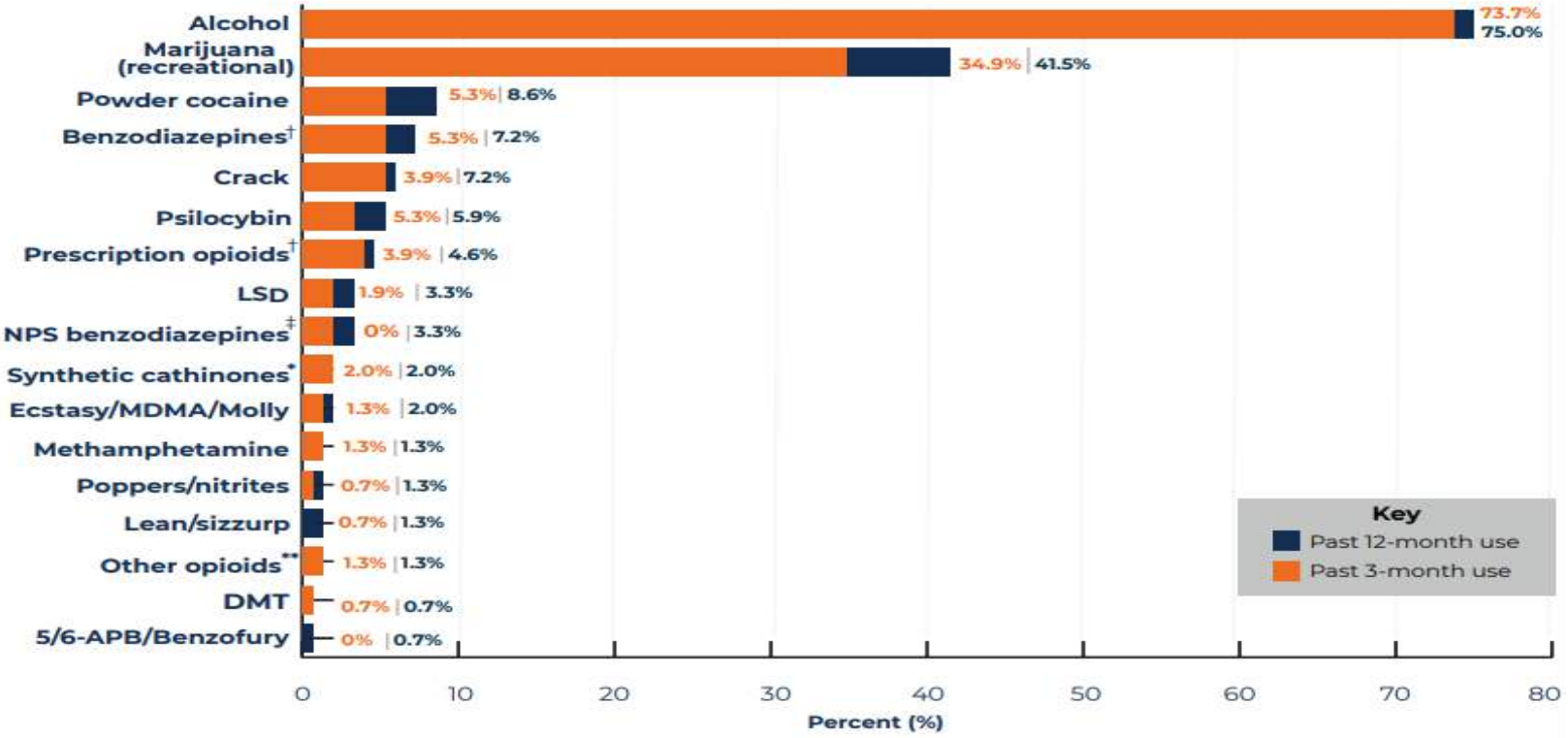
- White/Hispanic
- Insurance/Middle to Upper SES
- History of substance use (nicotine and etoh)
- No gender differences

Physician Data:

- 59% of Physicians suspected at least 1 patient to have misuse/malingering/diversion
- 10% suspected 5 or more
- Child and Adolescent Psychiatrist more likely to suspect than Child Neurologist or Pediatricians (Developmental/Behavioral)
- If you were a female DBP, you were less likely to suspect your patients.
- 35% of those surveyed (moderate and high prescribers) did not suspect their patients

Clemow, D.B., & Walker, D.J. (2014). The Potential for Misuse and Abuse of Medications in ADHD: A Review. *Postgraduate Medicine, 126*, 64 - 81.

The National Drug Early Warning System (NDEWS) Rapid Street Reporting (RSR) team visited Atlanta, GA, on January 28-30, 2022, for the RSR study. The RSR team conducted surveys within public spaces, such as sidewalks near downtown/college campuses, public parks, shopping mall areas, libraries, farmers' markets, and public transportation stops within Atlanta. Participants' (n=151) zip codes included 19 counties throughout the Atlanta Metro Area.

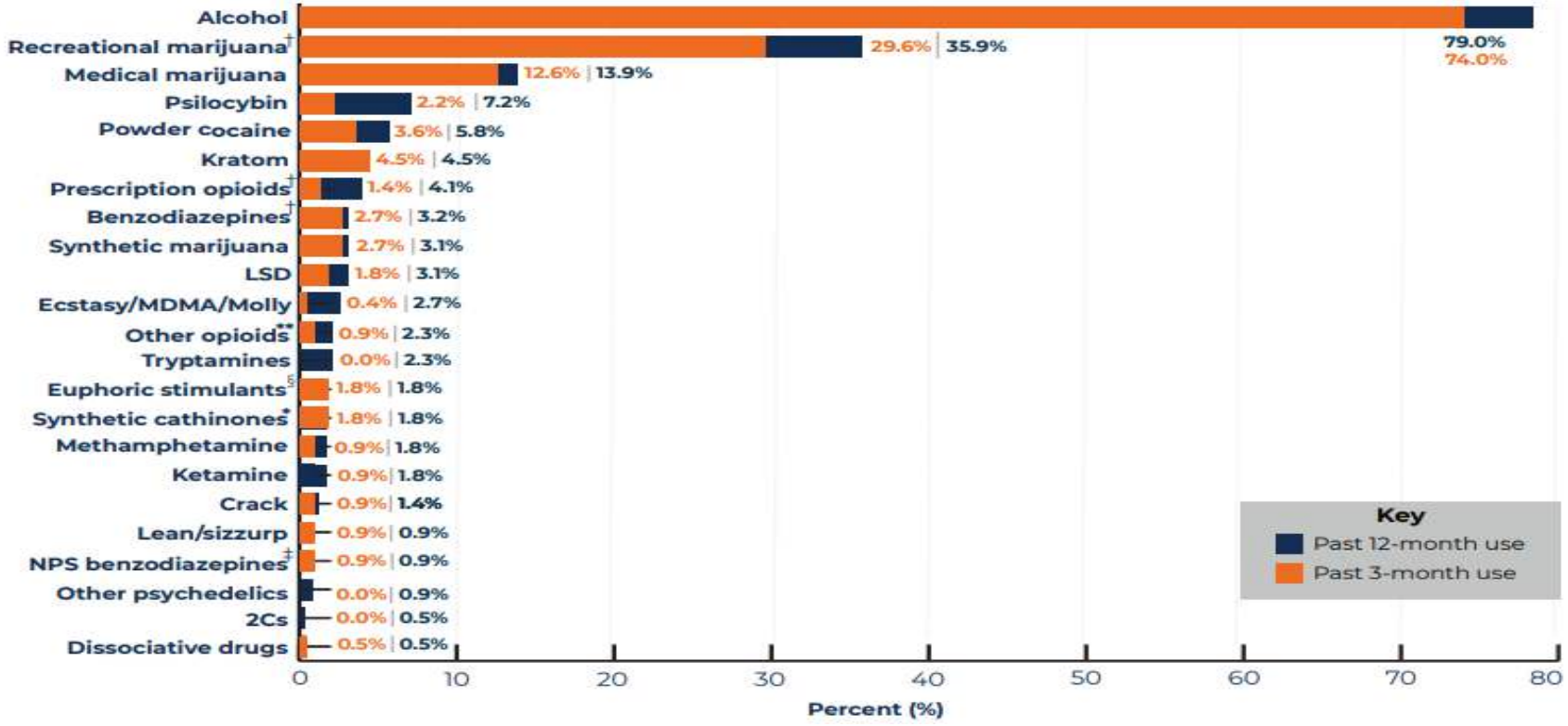


† Include non-medical use.
‡(NPS) benzodiazepines include: etizolam, pyramzolam, clonazolam, diclazepam, and flubromazepam.
* Synthetic cathinones also known as bath salts.
** Other opioids include fentanyl, heroin, U-47700/U4, pink and pinky.

Substance use in the past 12 months: Tampa, Florida
Survey dates: February 18-20, 2022
N= 223

Special Hotspot Alert Location

The National Drug Early Warning System (NDEWS) Rapid Street Reporting (RSR) team visited Tampa, FL on February 18-20, 2022. Tampa was chosen as a Hotspot location based on recent increases in drug-related 911 emergency medical services dispatches reported by biospatial.io. The RSR team conducted surveys in public spaces, including sidewalks near pedestrian walkways, downtown areas, public parks, shopping mall areas, skate parks, and nightlife areas such as bars and clubs within Tampa.



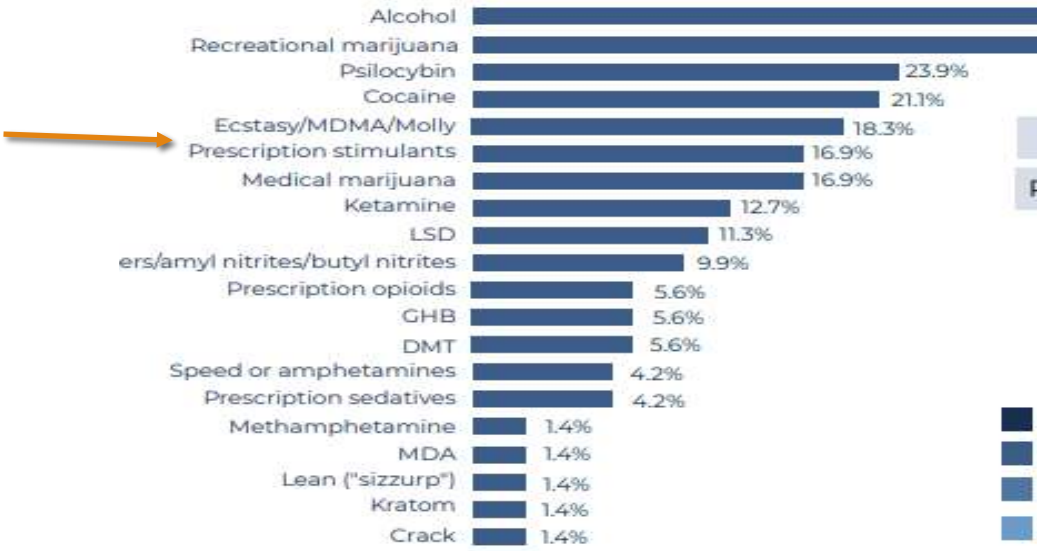
San Francisco Bay Area November 12-14, 2021

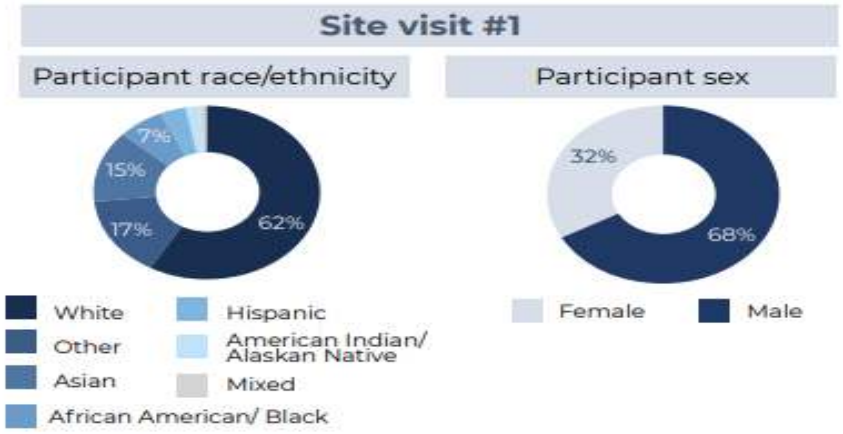
Report introduction

The NDEWS team has launched the Rapid Street Reporting (RSR) study, with the first weekend visit occurring November 12-14 in San Francisco. Delayed due to COVID-19, this national venue-intercept study to detect novel psychoactive substances will be conducted in each NDEWS sentinel site, along with five additional hotspots, throughout the next three years. Participant's zip codes were from: San Francisco, Contra Costa, Alameda, San Mateo, and Santa Clara counties. They were interviewed in public spaces, such as public parks, near bars/restaurants, shopping mall areas, and public transportation stops within San Francisco. The mean age of participants was 33.4 years (SD=12.4, range: 18-72), and participants reported an average of 15.6 years of education (SD=3.2, range: 5-24).

Substance use among participants within the past 3 months, surveyed over a weekend, from the Bay Area (n= 71). Data were reported during NDEWS San Francisco Rapid Street Reporting visit, November 12-13, 2021

*Participants reported the use of multiple substances





NDEWS is funded by the National Institute on Drug Abuse to the University of Florida (PI: Cottler, Co-Is: Goldberger, Nixon, Striley), New York University (Co-I: Palamar), and Florida Alantic University (Co-I: Barenholtz); Designed by Andrew Mike.

Mississippi non-fatal overdoses in the form of a monthly rapid alert report is an information sharing strategy to help communities reduce illicit and prescription drug misuse. Non-fatal overdose responses in hospital emergency departments and in communities by emergency medical services are reported per public safety district. Public health and public safety partners can review areas which may need additional resources to minimize further drug overdoses.

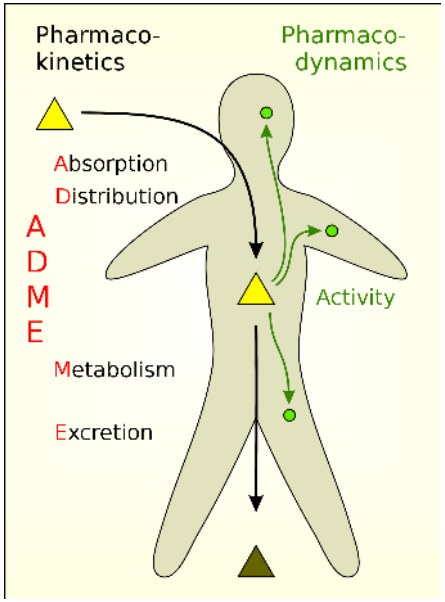
EMERGENCY DEPARTMENT (ED) VISITS

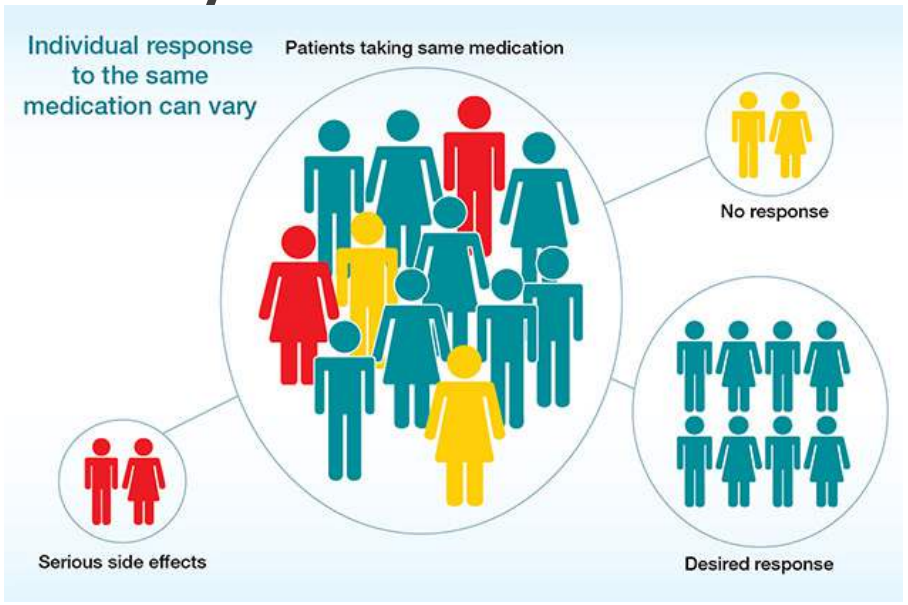
	Monthly Thresholds				January, 2023			
	All Drugs	Opioids	Heroin	Stimulants	All Drugs	Opioids	Heroin	Stimulants
Statewide	545	115	8	20	564	128	7	21
PSD 1	101	20	1	2	85	23	<5	<5
PSD 2	31	6	1	1	42	<5	<5	<5
PSD 3	61	13	0	2	67	17	<5	<5
PSD 4	43	4	0	1	50	7	<5	<5
PSD 5	36	4	0	1	37	<5	<5	<5
PSD 6	39	8	1	2	48	12	<5	<5
PSD 7	61	10	2	3	40	6	<5	<5
PSD 8	147	46	4	8	162	52	<5	9
PSD 9	26	4	1	1	33	<5	<5	<5

EMERGENCY MEDICAL SERVICES (EMS) RUNS

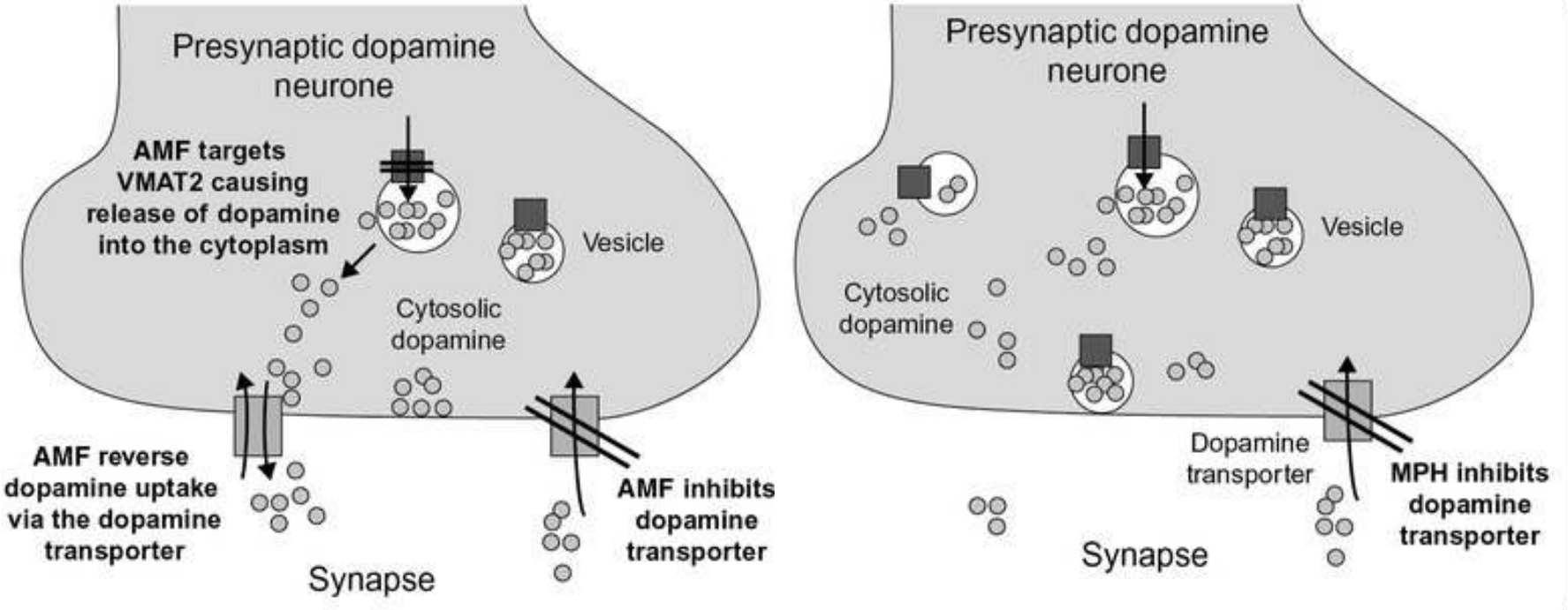
https://msdh.ms.gov/page/44,0,382,740.html
#overdose

WHY can medications for Attention Deficit-Hyperactivity Disorder become harmful/addictive?





2 Main Classes of ADHD Meds



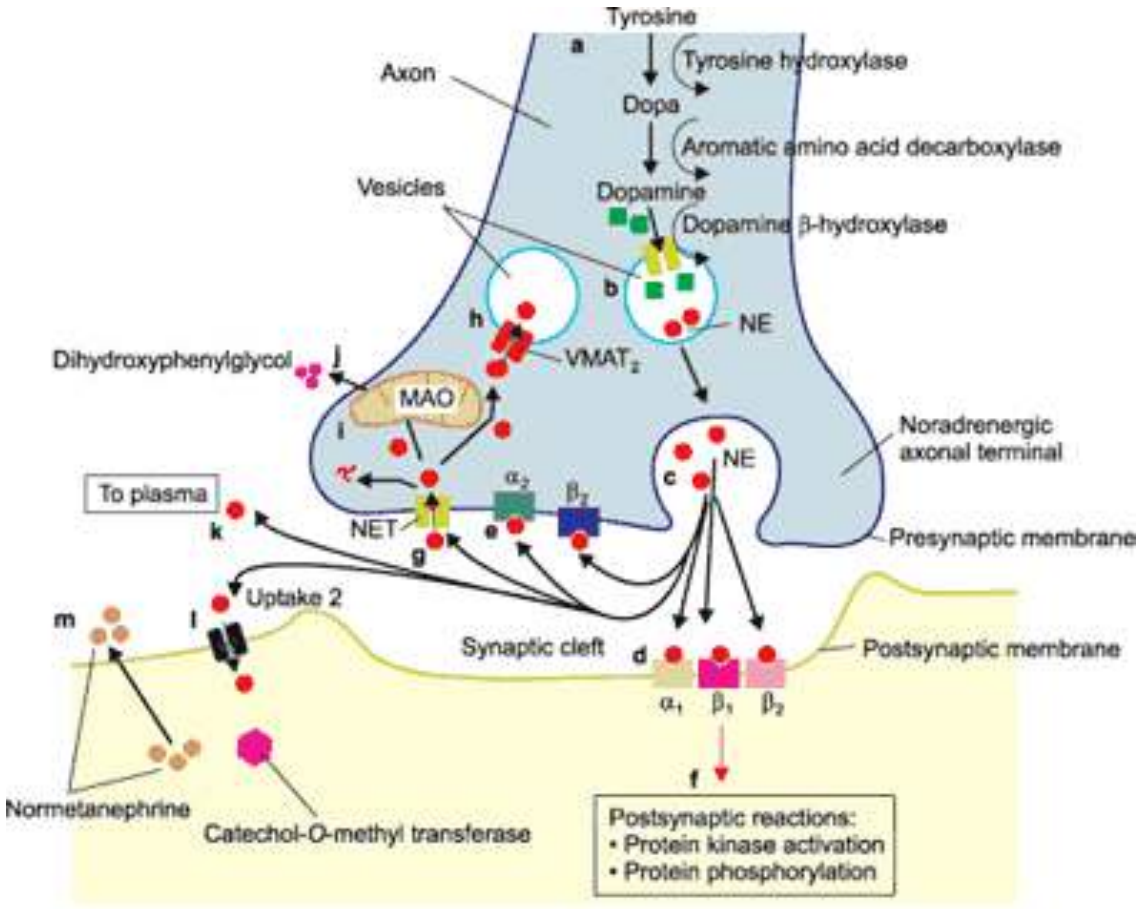
Class	Brand Name	Generic Name	Duration	Available Dosage Strengths
Amphetamine	Adderall ®	Amphetamine and dextroamphetamine mixed salts (tablet)	4–8 hours	5mg 7.5mg 10mg 12.5mg 15mg 20mg 30mg
	Adderall XR®	Amphetamine and dextroamphetamine mixed salts - extended-release (capsule)	8–12 hours	5mg 10mg 15mg 20mg 25mg 30mg
	Adzenys ER	amphetamine extended-release oral suspension (liquid)	9-12 hours	3.1mg/2.5ml 6.3mg/5ml 9.4mg/7.5ml 12.5mg/10ml 15.7mg/12.5ml 18.8mg/15ml
	Adzenys XR-ODT™	amphetamine extended-release (orally disintegrating tablet)	9–12 hours	3.1mg 6.3mg 9.4mg 12.5mg 15.7mg 18.8mg
	Desoxyn®	methamphetamine hydrochloride (tablet)	4-8 hours	5mg
	Dexedrine®	dextroamphetamine sulfate - extended-release (tablet)	6–9 hours	5mg 10mg 15mg
	Dyanavel® XR	amphetamine extended-release oral suspension (capsule)	8–12 hours	2.5mg/1ml 5mg/2ml 7.5mg/3ml 10mg/4ml 12.5mg/5ml 15mg/6ml 17.5mg/7ml 20mg/8ml
	Evekeo®	amphetamine sulfate (tablet)	4–6 hours	5mg 10mg
	Evekeo ODT ™	amphetamine sulfate - orally disintegrating (tablet)	4–6 hours	5mg 10mg 15mg 20mg
	Mydayis™	mixed salts of a single-entity amphetamine product - extended-release (capsule)	16 hours	12.5mg 25mg 37.5mg 50mg
	ProCentra®	dextroamphetamine sulfate (liquid)	4-8 hours	5mg/5ml
	Vyvanse®	lisdexamfetamine dimesylate (chewable tablet)	8-12 hours	10mg 20mg 30mg 40mg 50mg 60mg
	Vyvanse®	lisdexamfetamine dimesylate (capsule)	10–12 hours	10mg 20mg 30mg 40mg 50mg 60mg 70mg
	Zenzedi®	dextroamphetamine sulfate (tablet)	4–8 hours	2.5mg 5mg 7.5mg 10mg 15mg 20mg 30mg

Class	Brand Name	Generic Name	Duration	Available Dosage Strengths
Methylphenidate	Adhansia XR™	methylphenidate hydrochloride - extended-release (capsule)	16 hours	25mg 35mg 45mg 55mg 70mg 85mg
	Azstarys™	serdexmethylphenidate and dexmethylphenidate (capsule)	10+ hours	26.1mg/5.2mg 39.2mg/7.8mg 52.3mg/10.4mg
	Aptensio XR™	methylphenidate hydrochloride - extended-release (capsule)	7–8 hours	10mg 15mg 20mg 30mg 40mg 50mg 60mg
	Concerta®	methylphenidate hydrochloride - extended-release (tablet)	10–12 hours	18mg 27mg 36mg 54mg
	Cotempla™XR-ODT	methylphenidate extended-release (orally disintegrating tablet)	8–12 hours	17.3mg
	Daytrana®	methylphenidate (transdermal patch)	10–12 hours	10mg 15mg 20mg 30mg
	Focalin®	dexmethylphenidate hydrochloride (tablet)	3–5 hours	2.5mg 5mg 10mg
	Focalin XR®	dexmethylphenidate hydrochloride - extended-release (capsule)	12 hours	5mg 10mg 15m 20mg 25m 30mg 35mg 40mg
	Jornay PM™	methylphenidate hydrochloride - extended-release (capsule)	12+ hours	20mg 40mg 60mg 80mg 100mg
	Metadate CD®	methylphenidate hydrochloride - extended-release (capsule)	8 hours	10mg 20mg 30mg 40mg 50mg 60mg
	Metadate® ER	methylphenidate hydrochloride - extended-release (tablet)	8–12 hours	20 mg
	Methylin® Chewable	methylphenidate hydrochloride (chewable tablet)	3-5 hours	2.5mg 5mg 10mg
	Methylin® ER	methylphenidate hydrochloride - extended-release (tablet)	8 hours	10mg 20mg
	Methylin® Oral Solution	methylphenidate hydrochloride (liquid)	3–5 hours	5mg/5ml 10mg/5ml
	QuilliChew ER™	methylphenidate hydrochloride - extended-release (chewable tablet)	8–12 hours	20mg 30mg 40mg
	Quillivant XR®	methylphenidate hydrochloride - extended-release (liquid)	8, 10, and 12 hours	25mg/5ml (5mg/ml)
	Ritalin®	methylphenidate hydrochloride (tablet)	3–5 hours	5mg 10mg 20mg
	Ritalin-SR®	methylphenidate hydrochloride - sustained-release (tablet)	7–8 hours	20mg
	Ritalin LA®	methylphenidate hydrochloride - extended-release (capsule)	8 hours	10mg 20mg 30mg 40mg 60mg

Non-Stimulants

Class	Brand Name	Generic Name	Duration	Available Dosage Strengths
Norepinephrine reuptake inhibitor	Strattera®	atomoxetine hydrochloride (capsule)	24 hours	10mg 18mg 25mg 40mg 60mg 80mg 100mg
	Qelbree™	viloxazine extended-release (capsule)	24 hours	100mg 150mg 200mg
Alpha agonist	Kapvay®	clonidine hydrochloride - extended-release (tablet)	12–24 hours	0.1mg 0.2mg
	Intuniv®	guanfacine hydrochloride - extended-release (tablet)	12–24 hours	1mg 2mg 3mg 4mg

Non-Stimulants



Therapeutic Concepts

- Lack of response to one class does NOT preclude response to another
- Stimulants more effective treatment options vs. non-stimulants
- Children and adolescents respond better vs. adults
- In children and adolescents:
  - Amphetamines > efficacy
  - Methylphenidate > tolerability
- In adults:
  - Amphetamines > efficacy and tolerability

Different Formulations

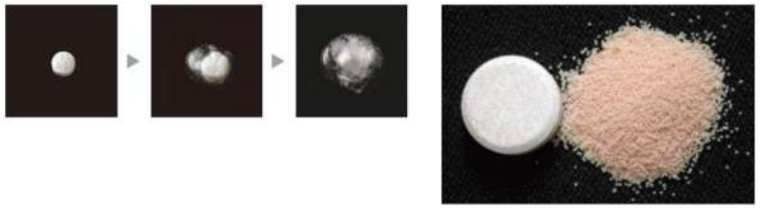
- Immediate Release
- Extended Release
- Liquids
- Orally disintegrating tablets (ODTs)
- Patches

What about once daily?

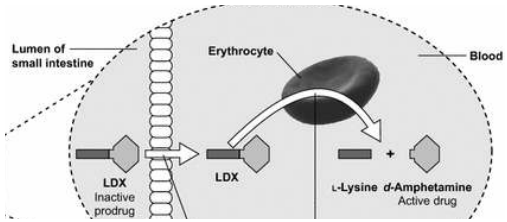
- Preferred treatments
- 8 – 12 hours of symptom control for most
  - 12 – 16 hours:
    - Mydayis (Mixed salts single entity amphetamine extended release)
    - Adhansia XR (Methylphenidate ER capsules)
    - Azstarys (Serdexmethylphenidate and dexmethylphenidate)
  - Almost 24 hours:
    - Jornay PM (Methylphenidate hydrochloride ER)
- Many products with IR + ER beads

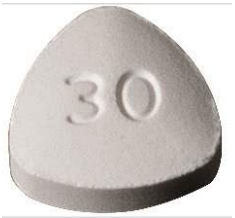
Trouble swallowing pills?

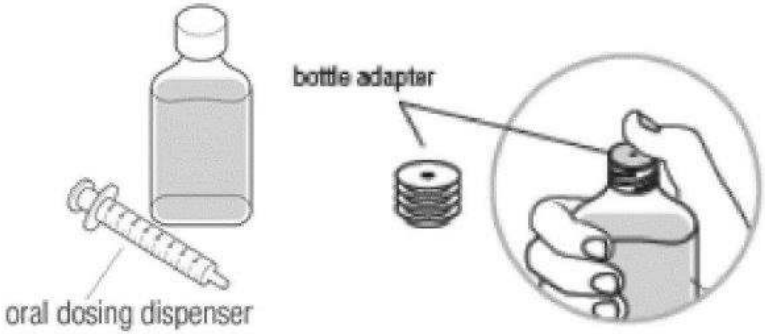
Oral disintegrating tablet technology



This is how tablets quickly disintegrate on contact with saliva







Adverse Reaction	Recommendation/ M anagement Strategy
Common	
Reduced appetite, weight loss	Give high-calorie meal when stimulant effects are low (at breakfast or at bedtime) or consider cyproheptadine at bedtime
Stomach ache	Administer stimulant on a full stomach; lower dose if possible
Insomnia	Give dose earlier in the day; lower the last dose of the day or give it earlier; consider a sedating medication at bedtime (guanfacine, clonidine, melatonin, or cyproheptadine)
Headache	Divide dose, give with food, or give an analgesic (eg, acetaminophen or
Rebound symptoms	Consider longer-acting stimulant trial, atomoxetine, or antidepressant
Irritability/jitteriness	Assess for comorbid condition (eg, bipolar disorder); reduce dosage; consider mood stabilizer or second-generation antipsychotic
Uncommon to Rare	
Dysphoria	Reduce dosage; reassess diagnosis; consider alternative therapy
Skin discoloration (chemical leukoderma)	Counsel regarding risk before using methylphenidate patch
Zombie-like state	Reduce dosage or change stimulant medication
Tics or abnormal movements	Reduce dosage; consider alternative medication
Priapism (painful erection)	Obtain medical assistance immediately; consider alternative treatment
Hypertension, pulse fluctuations	Reduce dosage; change medication
Hallucinations	Discontinue stimulant; reassess diagnosis; mood stabilizer and/or antipsychotic may be needed
Peripheral vasculopathy, including Raynaud's phenomenon	Obtain medical assistance if severe digital changes observed; consider reducing dosage or alternative medication

Personalized Pharmacotherapy

Methylphenidates

- Drug interactions vs. Amphetamines?
- Males vs. Females

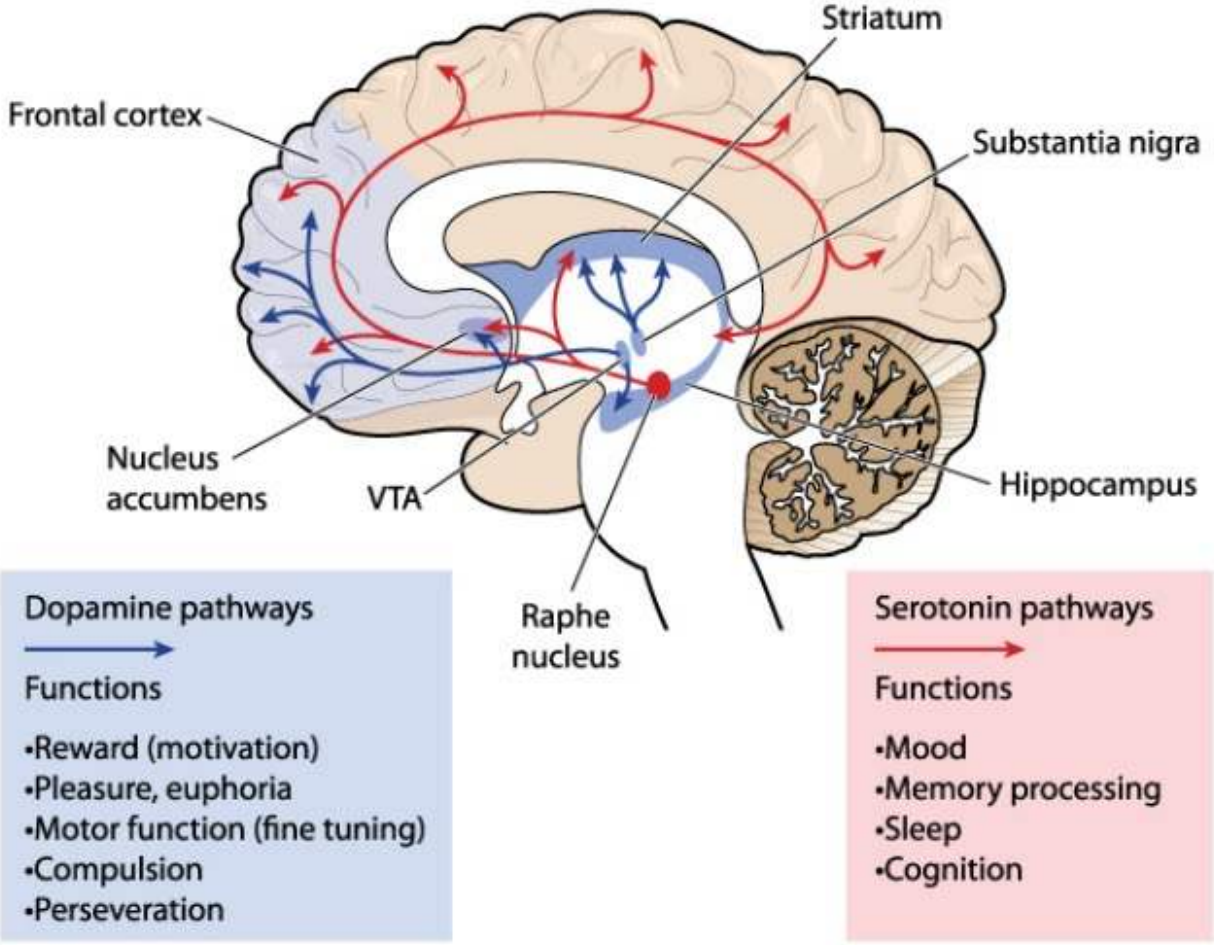
Amphetamines

- Bioavailability up to 4 – 8 x greater with Cyp2D6 inhibitor

Atomoxetine

- Dosing guideline for pediatric patients based on Cyp2D6 phenotype

Potential for Misuse and Abuse



Potential for Misuse and Abuse – Stimulants

MPH

- High school and college aged students more likely to report non-medical use of a stimulant than those in the upper 20's and 30's

AMP

- Potential for non-medical use – higher in adults vs adolescents
- Survey research – College students tend to misuse Amphetamines more than Methylphenidates
- Possibly due to AMP producing higher level of dopamine in the CNS reward centers vs. MPH

Potential for Misuse and Abuse – Non-stimulants

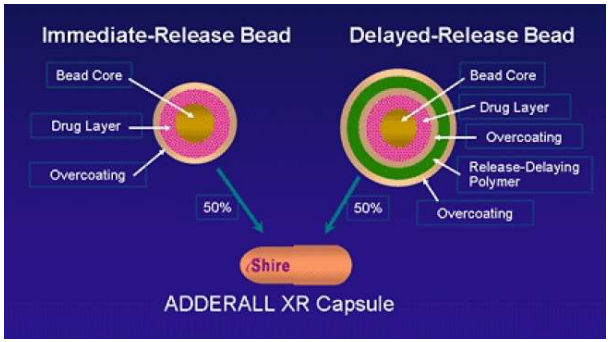
Guanfacine and Clonidine

- Alpha-2-receptor agonists for treating hypertension
- Increases brain executive functions without effects on dopamine levels or associated reward centers
- May have a role in reducing drug abuse potential

Atomoxetine

- Results in dose-dependent increase in both norepinephrine and dopamine in pre-frontal cortex
- No dopamine increase in the nucleus accumbens or in the striatum
- Lack of withdrawal symptoms

A Clinician's Guide



- Used to be a decision between short-acting amphetamines and methylphenidate

Adderall XR and Focalin XR

- SR formulations avoid need for mid-day dosing
- Beaded technology – IR brands plus beads coated with a pH-dependent layer to release 4 hours later in the less acidic small intestine

Mydayis – triple beads

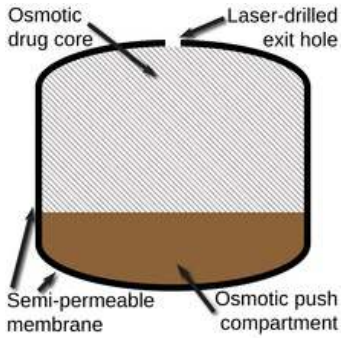
Aptensio and Adhansia – multi-layered release technology

- IR outer layer and an ER inner layer

A Clinician's Guide

Concerta

- Ongoing continuous release; osmotic pores in capsule



Vyvanse – prodrug

Transdermal option – Daytrana

Microparticle options – Contempla ODT and Adzenys ODT

- Quillivant and Quillichew (Methylphenidate)
- Dyanavel (Amphetamine)
  - Great for titrating in small increments for those sensitive to side effects
- Jornay PM – nighttime dosing

Practice Strategies to Mitigate Misuse and Diversion

Starts with Diagnosis
- Criteria
- Testing

Awareness and Education

Prescribing
- Long versus Short Acting
- Consider non-stimulants if concerned
- Pill Counts/Limiting number
- Medication Agreement

Use of Alternative Strategies—Behavioral/CBT

Questions

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