

REAL PSYCHIATRY

An Educational Experience Designed for and by APPs on the Frontline of Modern Practice

ATTENTION TO DETAIL OPTIMIZING ADHD TREATMENT ACROSS PATIENT LIFESPANS

— JANUARY 13, 2024 —



Project Overview

- Though estimates vary, up to ~8% of adults in the United States (US) may be affected by ADHD.¹ Yet, as most of these patients also have one or more comorbid psychiatric disorders, determining the optimal way to treat them can be challenging.
- Although stimulants are considered first-line treatment for ADHD, their potential for abuse, misuse, and addiction (schedule CII) has led to increasing prescribing restrictions and requirements.
- Coupled with recent shortages, likely related to growing demand and fears surrounding misuse, access has become broadly challenging.

ΟΒJΕCΤΙVΕ

To outline key challenges and potential solutions in the prescribing of stimulants for ADHD.



Faculty



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Psychiatric Nurse Practitioner Alay Psychiatry Pewaukee, WI



WHAT ADHD LOOKS LIKE ADULTS VS CHILDREN

0

Often more subtle!

Thought that only the minority of adults are diagnosed³

	CHILDREN ^{1,2} 6 SYMPTOMS IN EACH CATEGORY	ADULTS ^{1,2} (aged ≥17 years) 5 SYMPTOMS IN EACH CATEGORY
INATTENTION	Common (esp. in school children, adolescents) <i>May manifest as distractibility,</i> <i>not completing tasks</i>	More common May manifest as poor planning, difficulty with money/time
HYPERACTIVITY	 More common (esp. in preschoolers) May manifest as running or climbing where not appropriate 	Less common May manifest as restlessness, constant activity
IMPULSIVITY*	More common May manifest as interrupting, not waiting their turn, acting out	Common May manifest as thrill-seeking, quitting jobs, ending relationships, overspending

*Note: More common in males than females in children

1. Leffa DT et al. ADHD in children and adults: diagnosis and prognosis. In: Stanford SC, Sciberras, E, eds. New Discoveries in the Behavioral Neuroscience of Attention-Deficit Hyperactivity Disorder. Springer Nature; 2022:1-18. 2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th Ed. Text Revision. American Psychiatric Association; 2022. 3. Ginsberg Y et al. Underdiagnosis of attention-deficit/hyperactivity disorder in adult patients: a review of the literature. Prim Care Companion CNS Disord. 2014;16(3):PCC.13r01600.





COMORBID PSYCHIATRIC DISORDERS

BE ALERT! As many as 80% of adults with ADHD have at least one Psychomotor agitation Irritability coexisting psychiatric disorder MDD GAD · Enduring dysphoric mood or Exaggerated apprehension, anhedonia (≥ 2 weeks) worry (for > 6 months) Disturbed sleep, appetite Somatic GAD symptoms Fidgeting / Difficulty Suicide-related issues Nervousness / worrv completing tasks PREVALENCE Diminished energy levels **IN ADHD** Poor concentration. Difficulty with attention, ADHD attention, memory concentration/focus 44.65% GAD: Impaired social, Distractibility, agitation Bipolar SUD occupational, or · Enduring dysphoric or euphoric · Pathologic pattern of substance recreational functioning 42.28% mood use with social consequences MDD: Excessive talking Insomnia Physiologic, psychologic · Delusions, grandiosity tolerance & withdrawal Excessive involvement in pleasurable activities 35.12% SUD: Episodic changes from baseline Hyperactivity Mood swings 14.29% BD: Fidgeting/ restlessness

Katzam et al. Common psychiatric and metabolic comorbidity of adult attention-deficit/hyperactivity disorder • GAD: generalized anxiety disorder
 MDD: bipolar disorder • GAD: generalized anxiety disorder
 MDD: major depressive disorder • SUD: substance abuse disorder

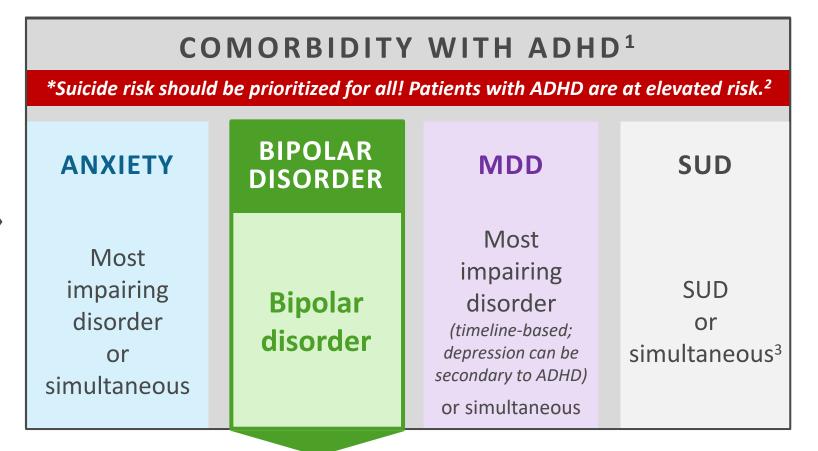




COMORBID DISORDERS WITH ADHD WHAT TO TREAT FIRST: EVOLVING VIEW

In general, * when should you consider treating ADHD in adults when it coexists with other psychopathologies?





Mood stabilization is key!

1. Katzman MA et al. *BMC Psychiatry*. 2017;17(1):302. **2.** Fitzgerald C et al. Suicidal behaviour among persons with attention-deficit hyperactivity disorder. The British Journal of Psychiatry, 2019. 215(4), 615-620. **3.** Kooij J et al. Updated European Consensus Statement on diagnosis and treatment of adult ADHD. European Psychiatry, 2019: 56;14-34.





TREATMENT GUIDELINES FOR ADULT ADHD

EUROPEAN,¹ UK,² AND CANADIAN³ CONSENSUS*

FIRST LINE: STIMULANTS

± psychotherapy and/or behavioral therapy

SECOND LINE: NONSTIMULANTS

Atomoxetine, viloxazine ER

THIRD LINE: OFF LABEL

Bupropion,⁴ modafinil, tricyclic antidepressants

MILLIONS of adults
 (+ millions of children and adolescents) have ADHD

That's **A LOT** of people who may need stimulants!

*There are no US ADHD treatment guidelines for adults

1. Kooij J et al. Updated European Consensus Statement on diagnosis and treatment of adult ADHD. European Psychiatry, 2019: 56;14-34. 2. NICE guideline: Attention deficit hyperactivity disorder: diagnosis and management. Available at https://www.nice.org.uk/guidance/ng87/chapter/Recommendations#managing-adhd. Updated September 2019. Accessed 11/29/23 3. Canadian ADHD Resource Alliance. Canadian ADHD Practice Guidelines 4.1 Edition. 2020. Available at https://adhdlearn.caddra.ca/wp-content/uploads/2022/08/Canadian-ADHD-Practice-Guidelines-4.1-January-6-2021.pdf. Accessed 11/29/23. 4. Clark A et al. Bupropion mediated effects on depression, attention deficit hyperactivity disorder, and smoking cessation. *Health Psychol Res.* 2023;11:81043.





THE CHALLENGES OF PRESCRIBING SHORTAGES

97% of independent pharmacies reported shortages in ADHD medications in 2023!

PBSO NEWS HOUR A 'perfect storm' led to an ADHD medication shortage. Here's why

Health Jul 18, 2023 2:04 PM EDT

St NEWS

ADHD medications still in shortage, frustrating patients and doctors

M health Life, But Better Fitness Food Sleep Mindfulness Relationships

ADHD drug shortage stresses families during back-to-school season

1. National Community Pharmacists Association. Report for Survey on Drug Shortages and Staffing, January 2023. Available at https://ncpa.org/sites/default/files/2023-02/drug-shortage-survey-23.pdf. Accessed 11/29/23.

Ryan Haight Online Pharmacy Act of 2008

FDA U.S. FOOD & DRUG

FDA Announces Shortage of Adderall

TABLE. Expected Shortages of Amphetamine Mixed Salts³

- Amphetamine mixed salts tablets C-II 5 mg, 100 (NDC 13107-068-01) Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 7.5 mg, 100 (NDC 13107-069-01)
 Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 10 mg, 100 (NDC 13107-070-01) Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 15 mg, 100 (NDC 13107-072-01) Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 20 mg, 100 (NDC 13107-073-01) Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 30 mg, 100 (NDC 13107-074-01) Estimated availability: December 2023
- Amphetamine mixed salts tablets C-II 5 mg, 100 (NDC 70010-111-01) Estimated availability: September 2023
- Amphetamine mixed salts tablets C-II 15 mg, 100 (NDC 70010-115-01) Estimated availability: September 2023
- Amphetamine mixed salts tablets C-II 5 mg, 100 (NDC 72516-016-01) Unavailable; estimated recovery: end of August 2023
- Amphetamine mixed salts tablets C-II 10 mg, 100 (NDC 72516-014-01) Unavailable; estimated recovery: end of August 2023
- Amphetamine mixed salts tablets C-II 15 mg, 100 (NDC 72516-013-01) Unavailable; estimated recovery: end of August 2023
- Amphetamine mixed salts tablets C-II 20 mg, 100 (NDC 72516-012-01) Unavailable; estimated recovery: end of August 2023
- Amphetamine mixed salts tablets C-II 30 mg, 100 (NDC 72516-011-01) Unavailable; estimated recovery: end of August 2023





AUDIENCE POLL

In general, how challenging have you found it to prescribe stimulants for your patients with ADHD in the past 5 years?

- a) Very challenging
- b) Somewhat challenging
- c) Not very challenging
- d) Easy

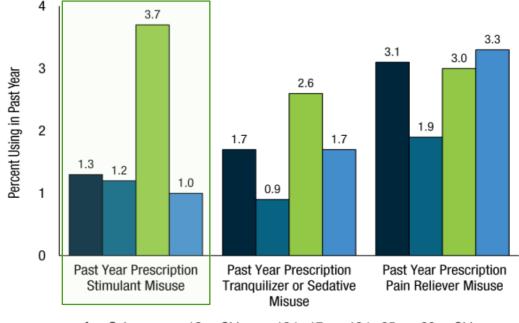




MORE CHALLENGES OF PRESCRIBING ABUSE AND MISUSE

- More than 50% of misused ADHD medications are gifted from family and friends¹
- Studies suggest that persons who misuse medical stimulants may be at greater risk of using other substances such as cocaine^{2,3}

PAST YEAR PRESCRIPTION MISUSE⁴



Age Category: ■ 12 or Older ■ 12 to 17 ■ 18 to 25 ■ 26 or Older

POTENTIAL FOR ABUSE AND MISUSE MAKES REGULATIONS AND ACCESS STRICTER

1. Compton WM 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 Aug 1;175(8):741-755. 2. Shearer RD et al. Associations between prescription and illicit stimulant and opioid use in the United States, 2015-2020. J Subst Abuse Treat. 2022;143:108894. 3. Teter CJ et al. Nonmedical Use of Prescription Stimulants Among US High School Students to Help Study: Results From a National Survey. J Pharm Pract. 2020;33(1):38-47. 4. SAMHSA. Results from the 2021 National Survey on Drug Use and Health: Graphics from the Key Findings Report. Available at https://www.samhsa.gov/data/sites/default/files/reports/rpt39443/2021 NNR figure slides.pdf. Accessed 12/1/2023





MORE CHALLENGES OF PRESCRIBING RISK OF COUNTERFEIT MEDS

Lack of access could prompt patients to look elsewhere



HOW CAN WE HELP PATIENTS GET THE MEDICATIONS THAT THEY NEED?

1. US Drug Enforcement Administration (DEA). One Pill Can Kill. Available at https://www.dea.gov/onepill. Accessed November 3, 2023.





ONE STEP FORWARD DEA UPDATE

Revised Regulation Allows DEA-Registered Pharmacies to Transfer Electronic Prescriptions at a Patient's Request

DEA Headquarters Division - Public Information Office

"At a patient's request, a DEA-registered retail pharmacy can now transfer an e-prescription for a controlled substance (schedules II-V) to another DEA-registered retail pharmacy"

Previously, patients had to go through their practitioner to cancel/re-issue prescriptions (taxing!)



Now it's easier to switch to a pharmacy that carries the med you want **ONE BARRIER SOLVED!**

1. DEA. Revised Regulation Allows DEA-Registered Pharmacies to Transfer Electronic Prescriptions at a Patient's Request. September 1, 2023. Available at https://www.dea.gov/stories/2023/2023-09/2023-09-01/revised-regulation-allows-dea-registered-pharmacies-transfer. Accessed 12/1/23





AUDIENCE POLL

In addition to the clinical interview, which of the following, if any, do you use routinely to evaluate adults with/suspected of ADHD? (SELECT ONE)

- a) Subjective scale (e.g., ADHD Self-Report scale [ASRS])
- b) Objective scale (e.g., ADHD Rating Scale [ADHD-RS])
- c) Objective test (e.g., computerized testing)
- d) A combination of the above
- e) None of the above





WHAT ELSE CAN WE DO? DOCUMENTATION WITH ASSESSMENTS

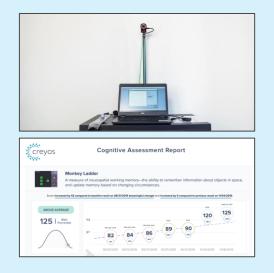
INSURANCE NEEDS TO SEE THE APPROPRIATE DIAGNOSIS AND PROGRESS

OBJECTIVE





COMPUTERIZED (e.g., QbTest, Creyos)^{2,3}



SUBJECTIVE

(e.g., Adult Self-Report Scale [ASRS])⁴

Pa	tient Name:	Today'	s Date:			
Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.		Never	Rarely	Sometimes	Often	Very often
1.	How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2.	How often do you have difficulty getting things in order when you have to do a task that requires organisation?					
з.	How often do you have problems remembering appointments or obligations?					
4.	When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5.	How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6.	How often do you feel overly active and compelled to do things, like you were driven by a motor?					

1. Anbarasan D et al. Screening for adult ADHD. *Curr Psychiatry Rep.* 2020;22(12):72. 2. QbTest: Rethinking the ADHD care pathway. Qbtech. Accessed October 26, 2023. https://www.qbtech.com/adhd-tests/qbtest/ 3. Agha S et al(. Young Adult ADHD Symptoms in the General Population and Neurocognitive Impairment. Journal of Attention Disorders, 2024. 28(1), 89-98. 4. Kessler RC et al. The WHO Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med.* 2005;35(2):245-256.





WHAT ELSE CAN WE DO? MONITOR FOR ABUSE, MISUSE, AND DIVERSION

PROVIDE EVIDENCE THAT THE MEDS ARE NOT BEING ABUSED

COMMON TYPES OF TESTING

- Oral
- Urine
 - Can include DNA testing
 - NOTE: Becoming easy to fake!
 Synthetic urine test strips may be important¹
- Blood: more precise
 - PMx testing can measure levels of medication in the system²

 PHARMACIES
 Image: Constraint of the state design of the stat

PRESCRIPTION DRUG MONITORING PROGRAM

MY PRACTICE: BLOOD TEST RANDOMLY!

1. Kim VJ et al. Can synthetic urine replace authentic urine to "beat" workplace drug testing?. *Drug Test Anal.* 2019;11(2):331-335. **2.** Sutherland J et al. Managing Psychotropic Medications in Complex, Real-World Patients Using Comprehensive Therapeutic Drug Monitoring. *ACS Chem Neuro*, 2017. 8 (8), 1641-1644.





AUDIENCE POLL



How often do you prescribe immediate release (IR) formulations of stimulants in ADHD?

- a) Always
- b) Often
- c) Sometimes
- d) Rarely
- e) Never





AUDIENCE POLL

On average, do you feel generic stimulants have the same clinical effect as brand name agents?

- a) Yes
- b) No
- c) It depends
- d) I do not know/I am unsure.





CONSIDERATIONS IN MEDICATION SELECTION REFRESH! THE BASICS OF DRUG MECHANICS

GENERIC:

+/- 20% to 25% of the molecule¹

BIOEQUIVALENT: ----

80% to 125% of the molecule¹

Bioavailability = the extent and rate to which an active drug ingredient/moiety is absorbed and becomes available at the site of action

• Predictive of clinical outcomes^{1,2}

Fundamental bioequivalence assumption: *"If two drug products are bioequivalent, they are generally therapeutically equivalent"*¹

APPROVAL OF GENERICS HINGES ON BIOEQUIVALENCE TESTING¹ AND GOOD MANUFACTURING PRACTICE (GMP)³

1. Chow SC. Bioavailability and bioequivalence in drug development. *Wiley Interdiscip Rev Comput Stat.* 2014;6(4):304-312. **2.** Uhl K et al. How the FDA ensures high-quality generic drugs. *Am Fam Physician.* 2018;97(11):696-697. **3.** FDA. Facts About the Current Good Manufacturing Practices (CGMP). Available at https://www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-good-manufacturing-practices-cgmp. Accessed 12/01/23.





CONSIDERATIONS IN MEDICATION SELECTION REFRESH! THE BASICS OF DRUG MECHANICS

GENERIC: +/- 20%-2 the molec BIOEQUI

80-125% o molecule²

THE PROBLEM WITH ASSUMPTIONS

- 80% to 125% is a big range!
- The FDA requires *roughly* the same blood levels of a drug and allows variation in binders, chemicals, fillers, colors, etc.²
 - Risk of lower blood levels: decreased efficacy
 - Risk of higher blood levels: more side effects

ΑΡΡΙ

ND GOOD MANUFACTURING PRACTICE (GMP)²⁶

1. Chow SC. Bioavailability and bioequivalence in drug development. *Wiley Interdiscip Rev Comput Stat.* 2014;6(4):304-312. 2. Uhl K et al. How the FDA ensures high-quality generic drugs. *Am Fam Physician.* 2018;97(11):696-697. 3. FDA. Facts About the Current Good Manufacturing Practices (CGMP). Available at https://www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-good-manufacturing-practices-cgmp. Accessed 12/01/23.

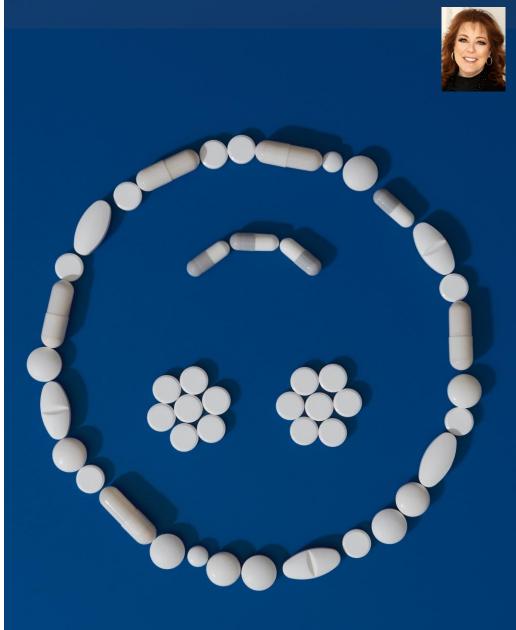


BRAND TO GENERIC CLINICAL IMPLICATIONS

Lower cost of medications

- Coupon codes of brand medications
- X Patient Assistance Program
- Cost-effective out-of-pocket pricing for commercially insured clients



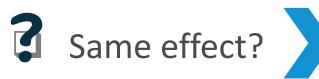




BRAND TO GENERIC CLINICAL IMPLICATIONS

Lower cost of medications

- Coupon codes of brand medications
- X Patient Assistance Program
- Cost-effective out-of-pocket pricing' for commercially insured clients



Switching to a generic may impact treatment success and/or safety







REFRESH! TYPES OF ADHD STIMULANTS

AMPHETAMINE



Main Formulation: Classic Coca Cola Offshoots: Diet Coke, Coke Zero, Vanilla Coke, etc...

METHYLPHENIDATE



Main Formulation: PepsiOffshoots: Diet Pepsi, Pepsi Zero Sugar, Cherry Pepsi, etc...





REFRESH! DIFFERENCES BETWEEN STIMULANTS

AMPHETAMINE



MORE POTENT

METHYLPHENIDATE









AUDIENCE POLL

Do you have a preferred delivery modality for stimulant medications that you prescribe?

a) Prodrug

- b) Ion exchange
- c) Multi-layered bead
- d) Osmotic pressure release
- e) Transdermal
- f) Whichever is cheapest
- g) I am unfamiliar with which agents correspond to these modalities





AUDIENCE POLL

Which of the following is/are your most commonly prescribed (or attempted to be prescribed) stimulant(s)? (SELECT ONE)

- a) Traditional IR formulations of either molecule (amphetamine, methylphenidate)
- b) Traditional ER/XR formulations of either molecule
- c) Adderall XR or Focalin XR
- d) Adzenys ER/XR or Dyanavel
- e) Azstarys
- f) Concerta
- g) Daytrana
- h) Quillivant/QuilliChew
- i) Vyvanse
- j) Other





MODERN LONG-ACTING DELIVERY METHODS

	METHOD FUNCTION		NTS
METHOD	FUNCTION	AMPHETAMINE	METHYLPHENIDATE
Prodrug	 Requires in vivo conversion Designed to be inactive until reaching target (Vyvanse: bloodstream, Azstarys: lower GI) 	Vyvanse	Azstarys
Ion exchange	exchange • Type 1: Coated resin complex -> not pH-dependent • Not affected by food, drink, PPIs • Can be crushed, swallowed, chewed • Type 2: Microparticles with cation exchange resin • pH-sensitive film, selective release in the SI		COATED RESIN Quillivant XR, QuilliChew ER MICROPARTICLES Cotempla XR-ODT
Multi-layered bead	pH-sensitive beads: as beads pass the GI tract, the drug is released	Mydayis, Adderall XR	Jornay PM, Focalin XR, Ritalin LA, Metadate CD, Aptensio XR
OROS (osmotic pressure release) Expansion of osmotic pump when water permeates membrane; partial, immediate release, with subsequent gradual release		N/A	Concerta
Transdermal	Permeates skin with controlled release into bloodstream	Xelstrym	Daytrana

1. Childress AC et al. An update on the pharmacokinetic considerations in the treatment of ADHD with long-acting methylphenidate and amphetamine formulations. *Expert Opin Drug Metab Toxicol*. 2019;15(11):937-974.

CD: controlled-delivery; ER, XR: extended-release; LA: long-acting; ODT: orally disintegrating tablet





MODERN LONG-ACTING DELIVERY METHODS

METHOD		A G E N T S		
ΜΕΤΗΟΟ	FUNCTION	AMPHETAMINE	METHYLPHENIDATE	
Prodrug	 Prodrug Prodrug Requires in vivo conversion Designed to be inactive until reaching target (Vyvanse: bloodstream, Azstarys: lower GI) 		Azstarys	
Ion exchange - Not affected by food, drink, PPIs Dyanavel XR Quillivar Ion exchange - Can be crushed, swallowed, chewed MICROPARTICLES MIC • Type 2: Microparticles with cation exchange resin Adzenys ER MIC		COATED RESIN Quillivant XR, QuilliChew ER MICROPARTICLE S Cotempla XR-ODT		
Multi-layered beadpH-sensitive beads: as beads pass the GI tract, the drug is releasedMydayis, Adderall XR				

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SER/DEXMETHYLPHENIDATE PRODRUG

PARTICIPANTS

• 23 healthy volunteers aged 18 to 55 years

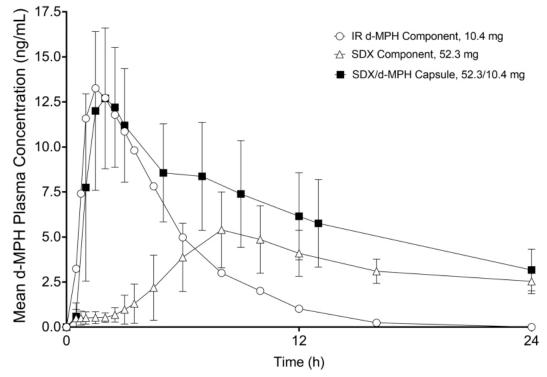
STUDY DESIGN

- Crossover fasted multi-dose design of serdexmethylphenidate/dexmethylphenidate (SDX/d-MPH) with a 96-hour washout period
- Followed by 4 consecutive uniform dosing days

RESULTS

- All doses saw a rapid rise and gradual decline in d-MPH
- SDX reached steady state after 1st dose, D-MPH before the 3rd dose
- May optimize symptom control from early morning to early evening

SDX/D-MPH COMPOSITE PK PROFILE



ONCE-A-DAY DOSING WITH BOTH IMMEDIATE AND DELAYED RELEASE (NO TROUGHS!)

1. Braeckman R et al. Dose Proportionality and Steady-State Pharmacokinetics of Serdexmethylphenidate/Dexmethylphenidate, a Novel Prodrug Combination to Treat Attention-Deficit/Hyperactivity Disorder. J Child Adolesc Psychopharmacol. 2022 Jun;32(5):288-295.





MODERN LONG-ACTING DELIVERY METHODS

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METHOD	FUNCTION	AMPHETAMINE	METHYLPHENIDATE
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Multi-layered bead	pH-sensitive beads: as beads pass the GI tract, the drug is released	Mydayis, Adderall XR	Jornay PM, Focalin XR, Ritalin LA, Metadate CD, Aptensio XR

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AMPHETAMINE ER ION EXCHANGE

PARTICIPANTS

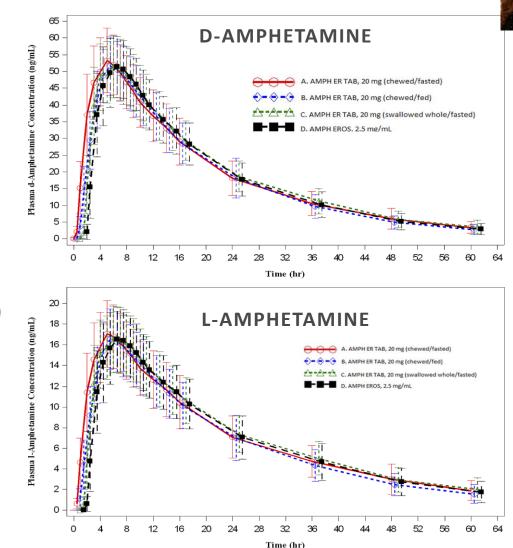
• 32 healthy volunteers aged 18 to 55 years

STUDY DESIGN

- Randomized to 1 dose of amphetamine ER (AMPH ER)
 - 20 mg tablets (TAB) swallowed (fasted) or chewed (fed/fasted)
 - 20 mg oral suspension (EROS) (fasted)

RESULTS

- Single doses of all formulations demonstrated comparable bioavailability
- No apparent food effect



MEAN PLASMA CONCENTRATIONS OVER TIME

STRONG EFFECT, ONCE-A-DAY DOSING, NO HINDRANCE FROM FOOD OR FORM!

1. Pardo A et al. Single-dose pharmacokinetics of amphetamine extended-release tablets compared with amphetamine extended-release oral suspension. *CNS Spectr*. 2020;25(6):774-781.





MODERN LONG-ACTING DELIVERY METHODS

METHOD		A G E N T S	
ΜΕΤΗΟΟ	FUNCTION	AMPHETAMINE	METHYLPHENIDATE
Prodrug	 Requires in vivo conversion Des Intil reaching target (Vyvanse: bloc 11 12 1 wer GI) 	Vyvanse	Azstarys
lon exchange	Food does not affect all but it prolongs the T-m (5.2 hours fasted to 7.7 hours th cation exchange resin	ax by 2.5 hours!	CODED RESIN Quillivant XR, QuilliChew ER MICROPARTICLE S Cotempla XR-ODT
Multi-layered bead	pH-sensitive beads: as beads pass the GI tract, the drug is released	Mydayis, Adderall XR	Jornay PM, Focalin XR, Ritalin LA, Metadate CD, Aptensio XR
OROS (osmotic pressure release)	Expansion of osmotic pump when water permeates membrane; partial, immediate release, with subsequent gradual release	N/A	Concerta

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	 Type 1: Coded resin complex -> not pH-dependent Not affected by food, drink, PPIs 		CODED RESIN Quillivant XR, QuilliChew EF	
Ion exchange	UPDATE [10-17-2016 and 11-4-16] FDA proposes to wi	thdraw approval of two	Another	
	generic versions of Concerta (methylphenidate hydro	chloride)	discontinued in 2023 ²	
Aulti-layered bead				
Aulti-layered bead OROS (osmotic pressure release)	generic versions of Concerta (methylphenidate hydro		in 2023² Jornay PM, Focalin XR, Ritalin LA, Metadate CD,	

1. Childress AC et al. An update on the pharmacokinetic considerations in the treatment of ADHD with long-acting methylphenidate and amphetamine formulations. *Expert Opin Drug Metab Toxicol*. 2019;15(11):937-974. 2. ASHP. Methylphenidate Extended Release Oral Presentations. Available at https://www.ashp.org/drug-shortages/current-shortages/drug-shortage-detail.aspx?id=896&loginreturnUrl=SSOCheckOnly

CD: controlled-delivery; ER, XR: extended-release; LA: long-acting; ODT: orally disintegrating tablet





AUDIENCE POLL

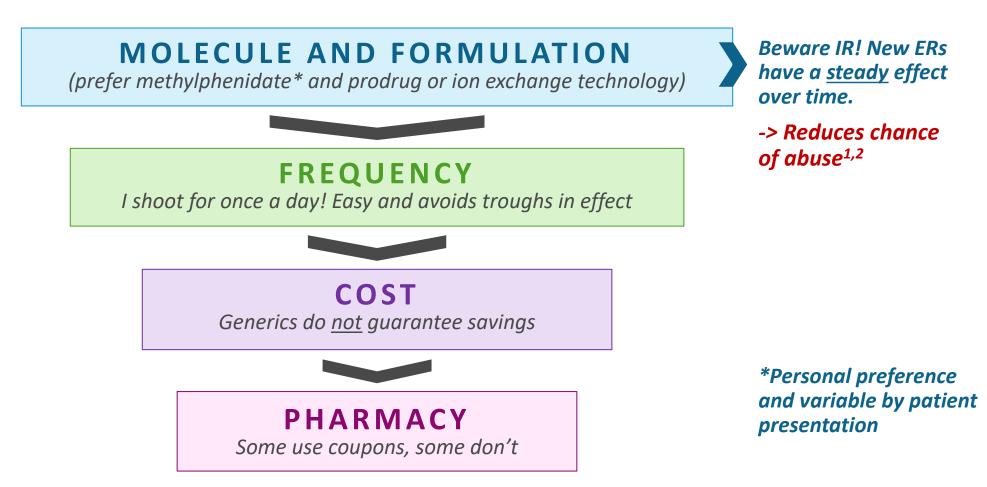
What is your number 1 priority when choosing a stimulant with your patients?

- a) Accessibility (i.e. ability to obtain insurance coverage)
- b) Cost
- c) Dosing frequency
- d) Pharmacy
- e) Molecule
- f) Formulation
- g) Other





CONSIDERATIONS IN FIRST-LINE AGENT SELECTION MY PRACTICE



1. Kooij J et al. Updated European Consensus Statement on diagnosis and treatment of adult ADHD. European Psychiatry, 2019: 56;14-34 **2.** Childress A. The safety of extended-release drug formulations for the treatment of ADHD. Expert Opin Drug Saf. 2017;16(5):603-615. doi:





LENGTH IT LASTS PACKAGE INSERT VS "FEELS LIKE"

AGENT	PI APPROXIMATE DURATION OF EFFECT
Azstarys	13 hours
Ritalin LA	8-10 hours
Concerta	12 hours
Dyanavel XR	13 hours
Adderall XR	12 hours
Vyvanse	10-13 hours
Mydayis	16 hours





1. Extrapolated from FDA prescribing information. Accessed November 2023

NONSTIMULANTS



NOREPINEPHRINE REUPTAKE INHIBITORS (NRIS)¹

GOAL: Help brain cells communicate -> improve concentration, impulse control, hyperactivity, etc.

AGENTS	CHALLENGES	
Viloxazine ER (NRI) ² (Practical advantages: faster onset, no hepatic warning, can be sprinkled on food)	Boxed warning, suicidal thoughts and behaviors	
Atomoxetine (SNRI)	Similar efficacy to each other but lower than stimulants	

COMMON OFF-LABEL AGENTS: *Bupropion, modafinil, tricyclic antidepressants*

ALPHA-ADRENERGIC RECEPTOR AGONISTS¹

GOAL: Regulate arousal and other cognitive processes (currently off-label in adults)

AGENTS	CHALLENGES
Clonidine ER ³	Sedating; rebound hypertension common (should be tapered)
Guanfacine ER*4	Less sedating; rebound hypertension less common (should still be tapered)

May help reduce certain side effects of stimulant therapy *Guanfacine has fewer side effects and a longer half-life⁴

RECOMMENDED SECOND LINE DUE TO LIMITED EFFICACY AND LONGER TIME TO EFFECT COMPARED WITH STIMULANTS¹

1. Groom MJ et al. Current pharmacological treatments for ADHD. In: Stanford SC, et al, eds. *New Discoveries in the Behavioral Neuroscience of ADHD*. Springer Nature; 2022:19-50 2 . Yu C et al. New Insights into the Mechanism of Action of Viloxazine: Serotonin and Norepinephrine Modulating Properties. J Exp Pharmacol. 2020 Aug 25;12:285-300. 3 Clonidine hydrochloride. Pl. Shionogi; 2020. 4. Guanfacine. Pl. Takeda; 2013. Accessed October 27, 2023.





CARDIOVASCULAR MONITORING

There are **no US guidelines** for cardiovascular monitoring in adults. However, the following pediatric guidelines¹ are consistent with prescribing information² for agents approved for adults



BEFORE MEDICATION

- Check for family history and presence of cardiovascular problems
 - E.g., Arrhythmias, heart murmur, HCM, long QT syndrome
- □ If any risk factors present, evaluate further (e.g., ECG, ECHO)



CARMEN'S TIPS:

Check if they had recent surgery-> may have recent ECG

DURING MEDICATION COURSE

Risk of cardiac adverse events is low!³ Data do not suggest a causal link

During treatment, monitor heart rate, blood pressure, and symptoms (e.g., chest pain, syncope)



1. Wolraich ML et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of ADHD in children and adolescents. *Pediatrics*. 2019;144(4):e20192528. 2 Adderall XR prescribing information. Available at <u>https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021303s036lbl.pdf</u>. Accessed 12/1/2023. 3. Man KKC et al. Long-term safety of methylphenidate in children and adolescents with ADHD: 2-year outcomes of the Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) study. *Lancet Psychiatry*. 2023;10(5):323-333.





SUMMARY OF CONSIDERATIONS



Prioritize comorbidities

Document WITH SCALES!

Consider **ONE-AND-DONE** daily dosing

Choose the **RIGHT PHARMACY**; transfer if they don't have your med

LISTEN TO PATIENTS about duration of effect



