

Assessment and Treatment of ADHD

Epidemiology

- prevalence of ADHD is between 3% and 8% of school-aged children
- prevalence in boys being 3-fold to 6-fold higher than in girls
- estimated that between 20% and 70% of will continue to be symptomatic as adults

Diagnosis



Symptoms of Inattention

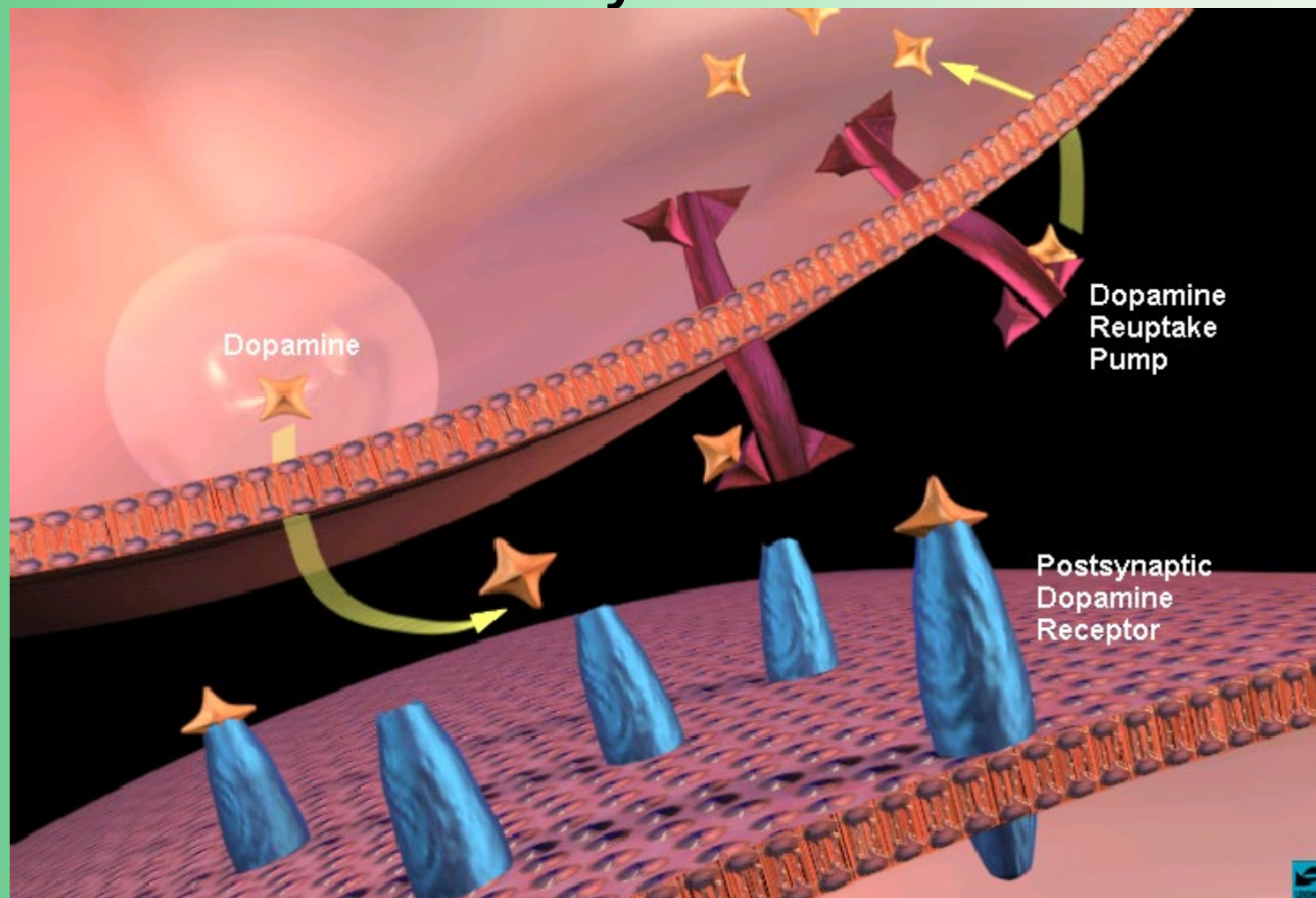
- Careless
- Difficulty sustaining attention in activity
- Doesn't listen
- No follow-through
- Avoids/dislikes tasks requiring sustained mental effort
- Can't organize
- Loses important items
- Easily distractible
- Forgetful in daily activities

Symptoms of Hyperactivity/Impulsivity

- Squirms and fidgets
- Can't stay seated
- Runs/climbs excessively
- Can't play/work quietly
- "On the go"/"driven by a motor"
- Talks excessively
- Blurts out answers
- Can't wait turn
- Intrudes/interrupts others

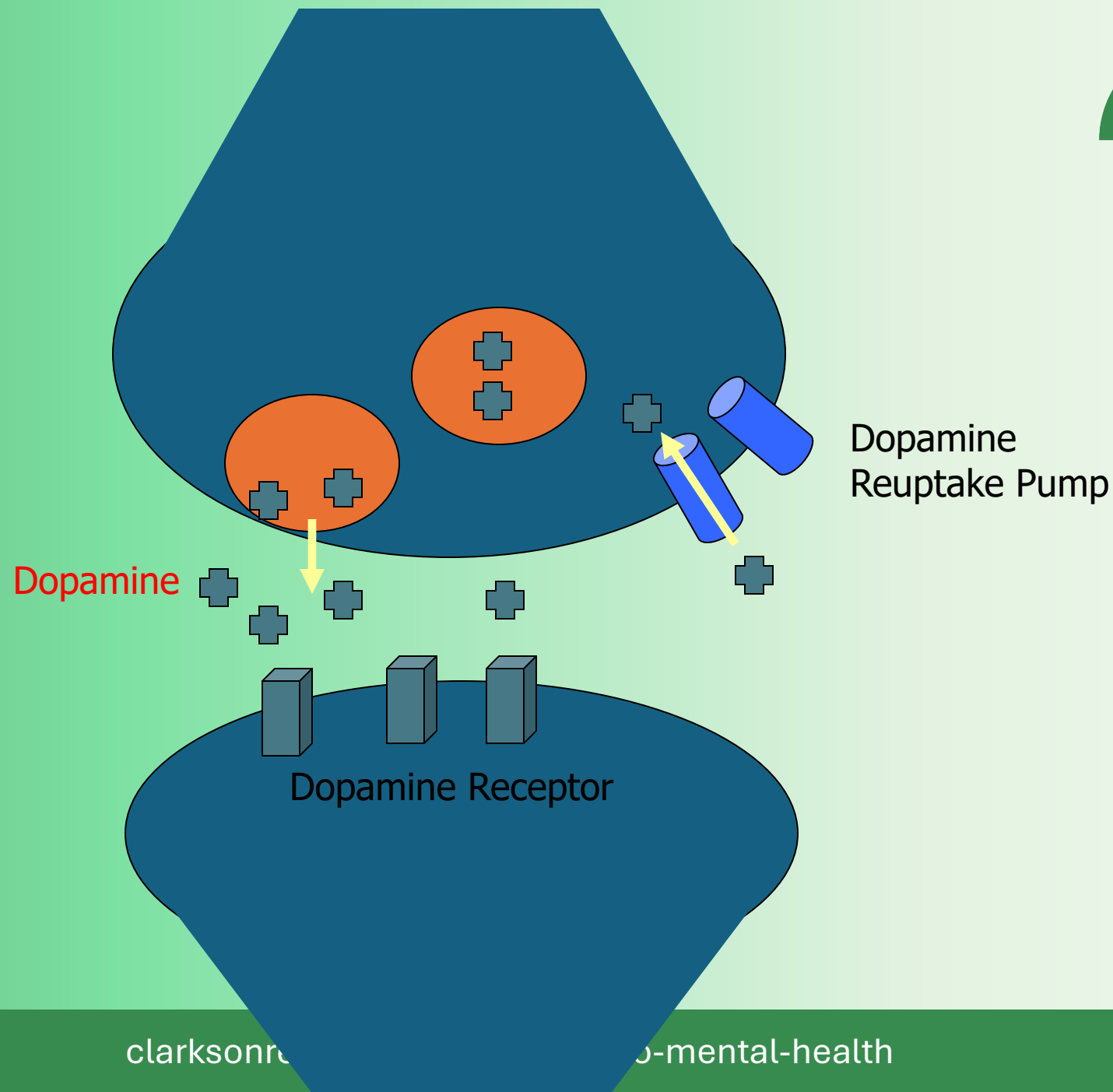
6/9 core symptoms (**5/9 if 17+**) for 6 months, starting before age 12, and causing significant impairment at home, at school, and/or in peer relations.

ADHD Treatments Primarily Affect Catecholamines



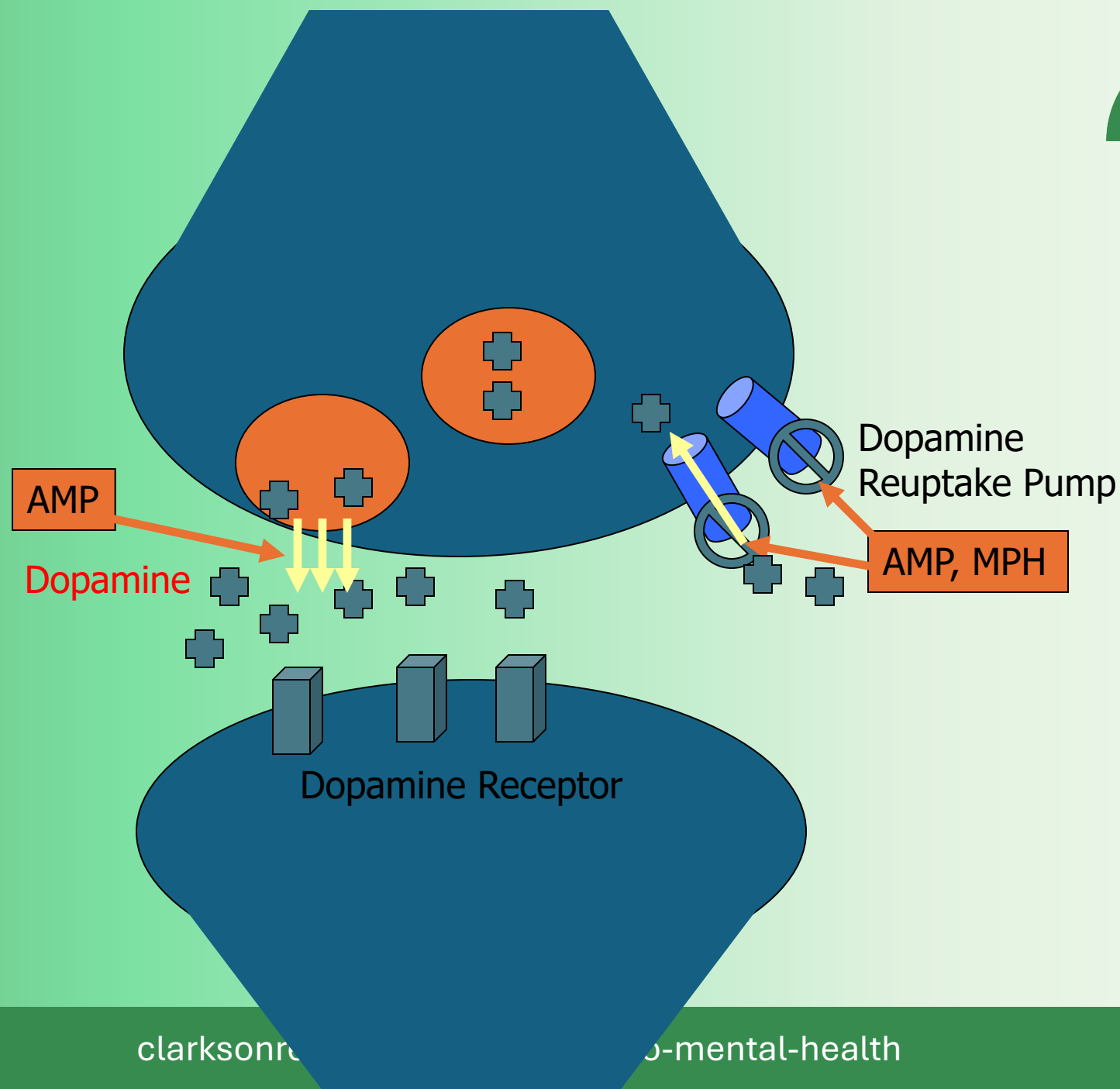


BRIDGES TO MENTAL HEALTH

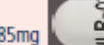
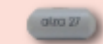
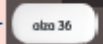
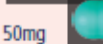
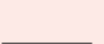
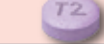
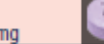
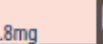
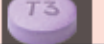
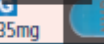
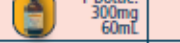
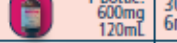
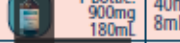
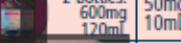
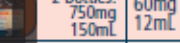
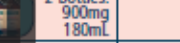
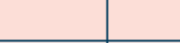
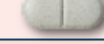
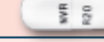
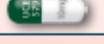
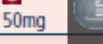
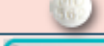
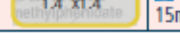
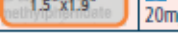
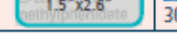
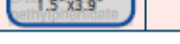




BRIDGES TO MENTAL HEALTH



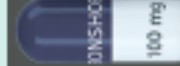
Medications used for ADHD

Methylphenidate Formulations – Long Acting** (Capsules and tablets in this section are shown at actual size)																		
Adhansia XR®*	6-17 Yrs: 25–70mg; SD: 25mg Adults: 25–85mg; SD: 25mg			25mg		35mg		45mg		55mg		70mg		85mg				
Concerta®†	6-12 Yrs: 18–54mg; SD: 18mg 13-17 Yrs: 18–72mg; SD: 18mg ≥18 Yrs: 18–72mg; SD: 18mg or 36mg		18mg		27mg		36mg		54mg		72mg	 + 		Methylphenidate ER 72mg (bioequivalent to 2 x 36 mg Concerta tablets)				
Aptensio® XR‡	6 Yrs–Adult: 10–60mg; SD: 10mg (biphasic – 40/60)		10mg		15mg		20mg		30mg		40mg		50mg		60mg			
Cotempla XR-ODT®§ (grape flavor)	6-17 Yrs: 8.6–51.8mg; SD: 17.3mg		8.6mg				17.3mg		25.9mg			34.6mg		43.2mg		51.8mg		69.7mg
Focalin® XR‡ (dexamethylphenidate)	6-17 Yrs: 5–30mg; SD: 5mg 18 Yrs–Adult: 5–30mg; SD: 5mg (biphasic – 50/50)		5mg		10mg		15mg		20mg		25mg		30mg		35mg		40mg	
Quilivant XR® (5mg/5mL, (5mg/mL) (bandana flavor)	6 Yrs–Adult: 20–60mg; SD: 20mg		10mg 2mL		20mg 4mL		30mg 6mL		40mg 8mL		50mg 10mL		60mg 12mL		70mg 14mL		90mg 18mL	
Quillichew ER®§ (cherry flavor)	6 Yrs–Adult: 20–60mg; SD: 20mg				20mg		30mg		40mg									
Ritalin® LA‡	6-12 Yrs: 10–60mg; SD: 20mg (biphasic – 50/50)		10mg		20mg		30mg		40mg		60mg							
Metadate® CD‡	6-17 Yrs: 10–60mg; SD: 20mg (biphasic – 30/70)		10mg		20mg		30mg		40mg		50mg		60mg					
Metadate® ER†	6 Yrs–Adult: 20–60mg; SD: 20mg		10mg		20mg		30mg											
Daytrana®	6-17 Yrs: 10–30mg; SD: 10mg (The color border around each patch reflects the packaging color, not the patch itself.)		10mg		15mg		20mg		30mg									

Medications used for ADHD

Methylphenidate Formulations – Long Acting/Delayed Onset**

(Medications in this section are shown at actual size)

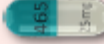
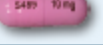
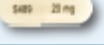
Jornay PM®†	6 Yrs–Adults: 20–100mg (dosed in the evening); SD: 20mg	20mg		40mg		60mg		80mg		100mg	
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Methylphenidate Formulations – Short Acting**

(Medications in this section are shown at actual size)

Focalin® (dexmethylphenidate)	6–17 Yrs: Daily: 5–20mg, divided BID; SD: 2.5mg BID			2.5mg		5mg		10mg		20mg	
Ritalin®	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID			5mg		10mg		20mg		30mg	
Methylphenidate Chewable ⁵ (grape flavor)	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID		2.5mg		5mg		10mg		20mg		
Methylin® Solution (grape flavor)	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID				5mg/5mL		10mg/5mL				

Medications used for ADHD

Amphetamine Formulations – Long Acting** (Medications in this section are shown at actual size)												
Dyanavel [®] XR (d- & l-amphetamine sulfate)	6 Yrs–Adults: 2.5–20mg; SD: 2.5 or 5mg		5mg		10mg		15mg		20mg			
Dyanavel [®] XR (d- & l-amphetamine sulfate) 2.5mg/mL (bubblegum flavor)	6 Yrs–Adults: 2.5–20mg; SD: 2.5 or 5mg	2.5mg 1mL 	5mg 2mL 	7.5mg 3mL 	10mg 4mL 	12.5mg 5mL 	15mg 6mL 	17.5mg 7mL 	20mg 8mL 			
Mydayis [®] ‡ (mixed amphetamine salts)	13–17 Yrs: 12.5–25mg; SD: 12.5mg Adults: 12.5–50mg; SD: 12.5mg	12.5mg 		25mg 		37.5mg 		50mg 				
Adzenys XR-ODT [®] § (d- & l-amphetamine) (orange flavor)	6–12 Yrs: 3.1–18.8mg; SD: 6.3mg 13–17 Yrs: 3.1–12.5mg; SD: 6.3mg Adults: 12.5mg		3.1mg 	6.3mg 	9.4mg 	12.5mg 	15.7mg 	18.8mg 				
Adzenys ER [®] (d- & l-amphetamine) 1.25mg/mL (orange flavor)	6–12 Yrs: 6.3–18.8mg; SD: 6.3mg 13–17 Yrs: 6.3–12.5mg; SD: 6.3mg Adults: 12.5mg		3.1mg 2.5mL 	6.3mg 5mL 	9.4mg 7.5mL 	12.5mg 10mL 	15.7mg 12.5mL 	18.8mg 15mL 				
Adderall XR [®] ‡ (mixed amphetamine salts)	6–17 Yrs: 5–30mg; SD: 10mg Adults: 5–30mg; SD: 20mg (biphasic – 50/50)		5mg 	10mg 	15mg 	20mg 	25mg 	30mg 				
Dexedrine Spansule [®] (d-amphetamine sulfate)	6–17 Yrs: 10–60mg; SD: 5mg 1-2x/day		5mg 	10mg 	15mg 							
Amphetamine Pro-Drug Formulations – Long Acting** (Medications in this section are shown at actual size)												
Vyvanse [®] ‡ (capsules) (lisdexamfetamine)	6 Yrs–Adults: 10–70mg; SD: 30mg	10mg 	20mg 	30mg 	40mg 	50mg 	60mg 	70mg 				
Vyvanse [®] ‡ (chewables) (lisdexamfetamine) (strawberry flavor)	6 Yrs–Adults: 10–70mg; SD: 30mg	10mg 	20mg 	30mg 	40mg 	50mg 	60mg 					

Medications used for ADHD

Amphetamine Formulations – Short Acting**																
(Medications in this section are shown at actual size)																
Evekeo® (d- & l- amphetamine sulfate)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg			10mg										
Evekeo® ODT (d- & l- amphetamine sulfate)	6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg			10mg			15mg		20mg					
Zenzedi® (d-amphetamine sulfate)	3–5 Yrs: SD: 2.5mg 1x/day 6–16 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day	2.5mg		5mg		7.5mg		10mg		15mg		20mg		30mg		
Adderall® (mixed amphetamine salts)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg		7.5mg		10mg		12.5mg		15mg		20mg		30mg	
ProCentra® (d-amphetamine sulfate) (bubblegum flavor)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg/5mL													

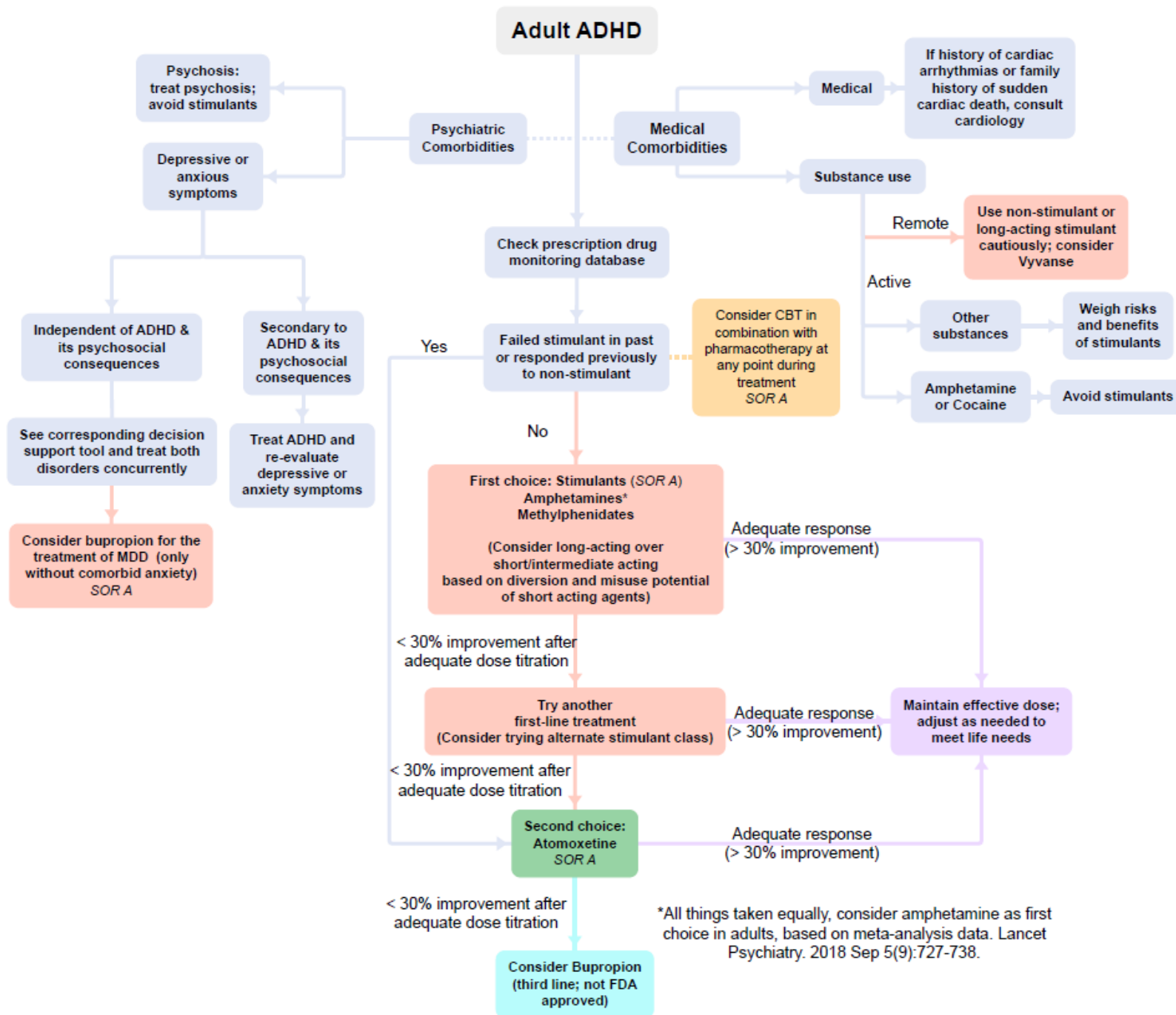
Metabolism

- Methylphenidate
 - Plasma esterases
- Amphetamine salts
 - Redundant hepatic metabolism
- Little P450 enzyme interaction problems for either

Medications used for ADHD

Non-Stimulants** (Medications in this section are shown at actual size)									
Intuniv®† (guanfacine, extended release)	6-12 Yrs: 1-4mg; SD: 1mg 13-17 Yrs: 1-7mg; SD: 1mg Weight-based dosing: SD: 0.05-0.08 mg/kg/day; may increase to 0.12 mg/kg/day	1mg		2mg		3mg		4mg	
Kapvay®† (clonidine, extended release)	6-17 Yrs: 0.1-0.2mg BID; SD: 0.1mg qHS	0.1mg		(only in dose pack) 0.2mg					
Strattera®† (atomoxetine)	≤70kg: 0.5mg/kg x ≤3days, then 1.2mg/kg (max: 1.4mg/kg, not to exceed 100mg) >70 kg: 40mg x ≤3days, then 80mg (max: 100mg)	10mg		18mg		25mg		40mg	
Qelbree®‡ (viloxazine)	6-11 Yrs: 100-400mg; SD: 100mg 12-17 Yrs: 200-400mg; SD: 200mg Adults: 200-600mg; SD: 200mg	100mg		200mg		300mg		400mg	

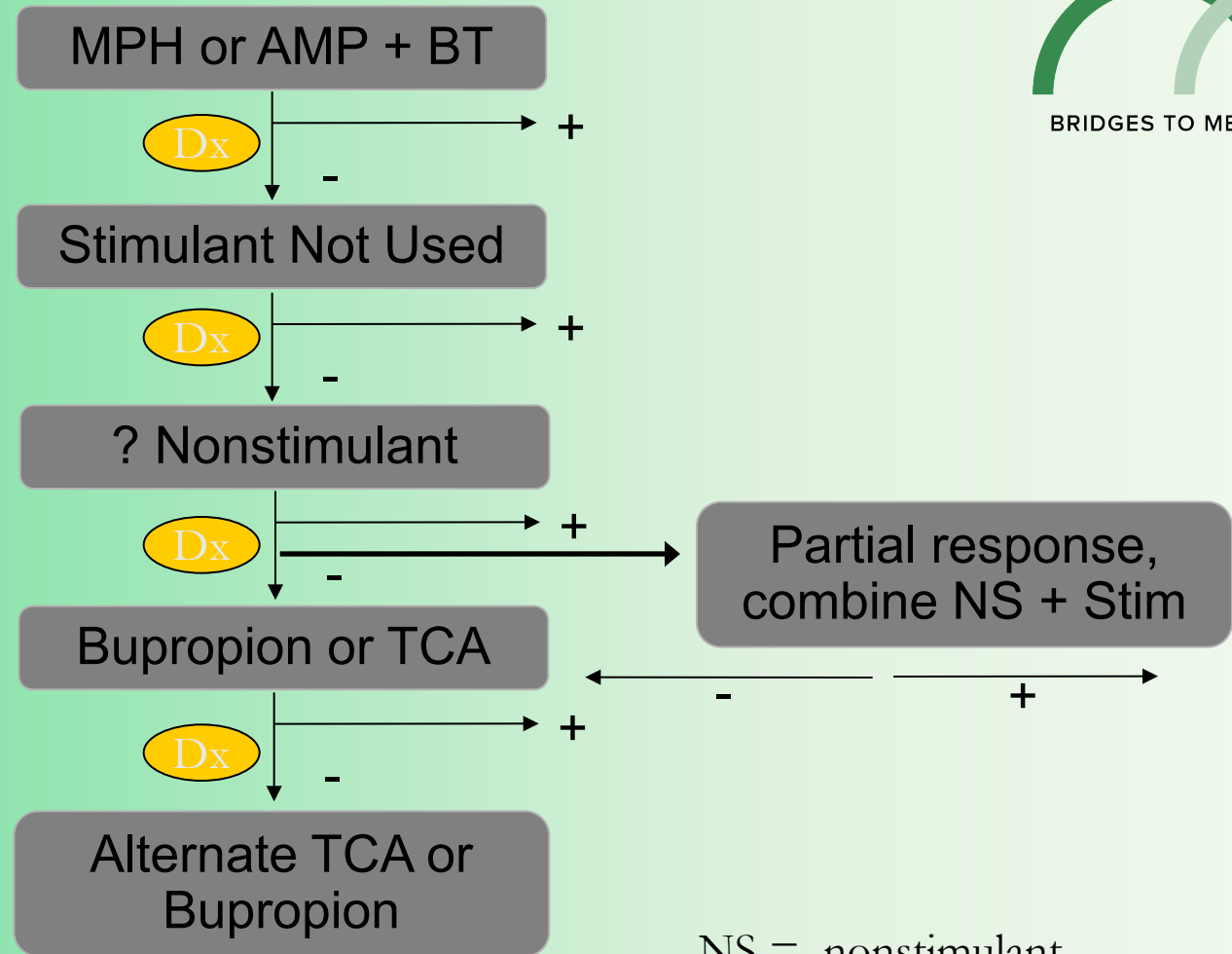
- Non-stimulants
 - bupropion (Wellbutrin, Wellbutrin-SR, Wellbutrin-XL) *
 - tricyclic antidepressants (imipramine, nortryptiline, desipramine, protryptiline) *
- * = no FDA indication for ADHD



Case

- Madison is a 19 year old who presents with symptoms since preschool of inattention and hyperactivity. At the time of referral, she has graduated from high school and started at a local community college. She had stopped her stimulant, thinking that she no longer needed it, in her Junior year of high school. A structured interview confirms ADHD, combined type. She does not meet criteria for another psychiatric disorder. Her sleep and appetite are good. She weighs 140 lbs.
- Madison does not have a history of substance use or tics. She is interested in getting back on a stimulant.

ADHD without major co- occurring disorder



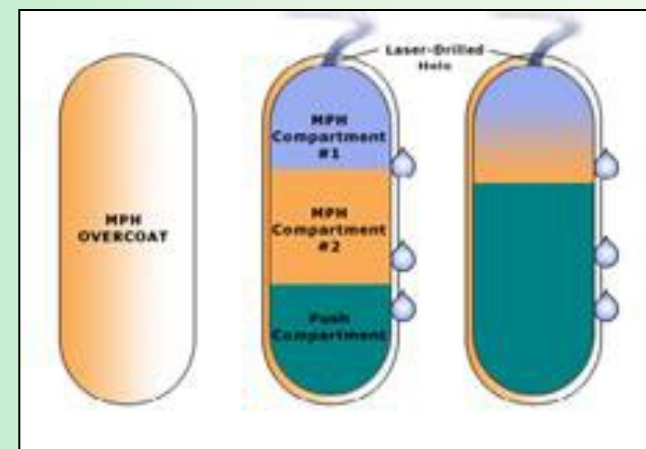
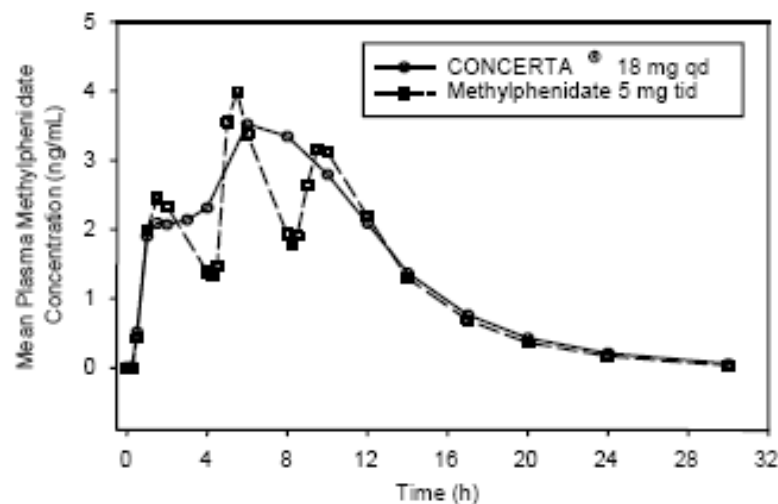
NS = nonstimulant
AMP = amphetamine
MPH = methylphenidate
TCA = Tricyclic Antidepressant

Case (cont.)

- You start a trial of OROS-methylphenidate (Concerta) at 18 mg. After 2 weeks there is improvement on the medication, but mild. You titrate to 36 mg.
- At a 1 month appointment, there has been some improvement but she still struggles. You titrate to 54 mg.
- In follow-up, there is marked improvement. Although she still struggles with distractibility, she is doing better in the classroom. She has been tired, though, and she says that her typical good sleep has been worse lately. She now takes 1-2 hours to fall asleep, is tired in the morning, and doesn't wake up until right before class, when she takes her pill, gobbles breakfast, and heads to school. She is now wondering about something for sleep.
- You take some time to review the pharmacokinetics of Concerta...

Concerta

22% Immediate
78% after 4 hours
Peak: 6.8 hours
T $\frac{1}{2}$: 3.5 hrs



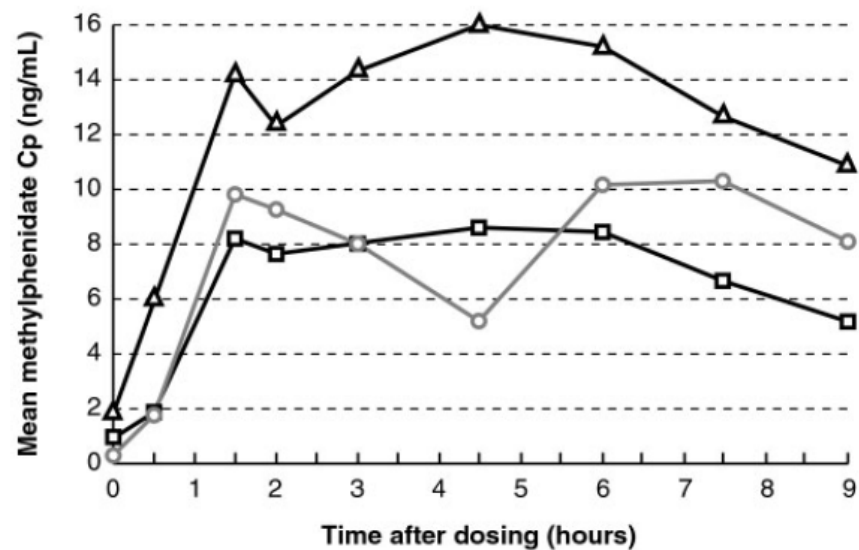
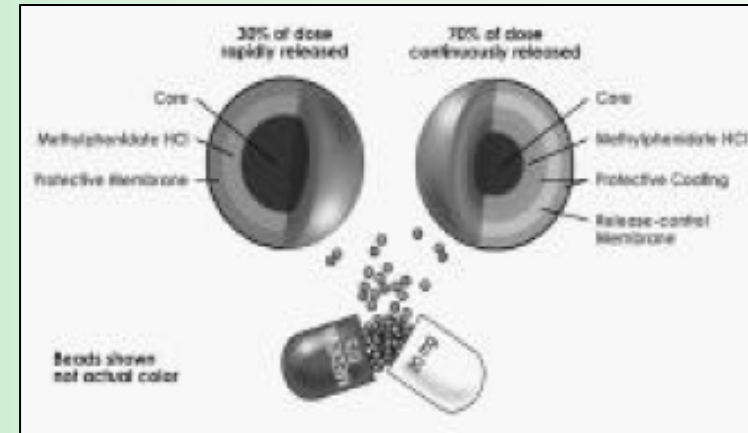
Metadate-CD

30% Immediate

70% after 4 hours

Peak(s): 1.5 h / 4.5 h

T $\frac{1}{2}$: 6.8 hrs



- 1 x 10 mg IR at 0 and 4 h (n=21)
- 1 x 20 mg METADATE CD (n=12)
- △ 2 x 20 mg METADATE CD (n=9-10)



Ritalin-LA/Focalin-XR

50% Immediate

50% after 4 hours

Peak(s): 2 h / 6.6 h

T $\frac{1}{2}$: 2.4 hrs

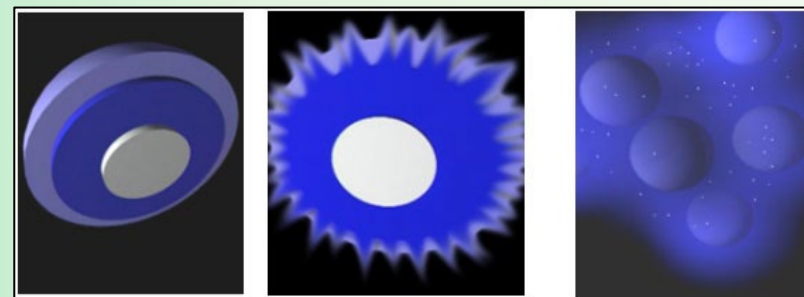
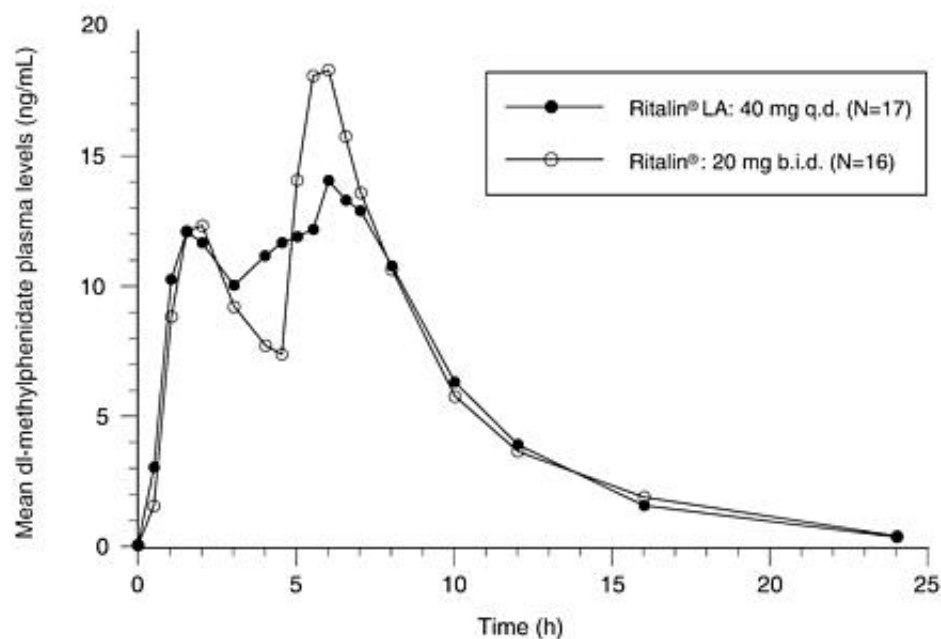
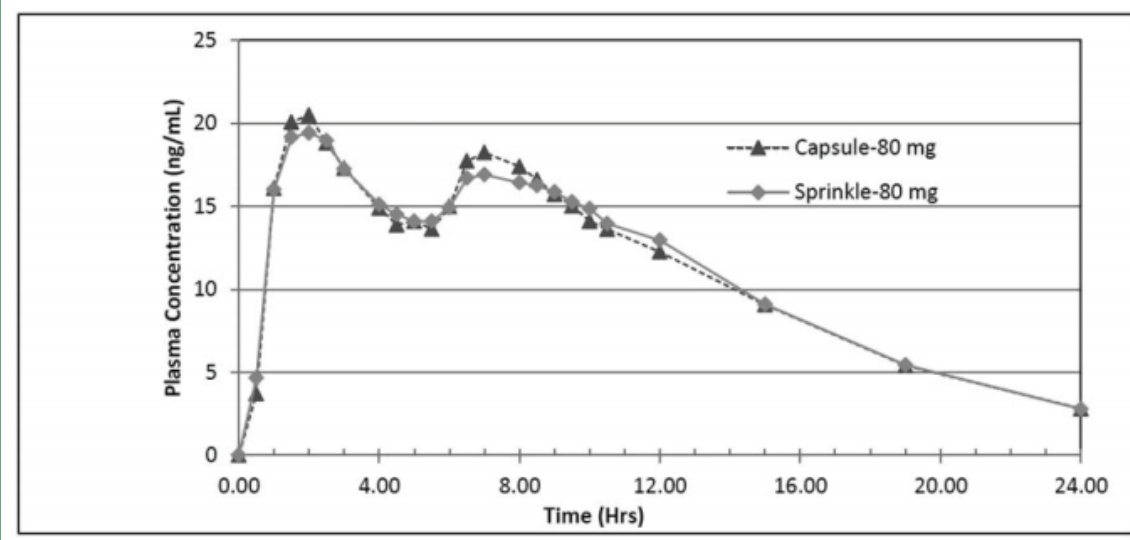


Figure 1. Mean plasma concentration time-profile of methylphenidate after a single dose of Ritalin® LA 40 mg q.d. and Ritalin® 20 mg given in two doses four hours apart

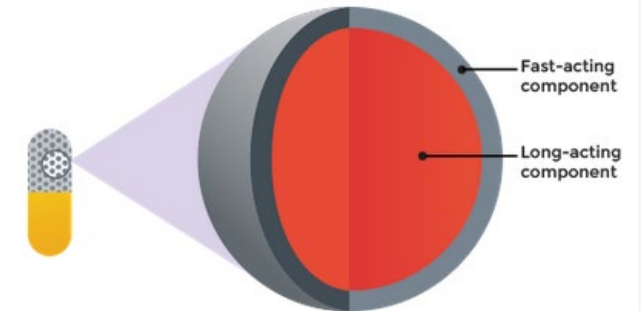


Aptensio-XR

40% Immediate
60% after 4 hours
Peak(s): 2 h / 7 h
T $\frac{1}{2}$: 5 hrs



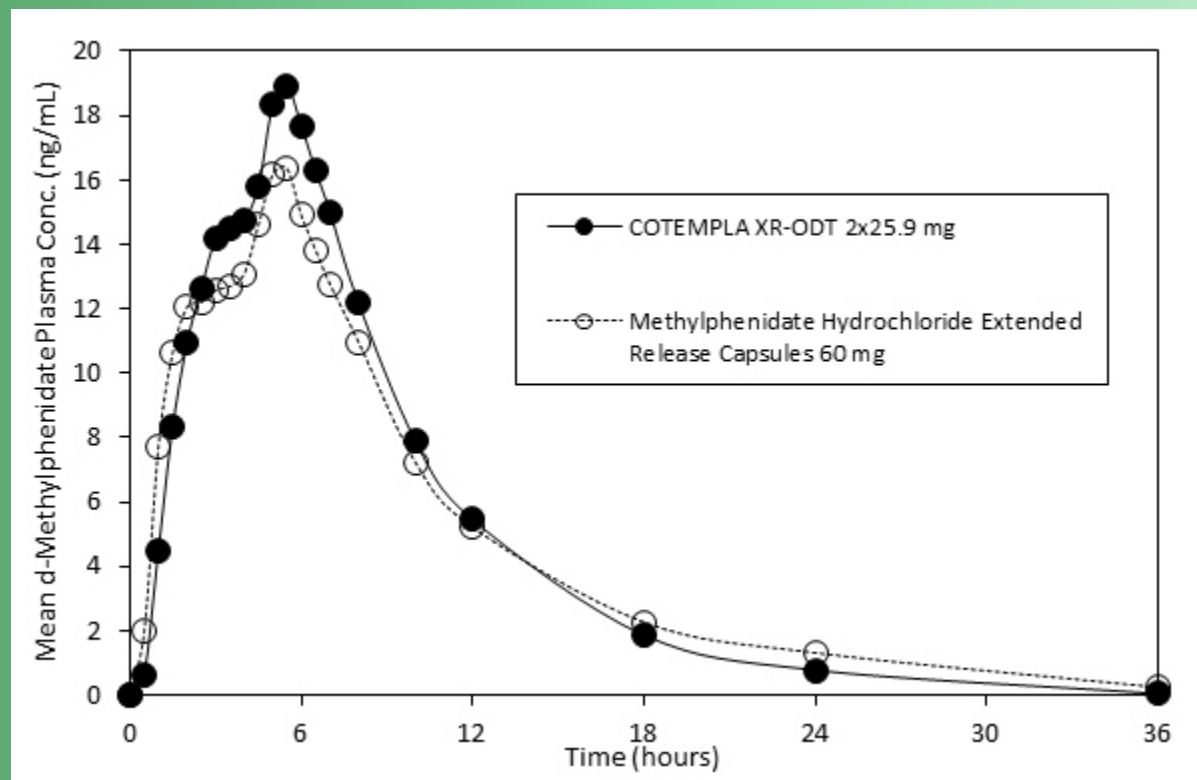
Aptensio XR is designed to deliver medicine from hour 1 to hour 12.



Cotempla-XL

Peak(s): 4.5-5 hr

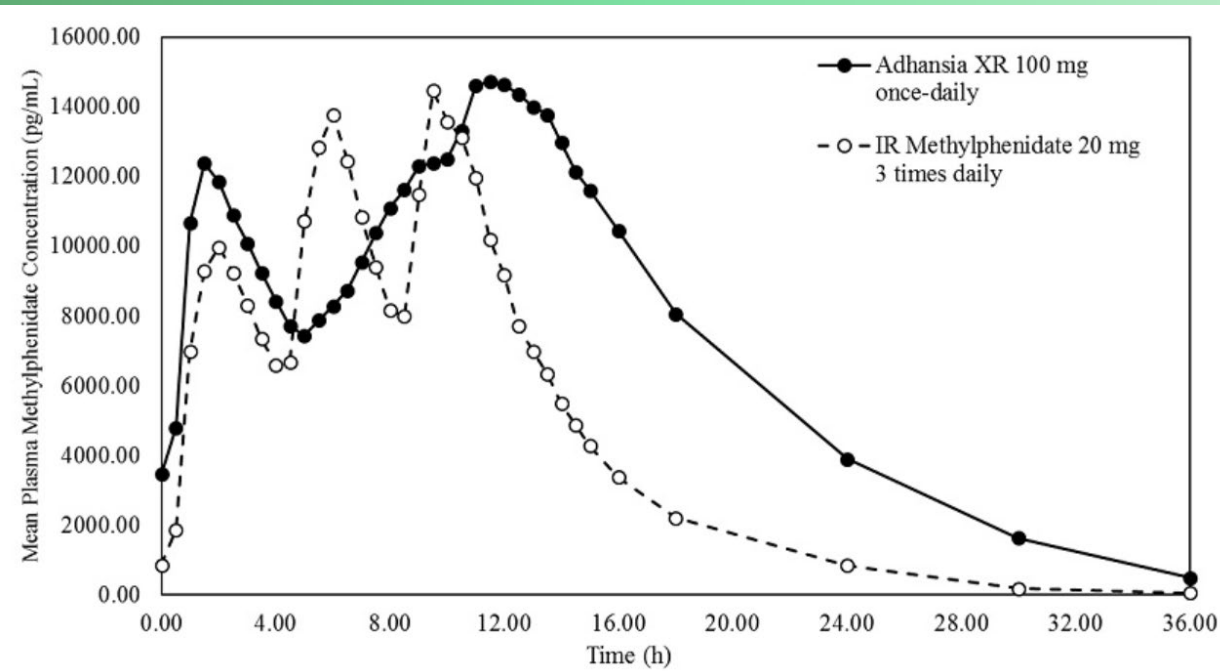
T $\frac{1}{2}$: 4 hrs



Adhansia XR

Peak(s): 1.5, 12

T $\frac{1}{2}$: 7 hrs



Within the once-daily capsule, each bead releases the dose in two phases¹⁻³

One methylphenidate dose is released immediately, and one is released later^{3,5}

Outer immediate-release layer contains

~20%
of the dose

Inner controlled-release layer contains

~80%
of the dose



- 1 Methylphenidate HCl layer
- 2 Delayed-release coating
- 3 Controlled-release coating
- 4 Methylphenidate HCl layer
- 5 Sugar sphere

Adderall-XR

50% Immediate

50% after 4 hours

Peak: 7 hours

T $\frac{1}{2}$: 10-13 hrs (but variable!)

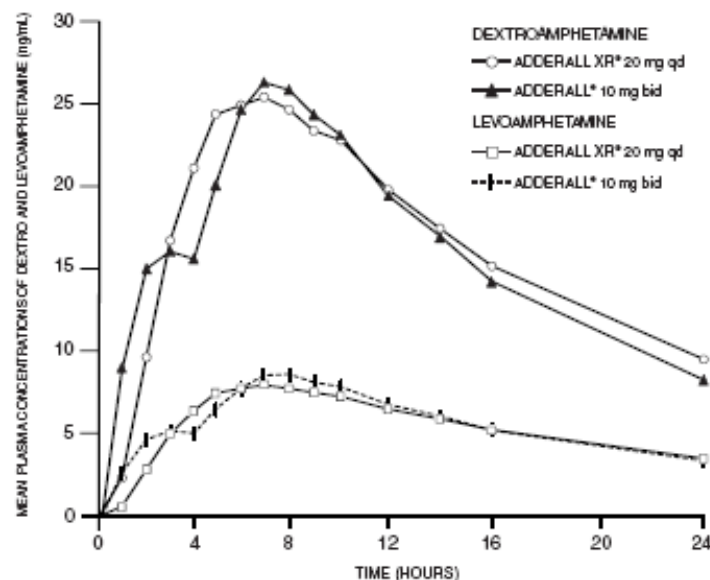
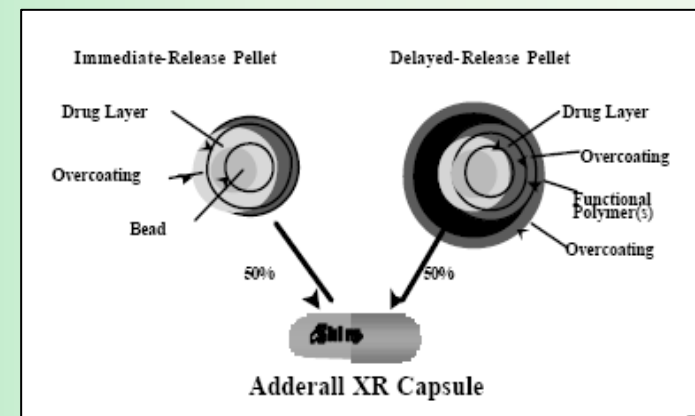


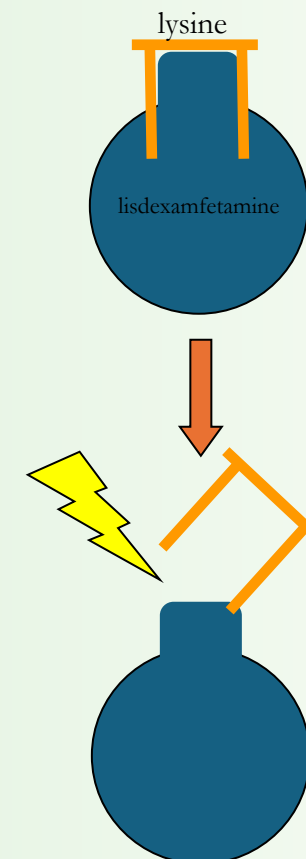
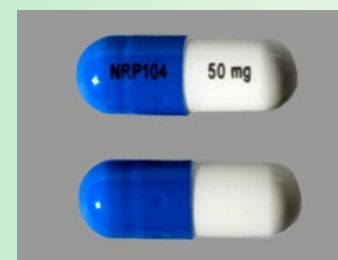
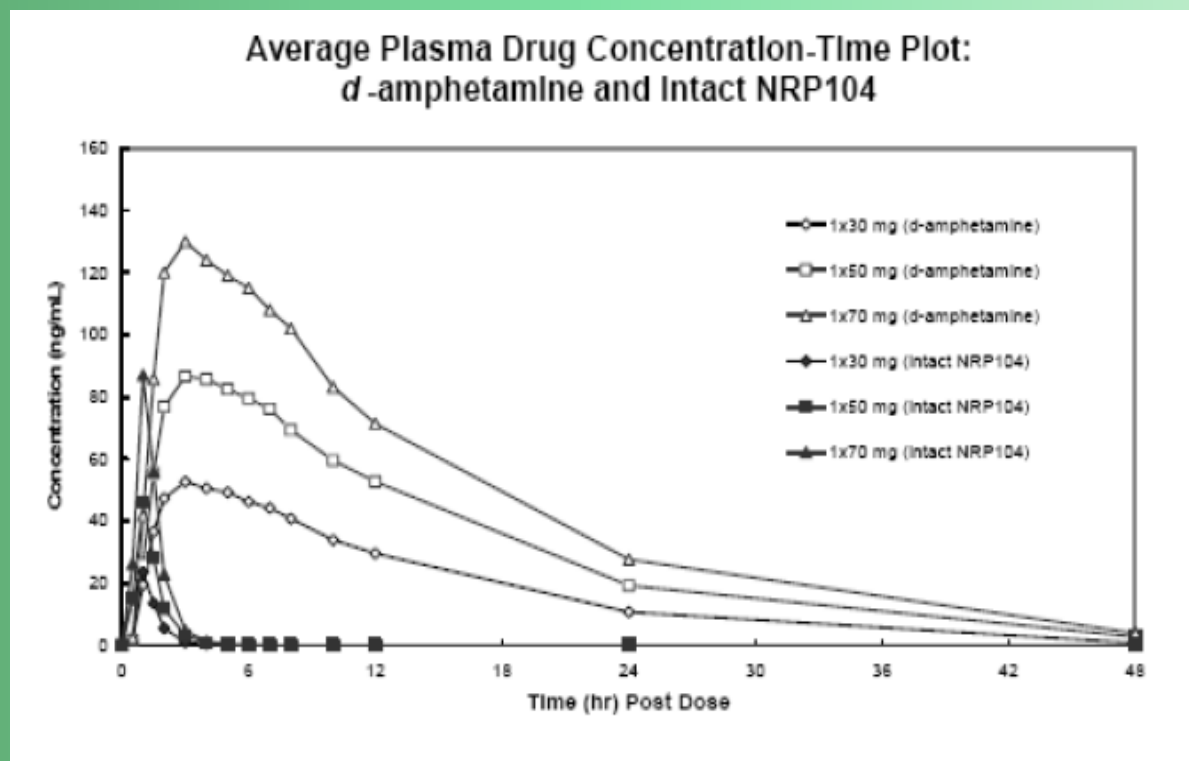
Figure 1 Mean d-amphetamine and l-amphetamine plasma concentrations following administration of ADDERALL XR® 20 mg (8 am) and ADDERALL® (immediate-release) 10 mg bid (8 am and 12 noon) in the fed state.



Lisdexamfetamine mesylate (Vyvanse)

Peak: 3.5 hours

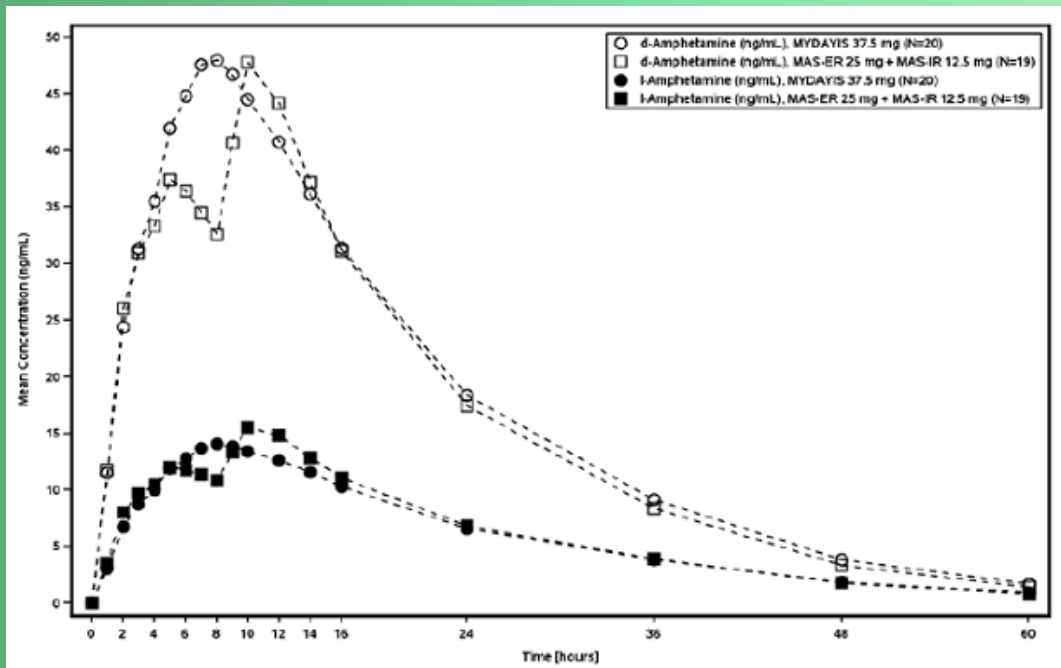
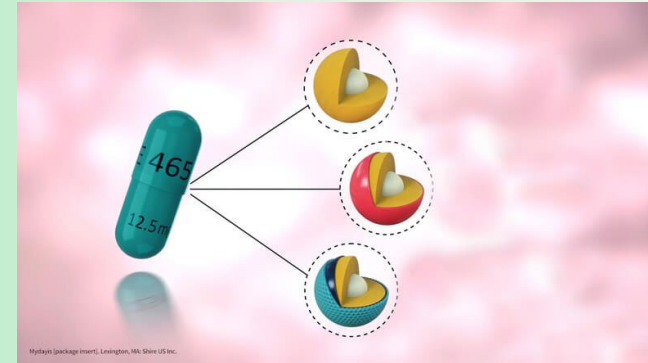
T $\frac{1}{2}$: 9.6 hours



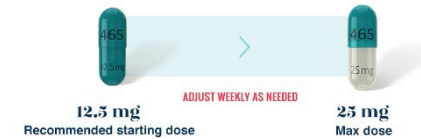
MyDayis

Peak(s): 7-10 hours

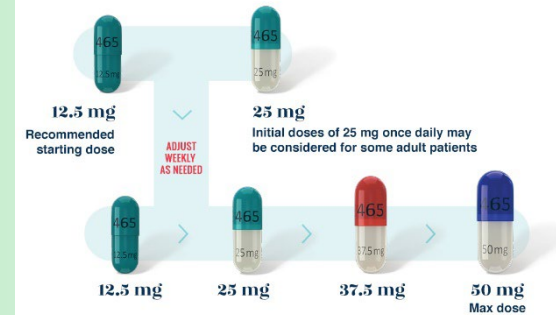
T $\frac{1}{2}$: 11-13 hrs



ADOLESCENT TITRATION



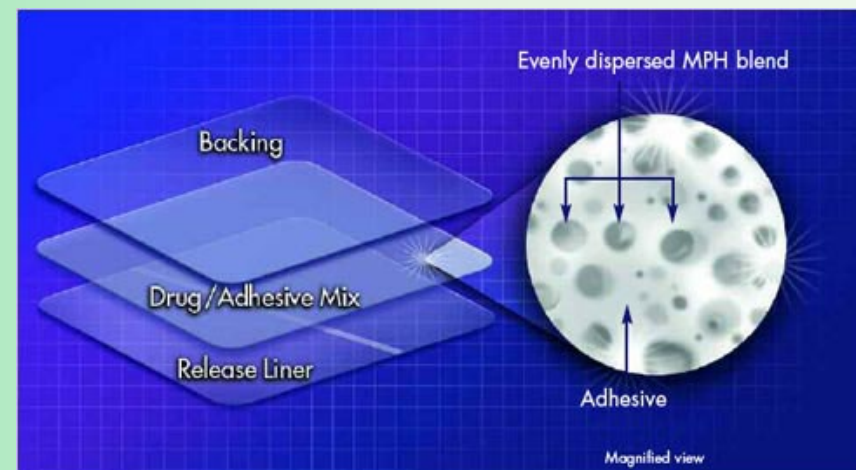
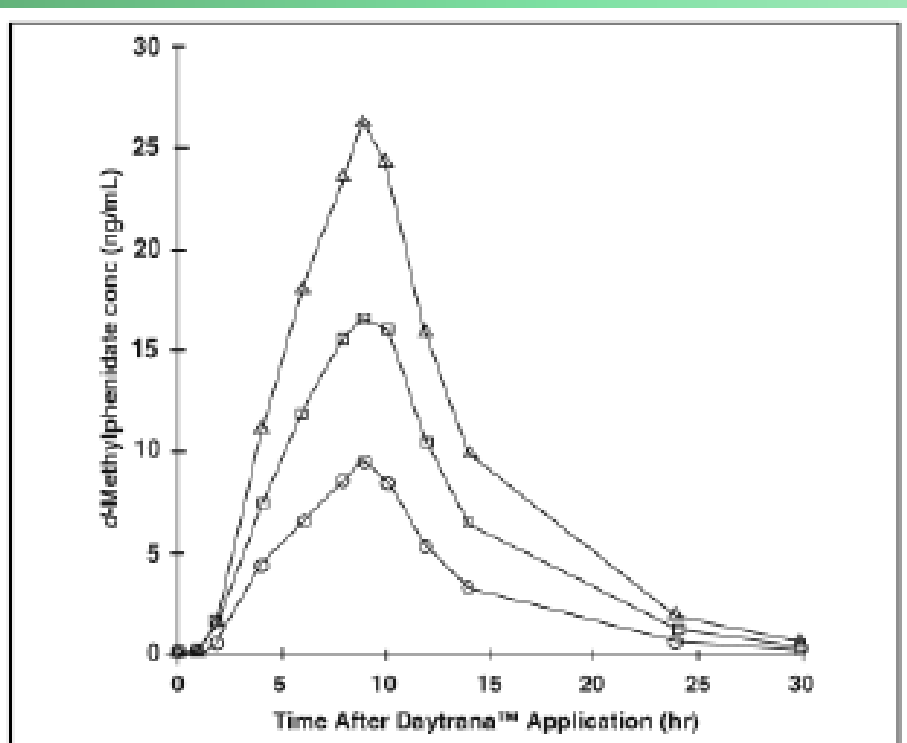
ADULT TITRATION



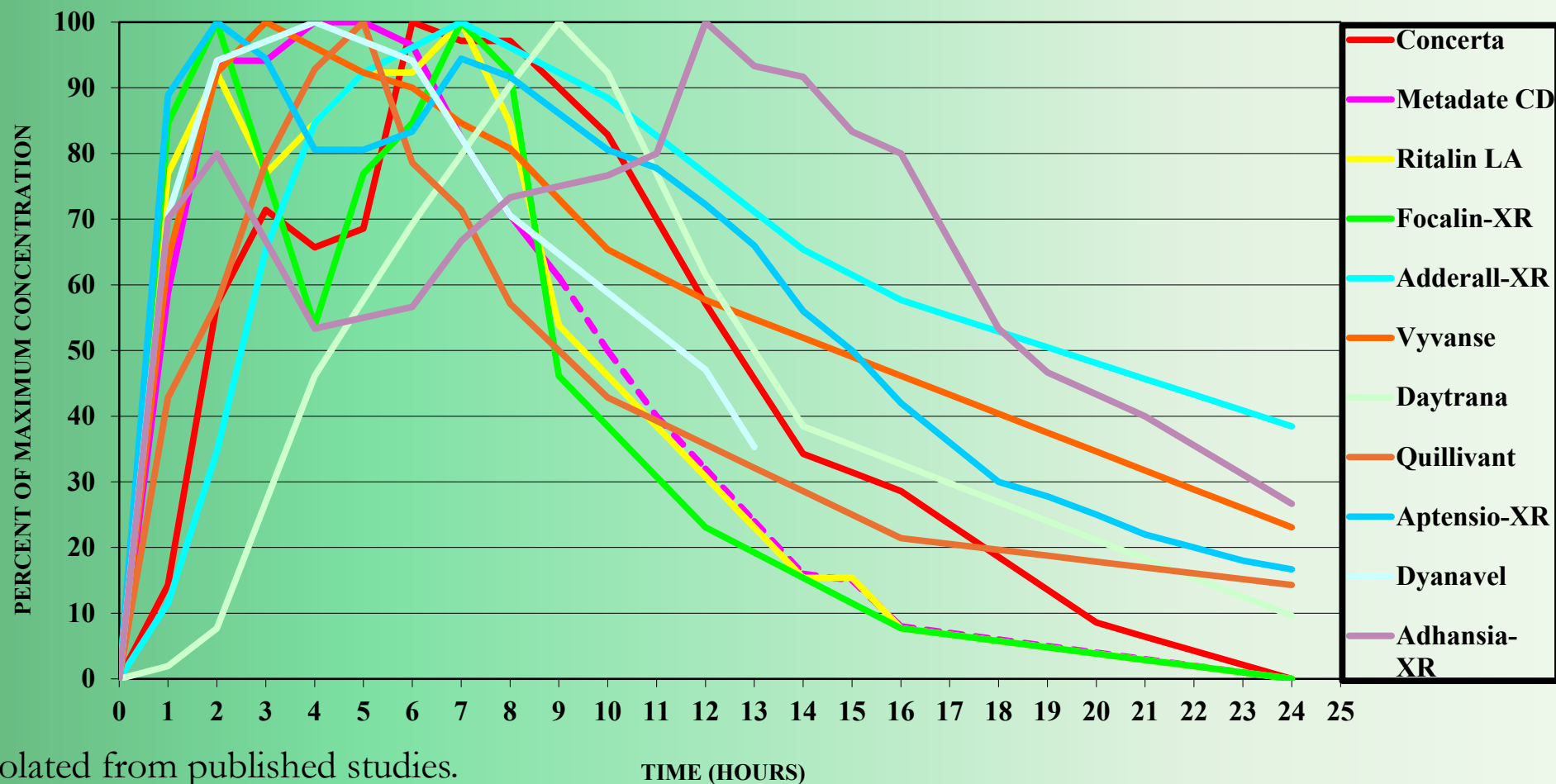
Daytrana

Peak: 9 hours after application

T $\frac{1}{2}$: 3-4 hrs after removal



Rough Comparison* of Long-Acting Stimulant Serum Concentrations



*Data interpolated from published studies.

Case (cont)



- You opt for a change to Focalin-XR. Madison's sleep returns to normal and her school performance improves.

Safety of Stimulants: Common Reactions



- Headache, upper respiratory tract infection, abdominal pain, vomiting, loss of appetite, insomnia, increased cough, pharyngitis, sinusitis, dizziness, irritability, dysphoria

Safety of Stimulants: Common Reactions



- Of the problematic reactions:
 - Loss of appetite can be partly mitigated by dosing with or after breakfast
 - Insomnia can be partly mitigated by the use of longer acting once daily medications
 - Most of the other side effects decreased by either waiting or decreasing the dose

Safety of Stimulants: Adverse Events



- Weight loss and slowed longitudinal growth
- New onset of tics or Gilles de la Tourette
- Liver toxicity
- Sudden cardiac death
- Substance abuse

Conclusions

- There are multiple treatment options available for the management of ADHD
- Since ADHD is typically seen in the context of co-occurring disorders, it is likely that strategies will need to be modified for those conditions.
- Most treatment-emergent side effects are time-limited and respond to a modification of the treatment regimen