BRIDGES TO MENTAL HEALTH

Assessment and Treatment of ADHD

Epidemiology

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- 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

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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.

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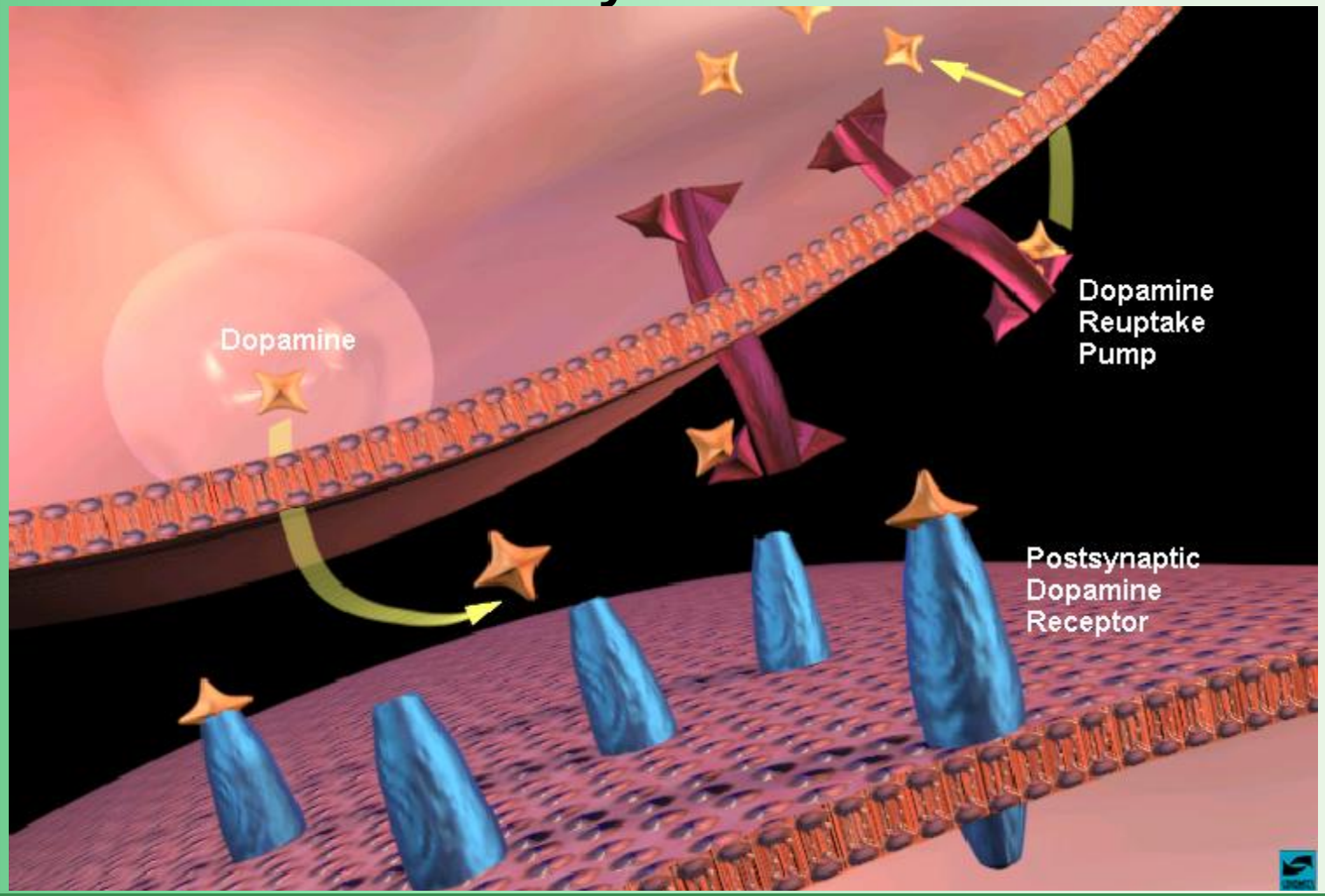
ADHD Treatments Primarily Affect Catecholamines



Adapted from NIDA presentation: The Brain & the Actions of Cocaine, Opiates, and Marijuana

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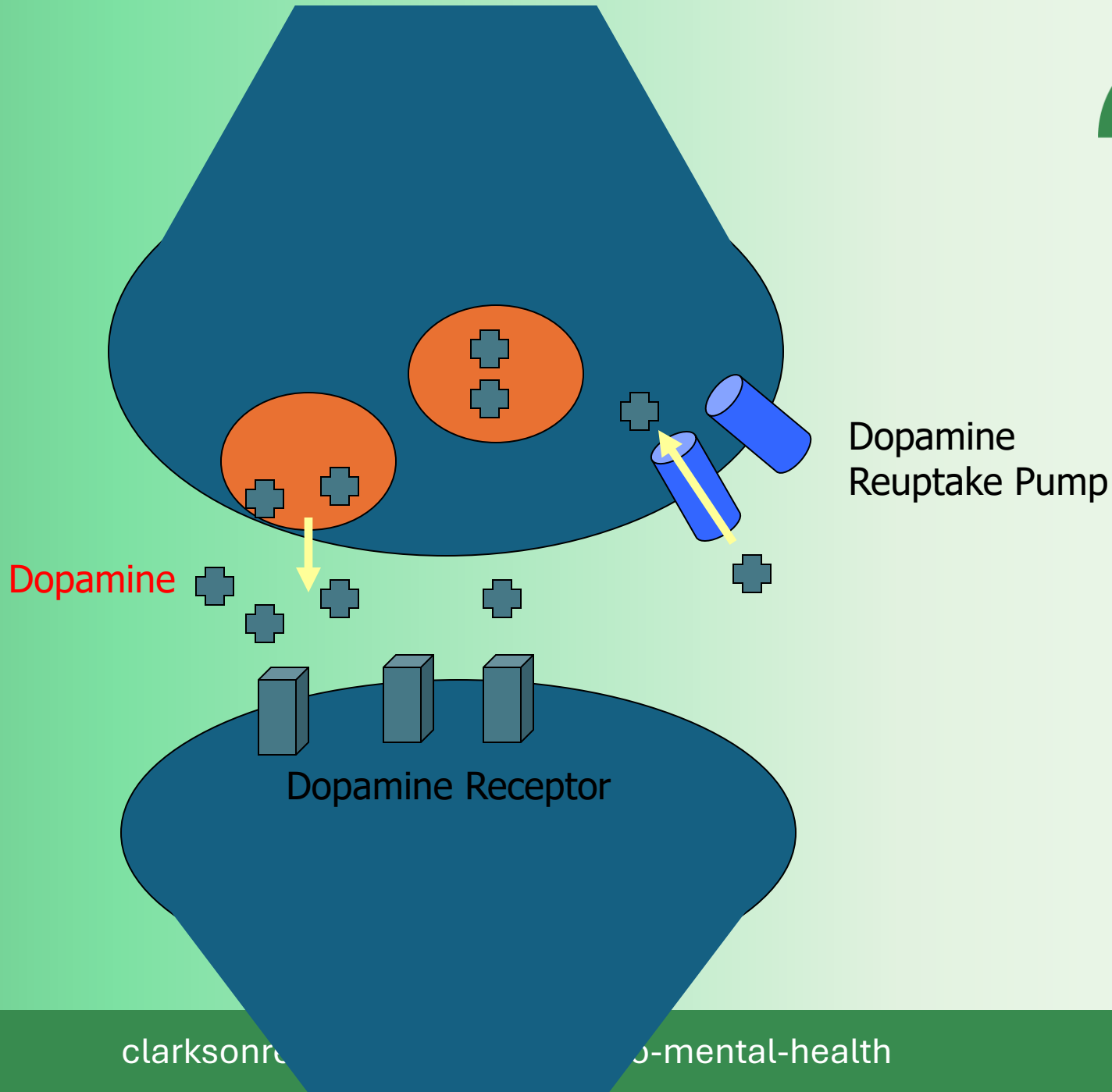
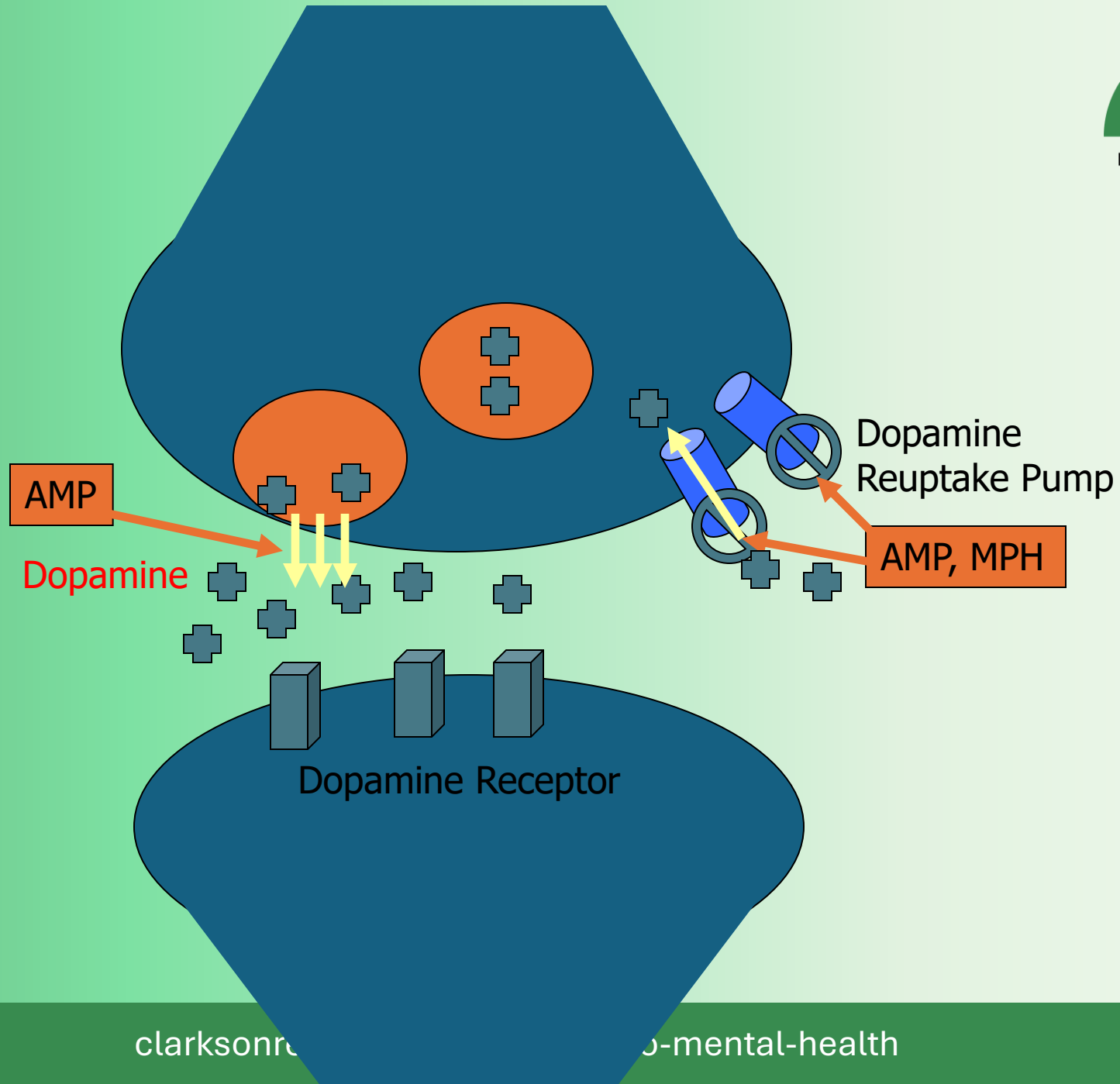
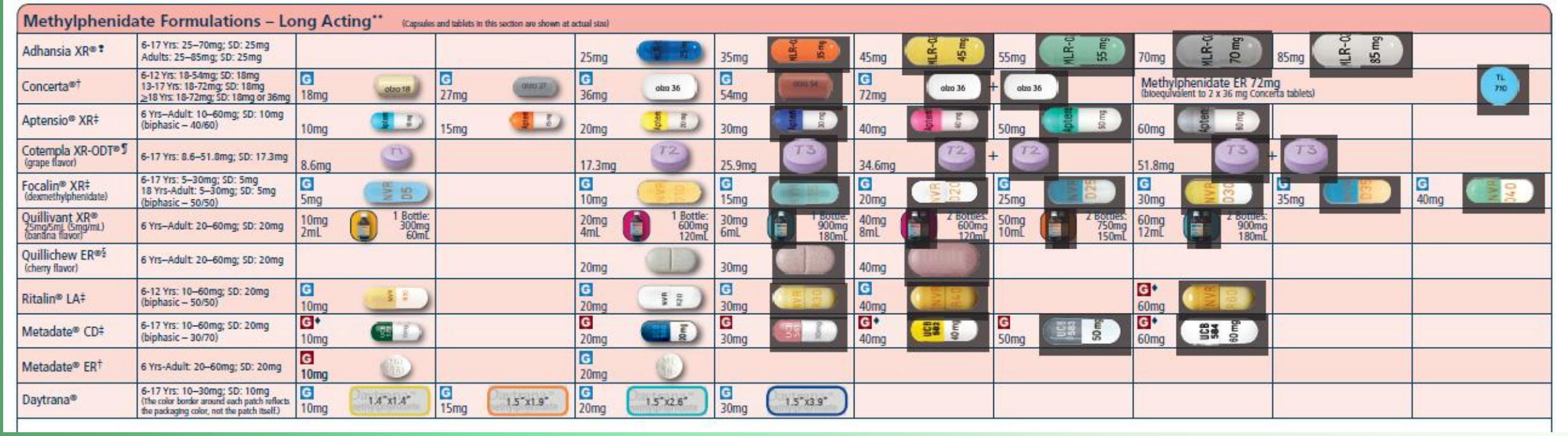


BRIDGES TO MENTAL HEALTH



Medications used for ADHD

BRIDGES TO MENTAL HEALTH



Medications used for ADHD

BRIDGES TO MENTAL HEALTH

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	

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			G 2.5mg		G 5mg		G 10mg			
Ritalin®	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID			G 5mg		G 10mg		G ♦ 20mg			
Methylphenidate Chewable§ (grape flavor)	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID	G ♦ 2.5mg		G ♦ 5mg		G ♦ 10mg					
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			G 5mg/5mL		G 10mg/5mL					

Medications used for ADHD

BRIDGES TO MENTAL HEALTH

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)		G 5mg	G 10mg	G 15mg	G 20mg	G 25mg	G 30mg		
Dexedrine Spansule® (d-amphetamine sulfate)	6-17 Yrs: 10–60mg; SD: 5mg 1-2x/day		G♦ 5mg	G♦ 10mg	G 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

BRIDGES TO MENTAL HEALTH

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	G 5mg	7.5mg	G 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		G 5mg	G 7.5mg	G 10mg	G 12.5mg	G 15mg	G 20mg	G 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		G 5mg/5mL							

Metabolism

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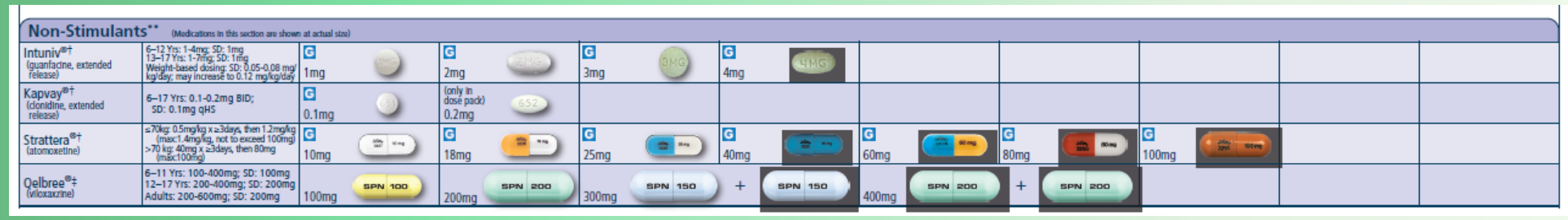
- Methylphenidate
  - Plasma esterases
- Amphetamine salts
  - Redundant hepatic metabolism

- Little P450 enzyme interaction problems for either

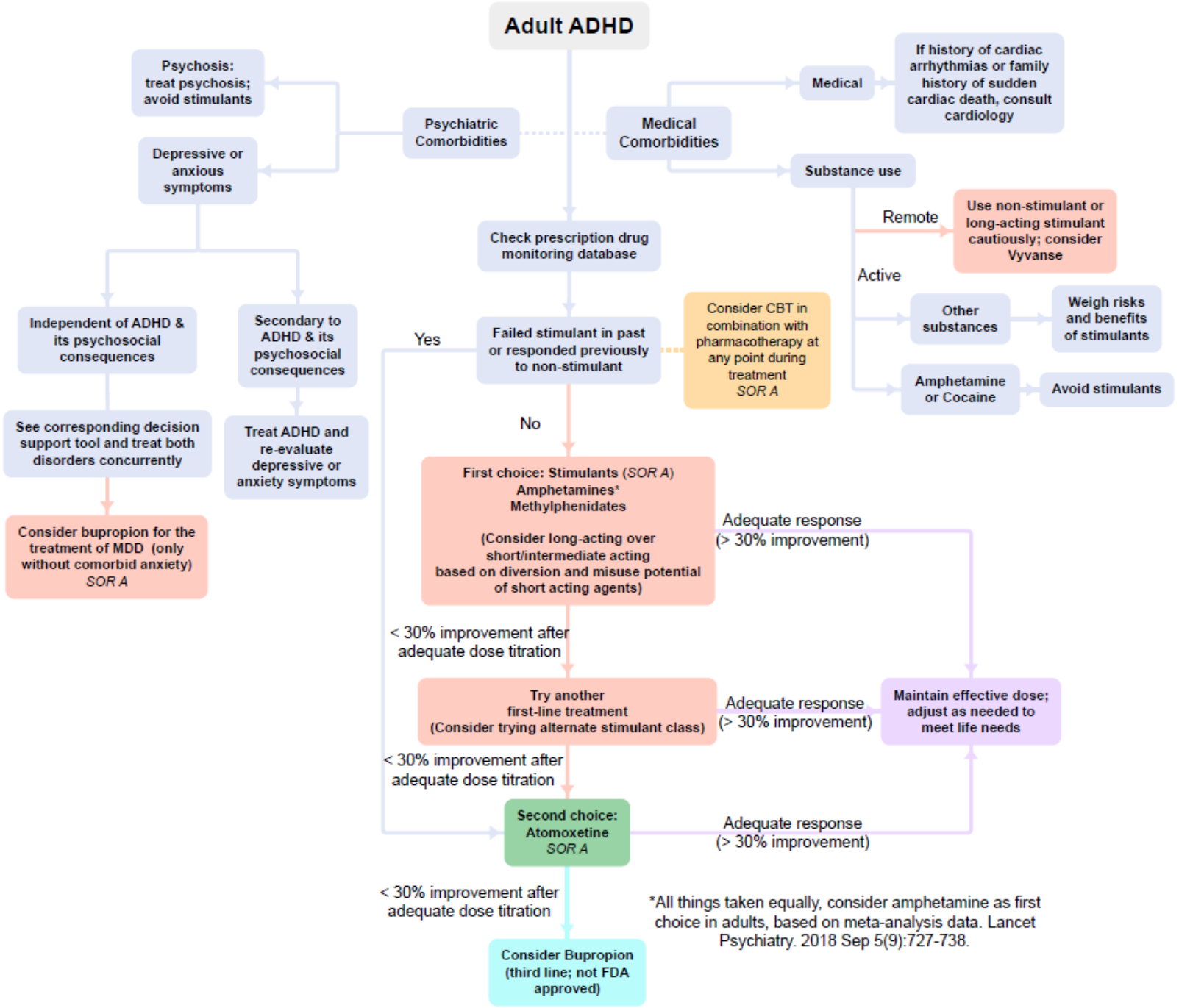
Medications used for ADHD

BRIDGES TO MENTAL HEALTH



- Non-stimulants
  - bupropion (Wellbutrin, Wellbutrin-SR, Wellbutrin-XL) *
  - tricyclic antidepressants (imipramine, nortryptyline, desipramine, protryptyline) *

- * = no FDA indication for ADHD



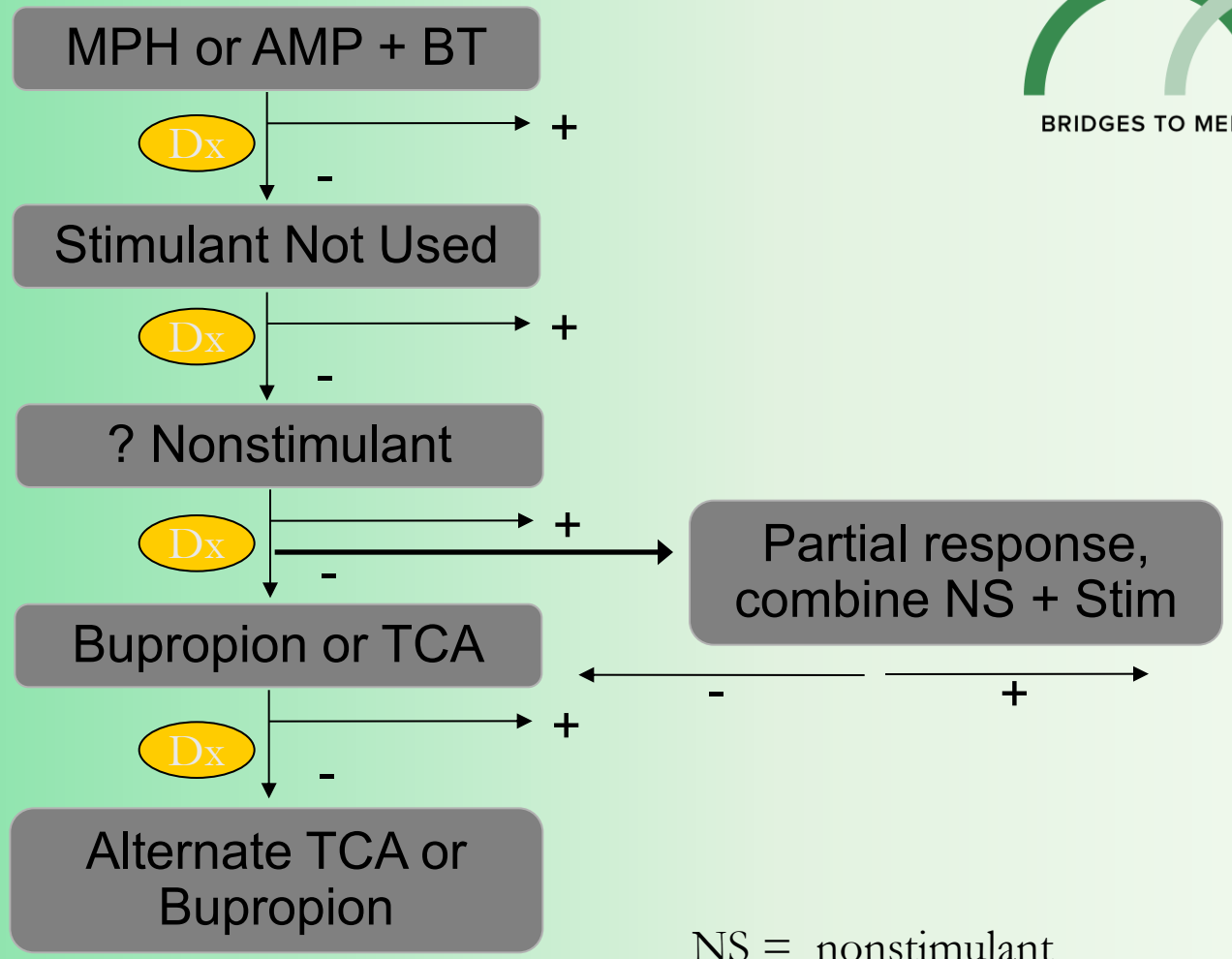
BRIDGES TO MENTAL HEALTH

Case

BRIDGES TO MENTAL HEALTH

- 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

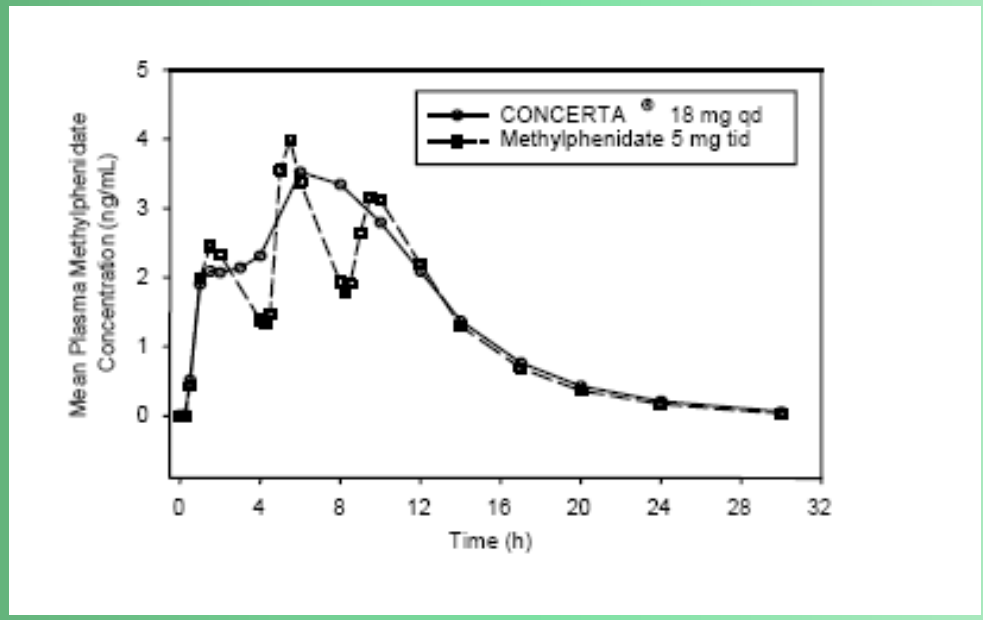
Case (cont.)

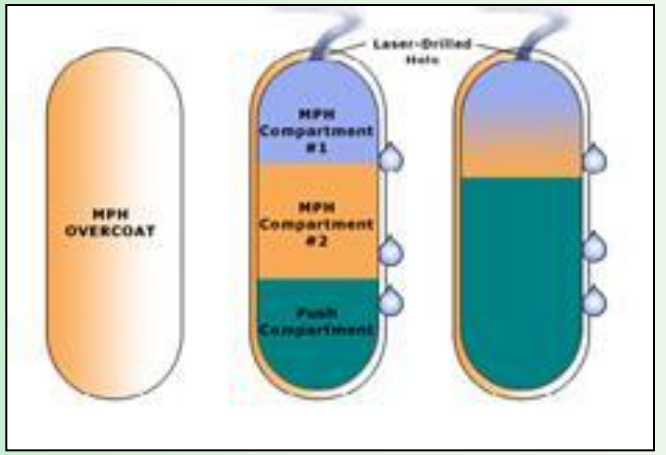
BRIDGES TO MENTAL HEALTH

- 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

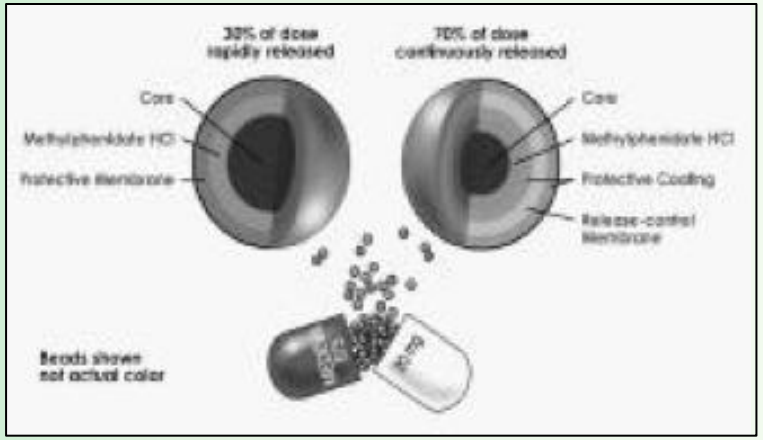
22% Immediate
78% after 4 hours
Peak: 6.8 hours
T ½: 3.5 hrs

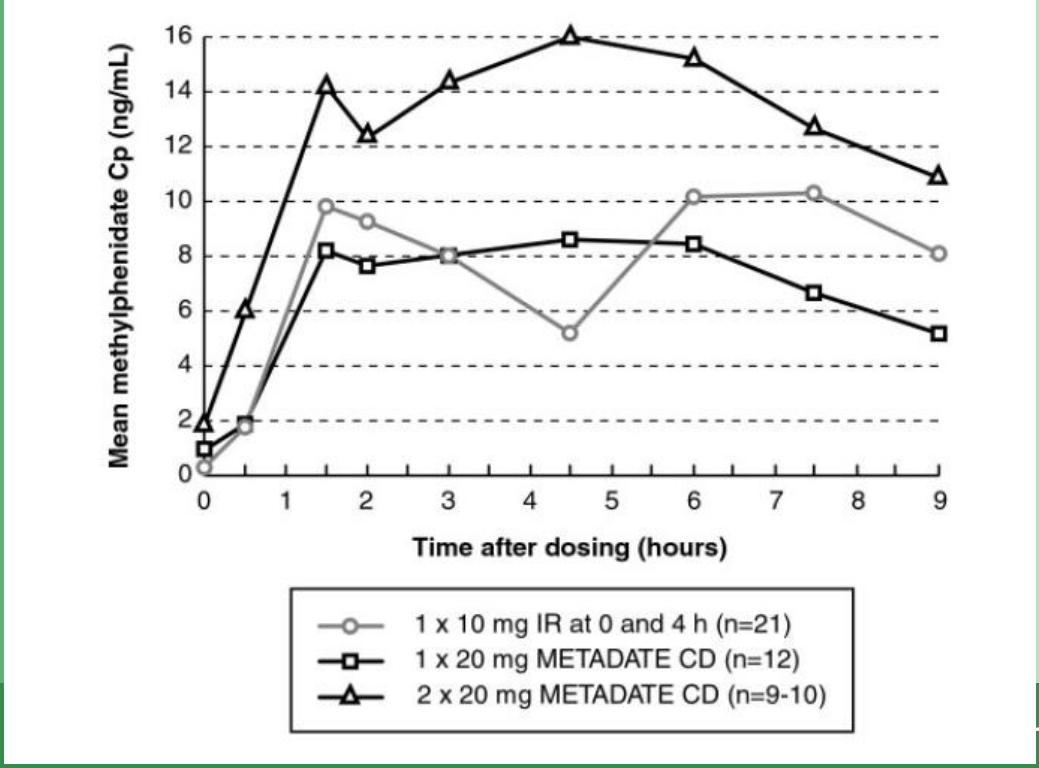




Metadate-CD

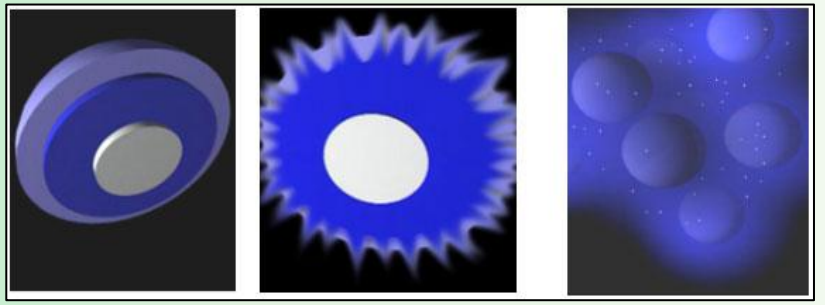
30% Immediate
70% after 4 hours
Peak(s): 1.5 h / 4.5 h
T ½: 6.8 hrs

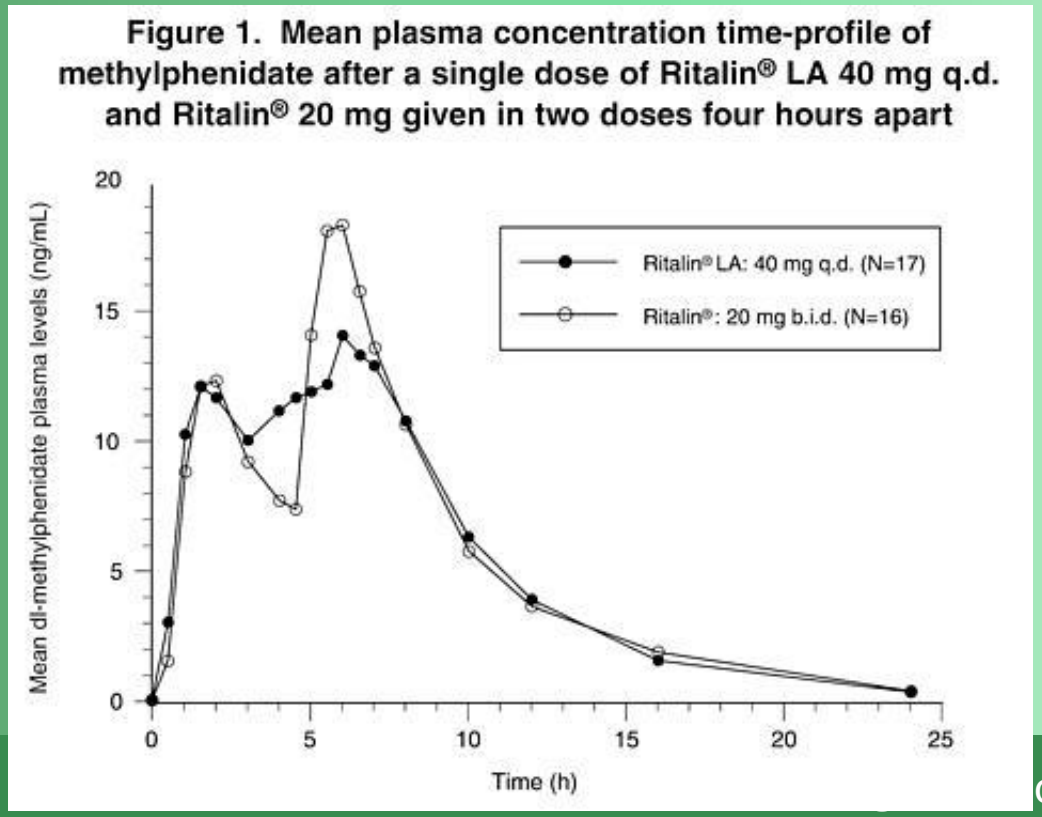




Ritalin-LA/Focalin-XR

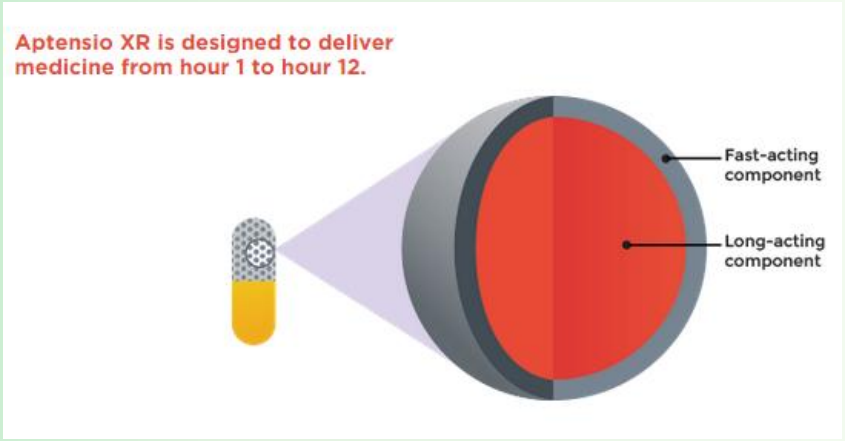
50% Immediate
50% after 4 hours
Peak(s): 2 h / 6.6 h
T ½: 2.4 hrs

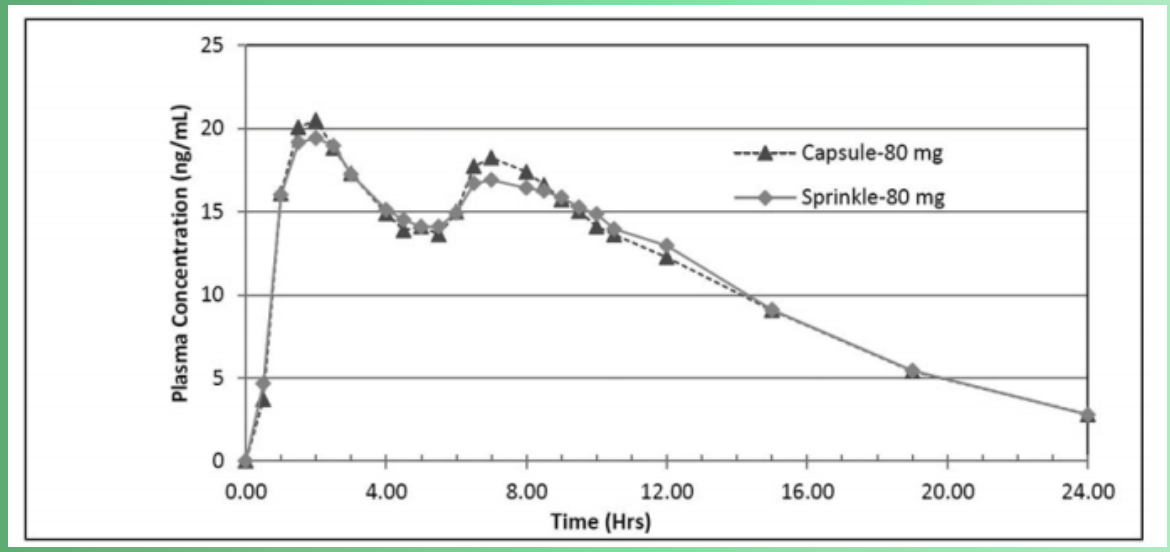




Aptensio-XR

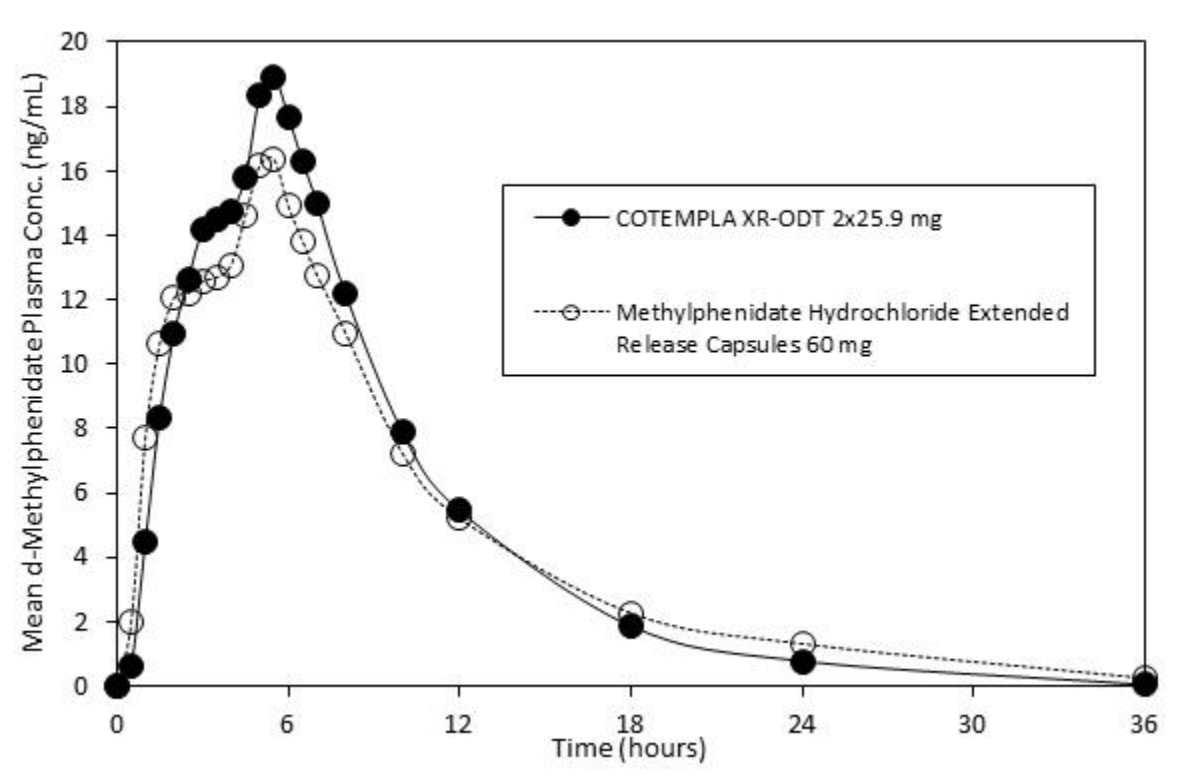
40% Immediate
60% after 4 hours
Peak(s): 2 h / 7 h
T ½: 5 hrs





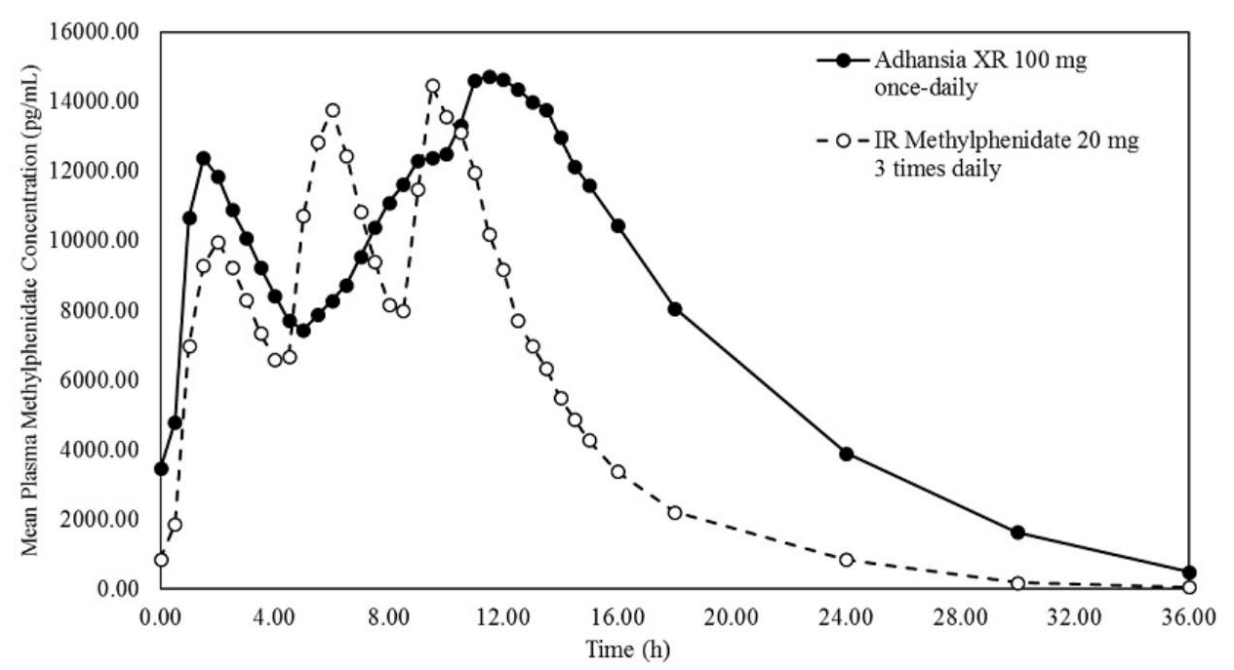
Cotempla-XL

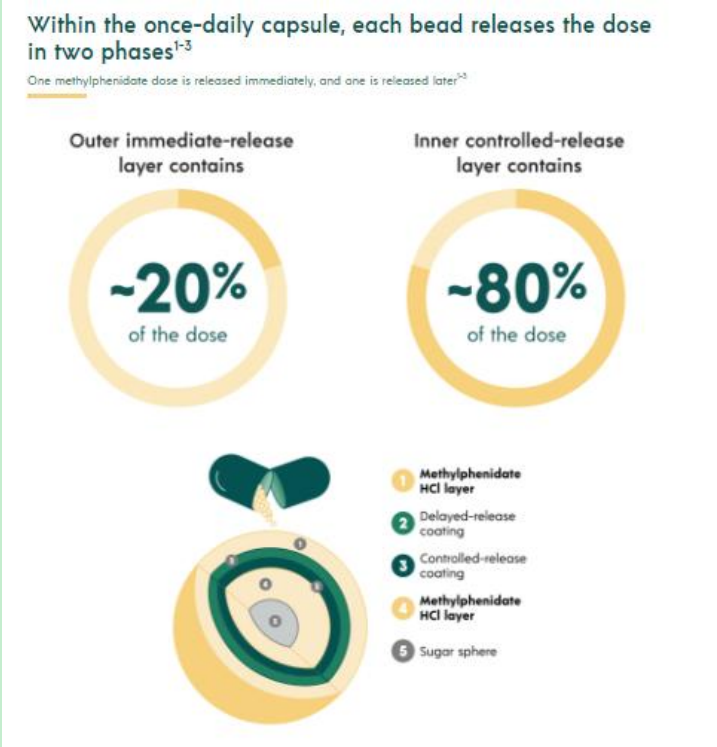
Peak(s): 4.5-5 hr
T ½: 4 hrs



Adhansia XR

Peak(s): 1.5, 12
T ½: 7 hrs





Adderall-XR

50% Immediate
50% after 4 hours
Peak: 7 hours
T ½: 10-13 hrs (but variable!)

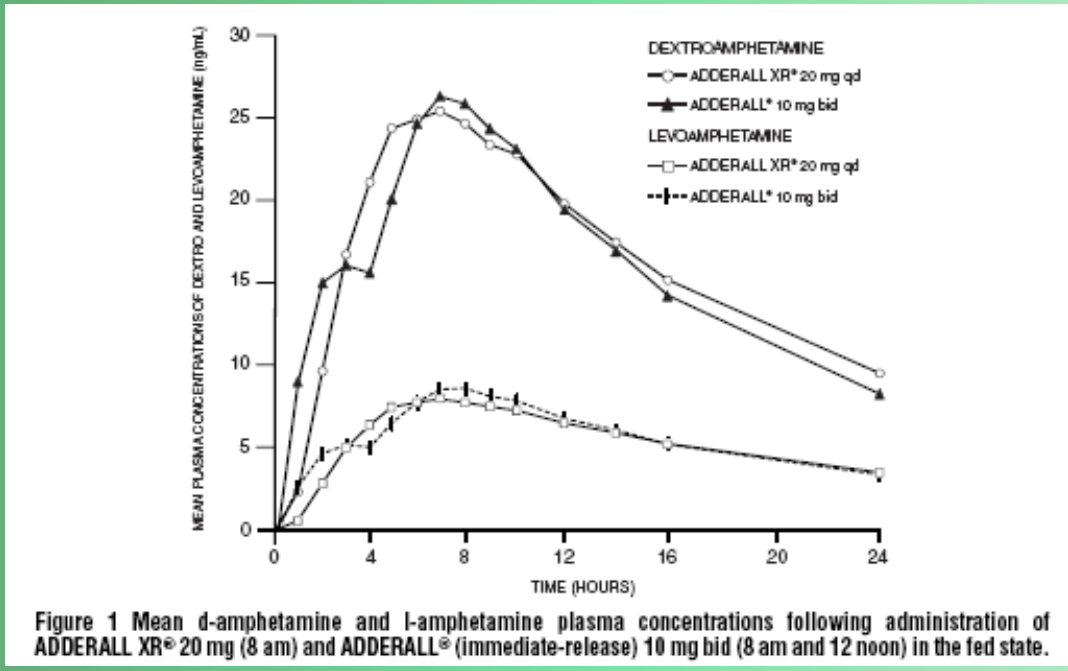
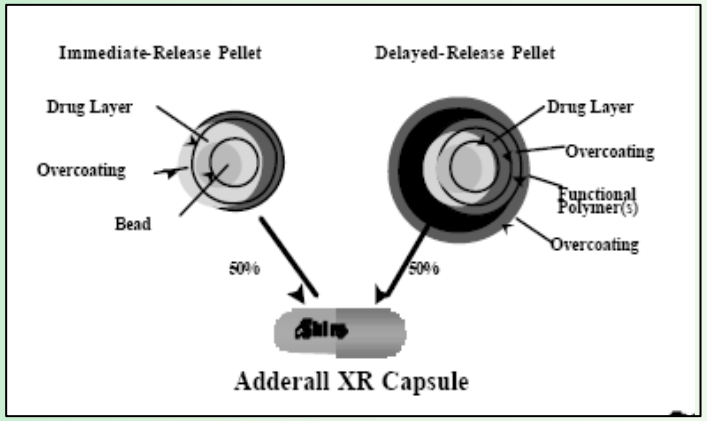
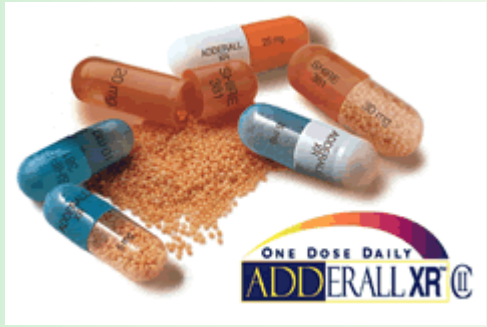


Figure 1 Mean d-amphetamine and l-amphetamine plasma concentrations following administration of ADDERALL XR® 20 mg (8 am) and ADDERALL® (immediate-release) 10 mg bid (8 am and 12 noon) in the fed state.



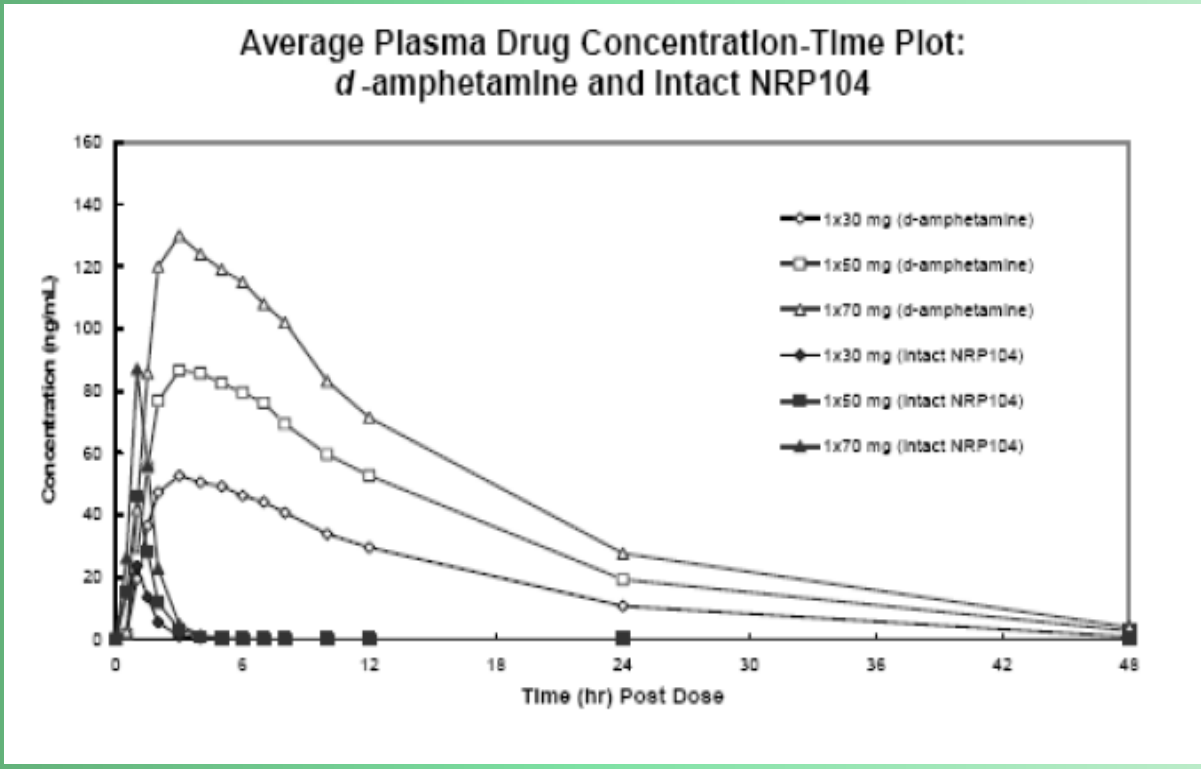
Adderall XR Capsule

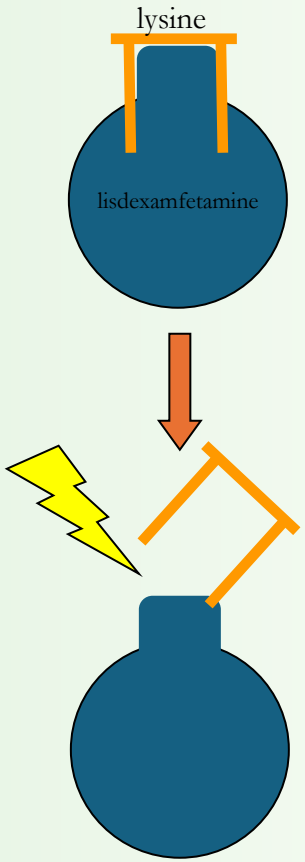


Lisdexamfetamine mesylate (Vyvanse)

BRIDGES TO MENTAL HEALTH

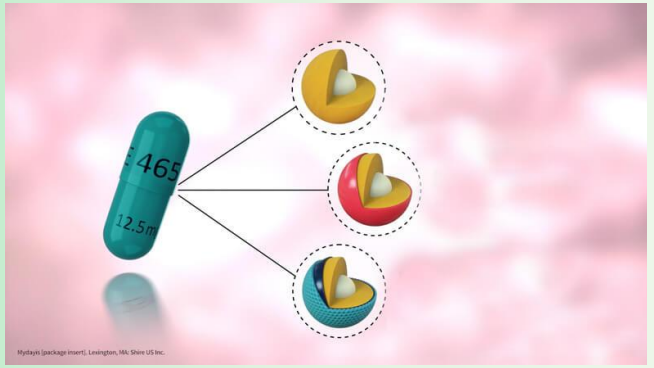
Peak: 3.5 hours
T ½: 9.6 hours

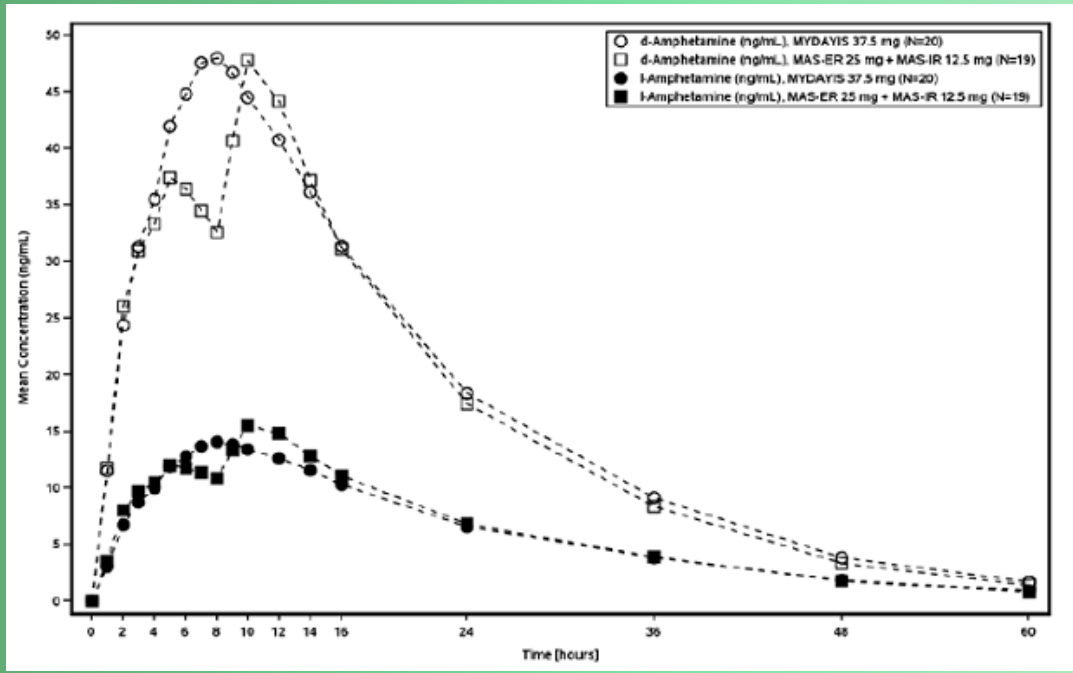


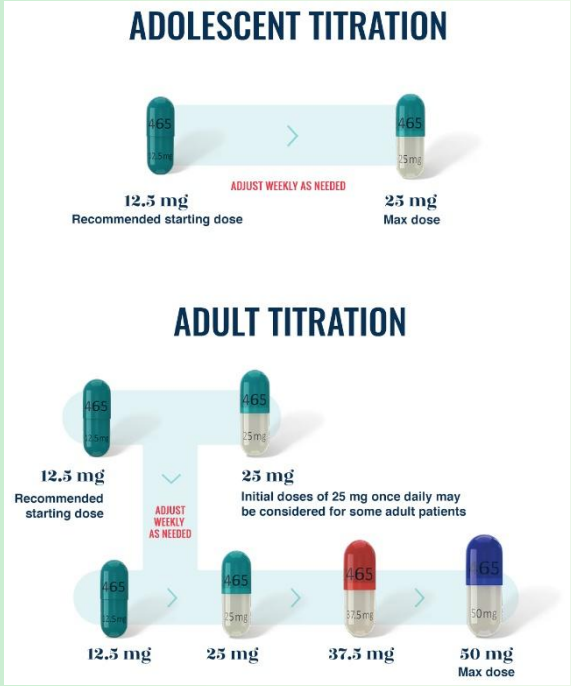


MyDayis

Peak(s): 7-10 hours
T ½: 11-13 hrs

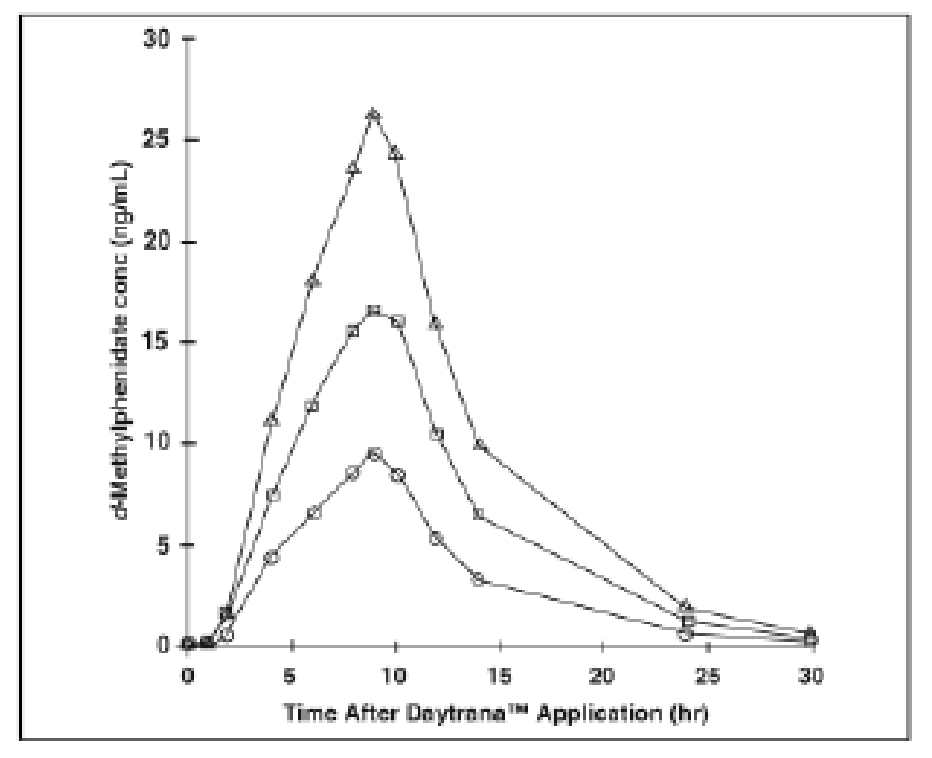


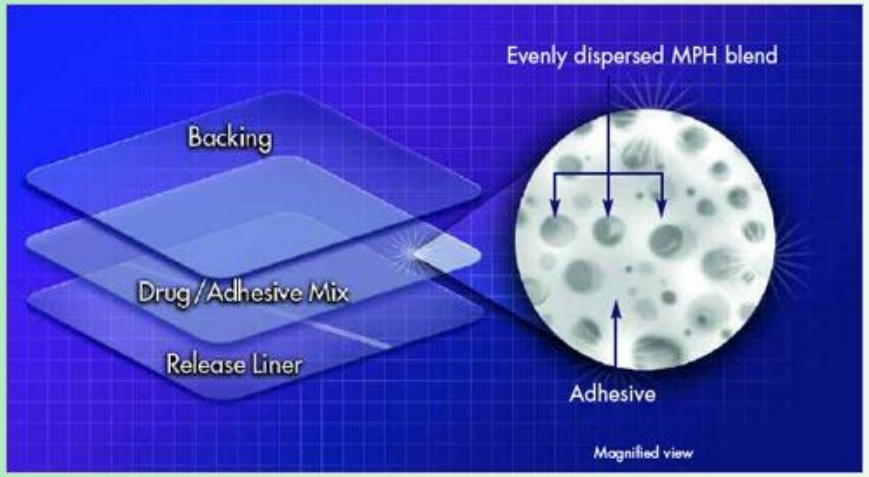




Daytrana

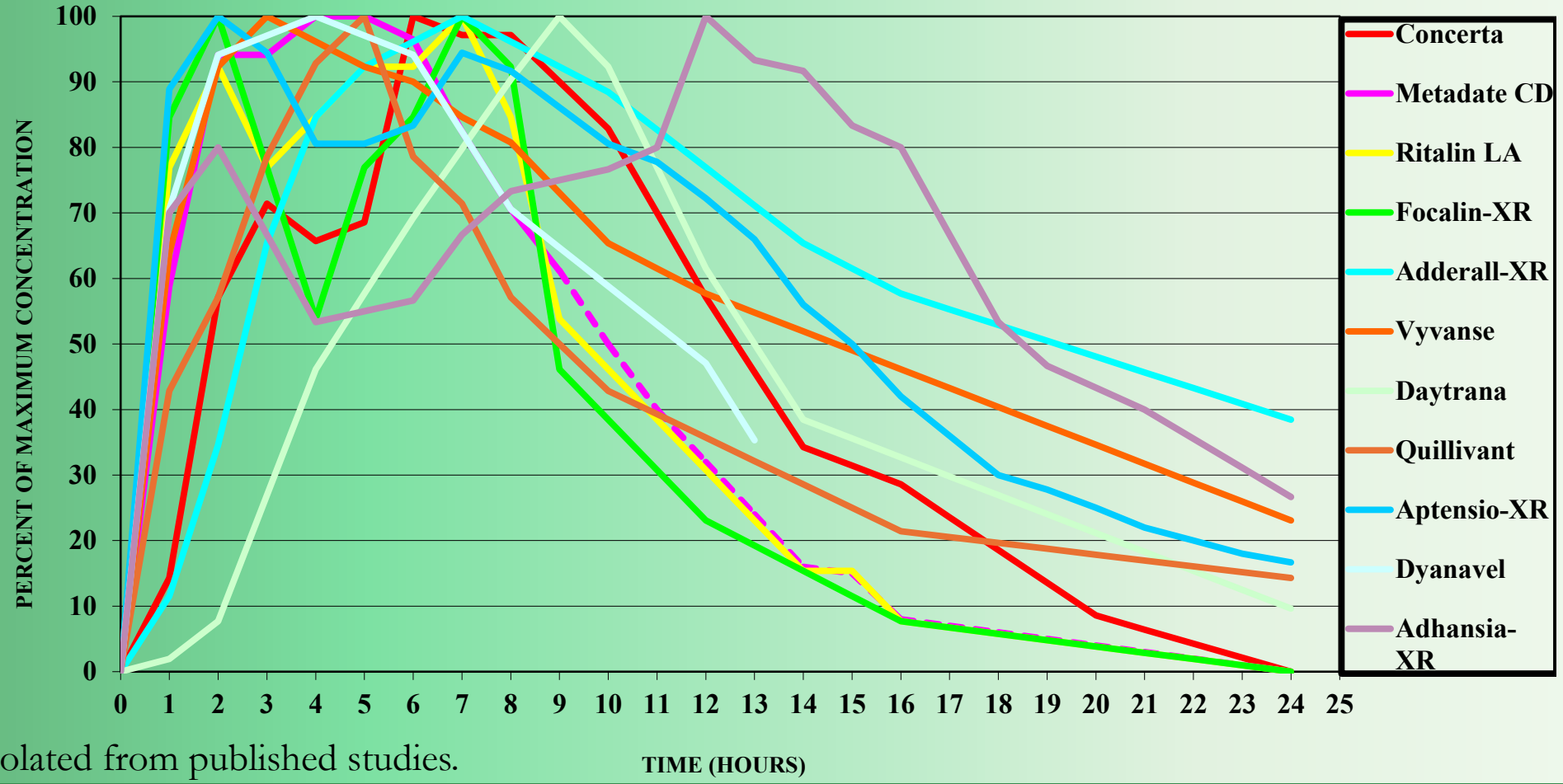
Peak: 9 hours after application
T ½: 3-4 hrs after removal





Rough Comparison* of Long-Acting Stimulant Serum Concentrations

BRIDGES TO MENTAL HEALTH



*Data interpolated from published studies.

Case (cont)

BRIDGES TO MENTAL HEALTH

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

Safety of Stimulants: Common Reactions

BRIDGES TO MENTAL HEALTH

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

Safety of Stimulants: Common Reactions

BRIDGES TO MENTAL HEALTH

- 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

BRIDGES TO MENTAL HEALTH

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

Conclusions

BRIDGES TO MENTAL HEALTH

- 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