

How to Select a Stimulant Formulation



A Carlat Webinar

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Conflicts and Disclosures

None

Learning Objectives

After the webinar, clinicians should understand:

Isomers

1. The risks and benefits of dextro- vs. levo-amphetamine
2. The risks and benefits of dex- vs. levo-methylphenidate

Modified Release Mechanisms

3. Key differences among modified release mechanisms
4. How to select the right isomer mix and modified release mechanism for your patient

Methylphenidate

Bottom Line

Safer, particularly with complex comorbidities

Better tolerated

Less effective in some patients

BEST CHOICE

Amphetamine

Bottom Line

Riskier, particularly in the young, elderly, and those at risk for abuse, mania, or psychosis

More effective in some patients

2ND CLASS

Methylphenidate

Ritalin
Methylin
Ritalin SR
Methylin ER
Metadate ER
Ritalin LA
Metadate CD
Aptensio XR
Adhansia XR
Concerta
QuilliChew ER
Quillivant XR
Cotempla XR-ODT
Daytrana
Jornay PM
Azstarys
Focalin
Focalin XR

Amphetamine

Adderall
Adderall XR
Adzenys XR-ODT
Adzenys ER liquid
Dyanavel XR liquid
Mydayis
Evekeo
Evekeo ODT
Dexedrine
Zenzedi
Dexedrine Spansules
Vyvanse



Isomers: Levo vs. Dex

For amphetamines...

Dextro- more potent (2-4 times vs levo)

Levo- longer duration, more cardiac side effects

For methylphenidate...

Dex- accounts for all efficacy

Levo- is practically inert

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Methylphenidates

Ritalin, Concerta, etc

Methylphenidate

50/50 Dex/Levo

Ritalin 1955

Ritalin SR 1987

Methylin ER

Metadate ER

Ritalin LA 2000

Metadate CD 2001

Concerta 2001

Daytrana patch 2006

Quillivant XR 2012

QuilliChew ER 2015

Cotempla XR-ODT '17

Jornay PM 2018

Aptensio XR 2015

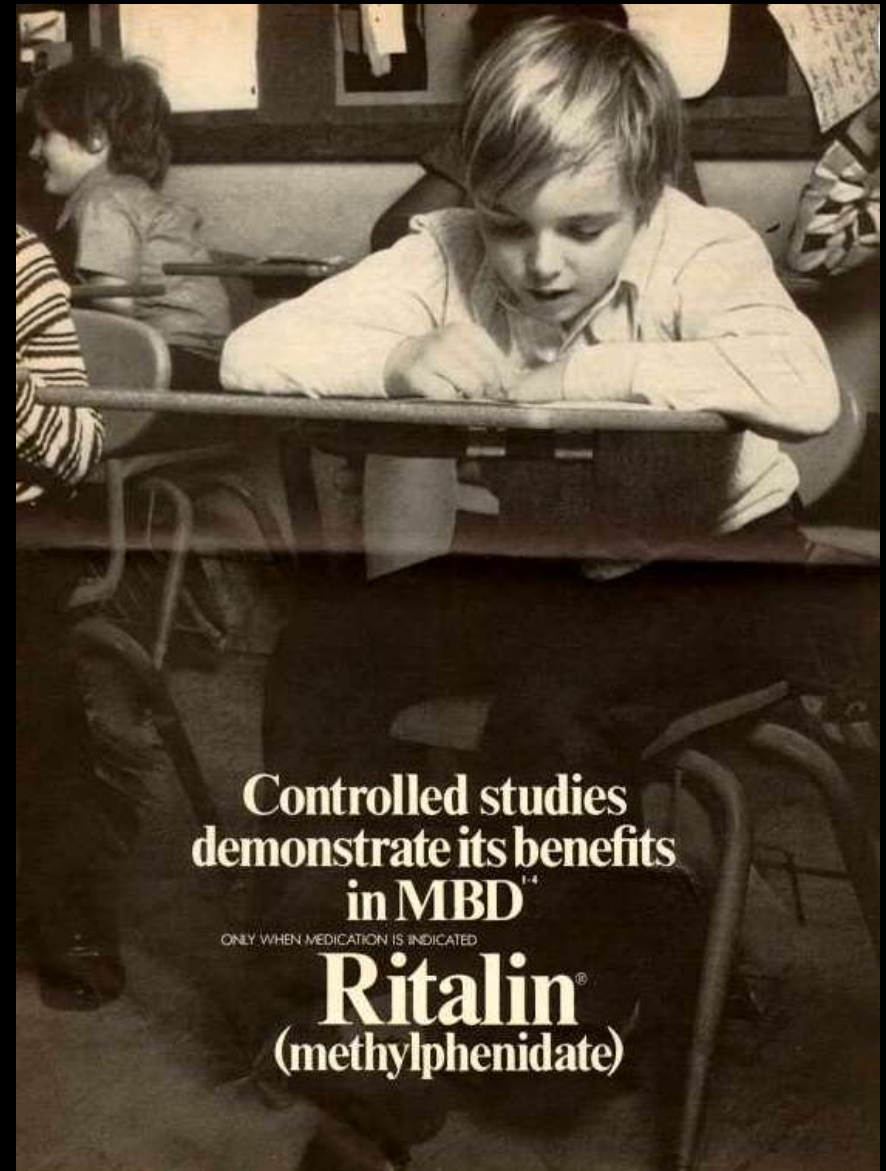
Adhansia XR 2019

100% Dexmethylphenidate

Focalin 2001

Focalin XR 2005

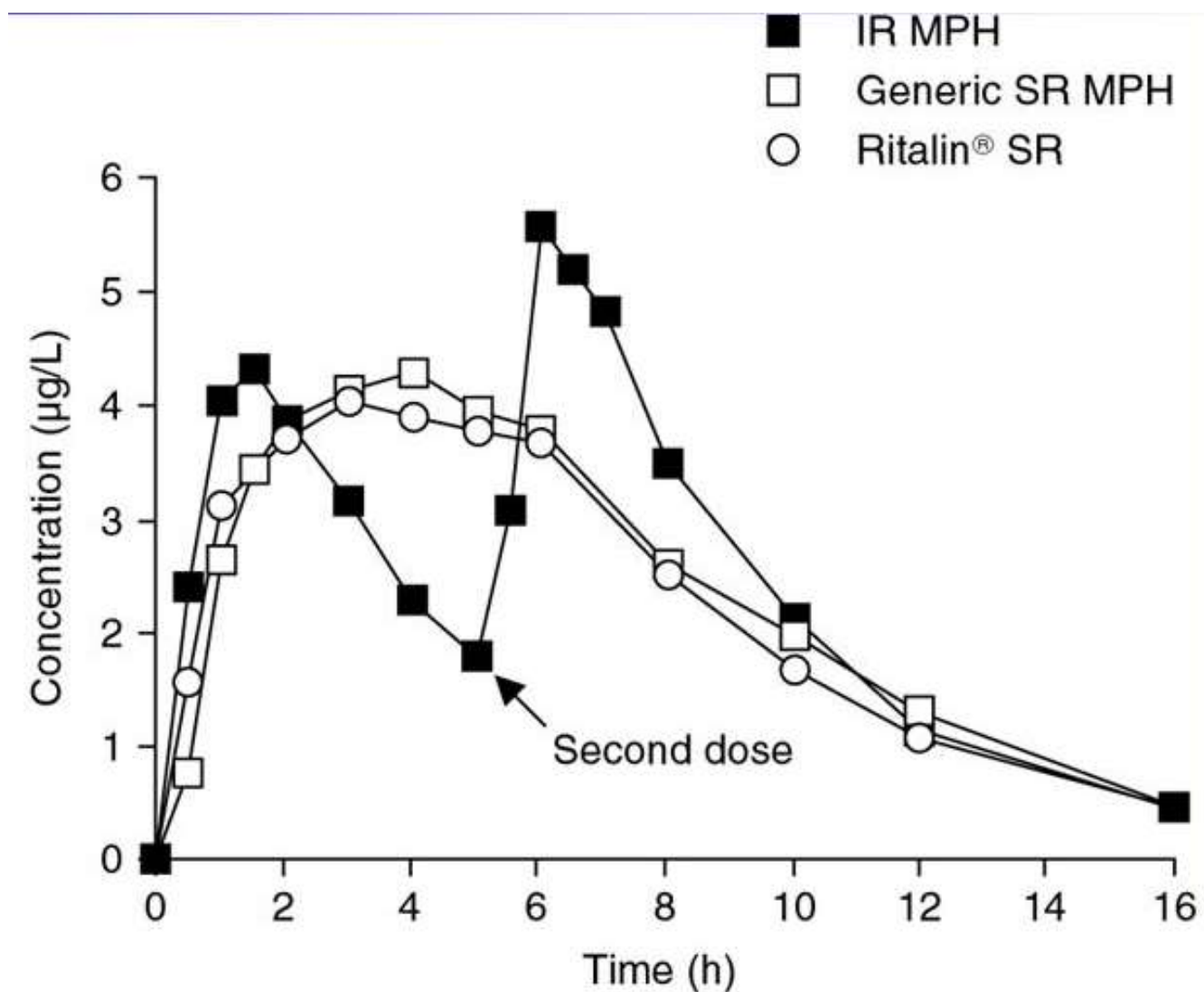
Azstarys 2022



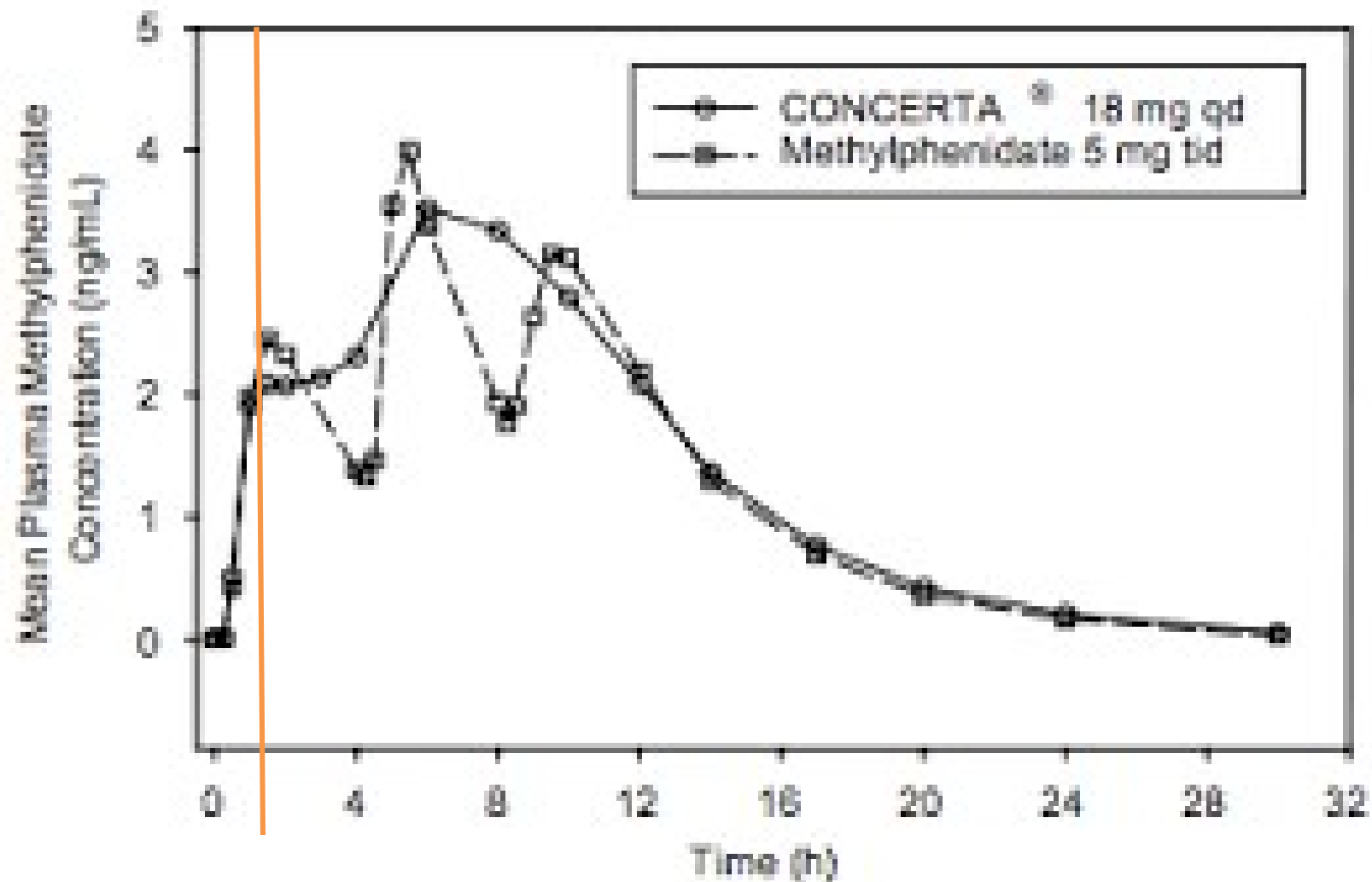
Methylphenidates 50/50 dex:levo

	Form	Dur	Max	Cost	Notes
GENERIC	Methylphenidate IR	3-5 hr	60mg	\$20	Rapid onset (15-30 min) Tabs, Methylin chewable tabs, liquid
	Methylphenidate SR	4-8	60mg	\$25	Waxy release mechanism has inconsistent effects Ritalin SR, Methylin ER, Metadate ER
	Metadate CD	8-9	60mg	\$40	50% instant, 50% delayed
	Methylphenidate LA	6-9		\$50	30% instant, 70% delayed (wax-coated) release caps
	Methylphenidate OROS ER (Concerta)	12	72mg	\$40	22% instant, 78% delayed. Slow onset (1-2 Hr), but greater efficacy in later part of day
BRAND ONLY	QuilliChew ER	8	60mg	\$337	Fast onset (45 min). Cherry chews
	Quillivant XR	8-12	60mg	\$289	Banana liquid. Onset in 1 hr
	Cotempla XR-ODT	12	51.8mg	\$348	Similar to Concerta but orally dissolving To convert to methylphenidate, multiply by 1.16
	Daytrana patch	9-12	30mg	\$350	Risk = chemical leukoderma, skin irritation, falls off. Slow onset (2 hr), lasts 2-3 hr after patch is removed.
	Aptensio XR	12	60mg	\$250	Onset 1 hr
	Jornay PM	9-12	100mg	\$300	Taken at night with onset upon waking To convert to methylphenidate, multiply by 0.74
	Adhansia	13-16	85mg	\$350	Onset 1 hr

Ritalin SR vs instant release

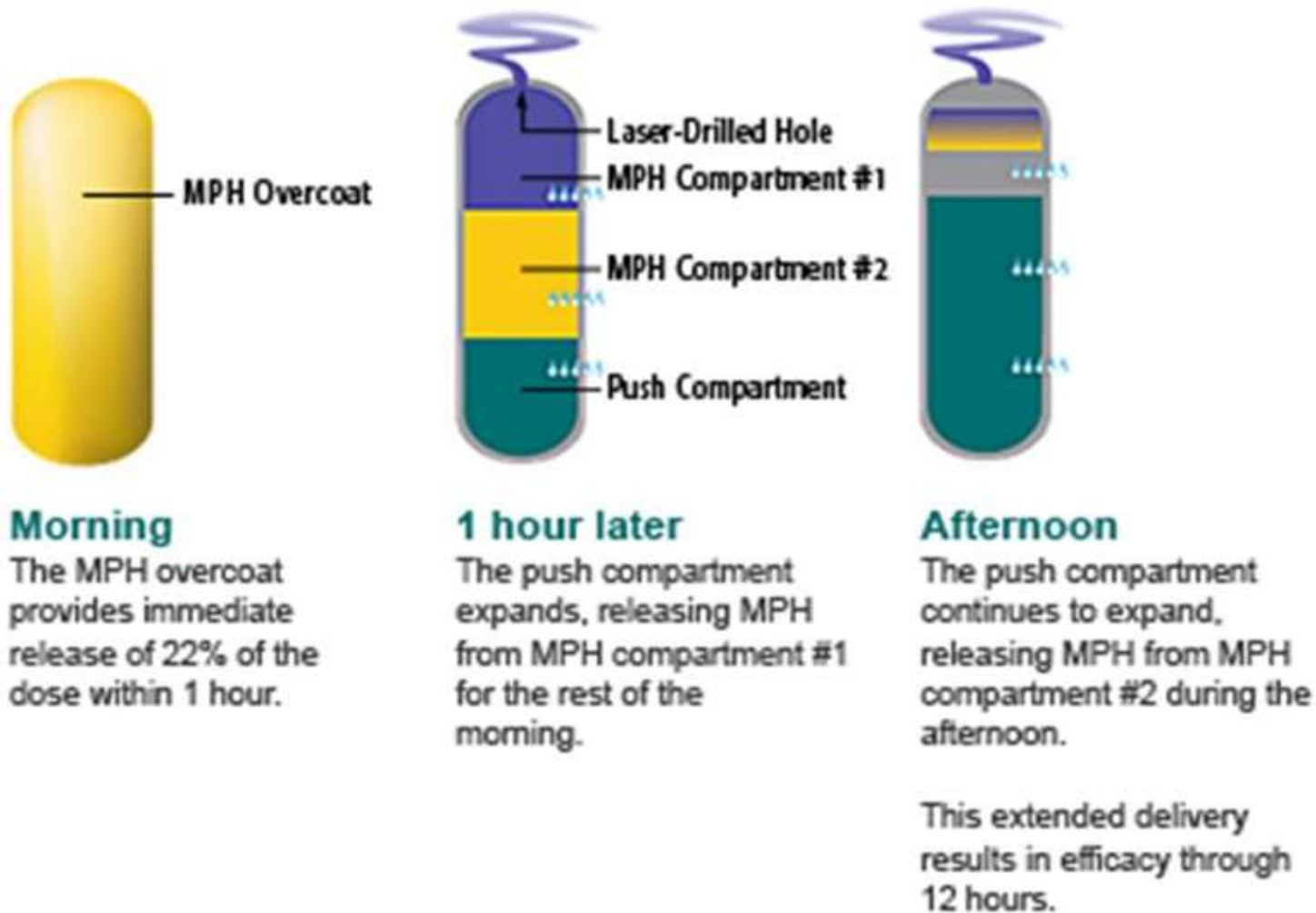


Concerta vs instant release

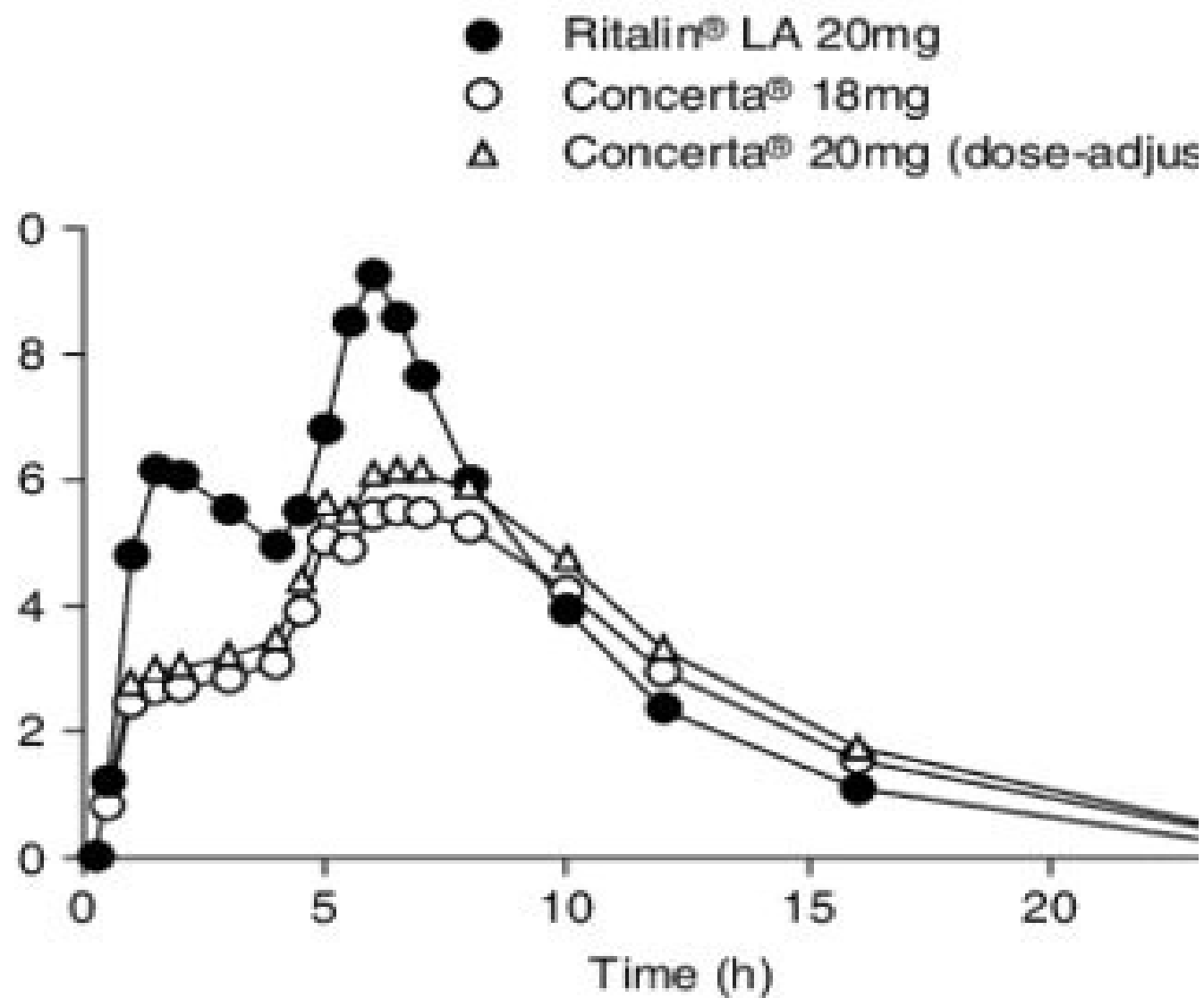


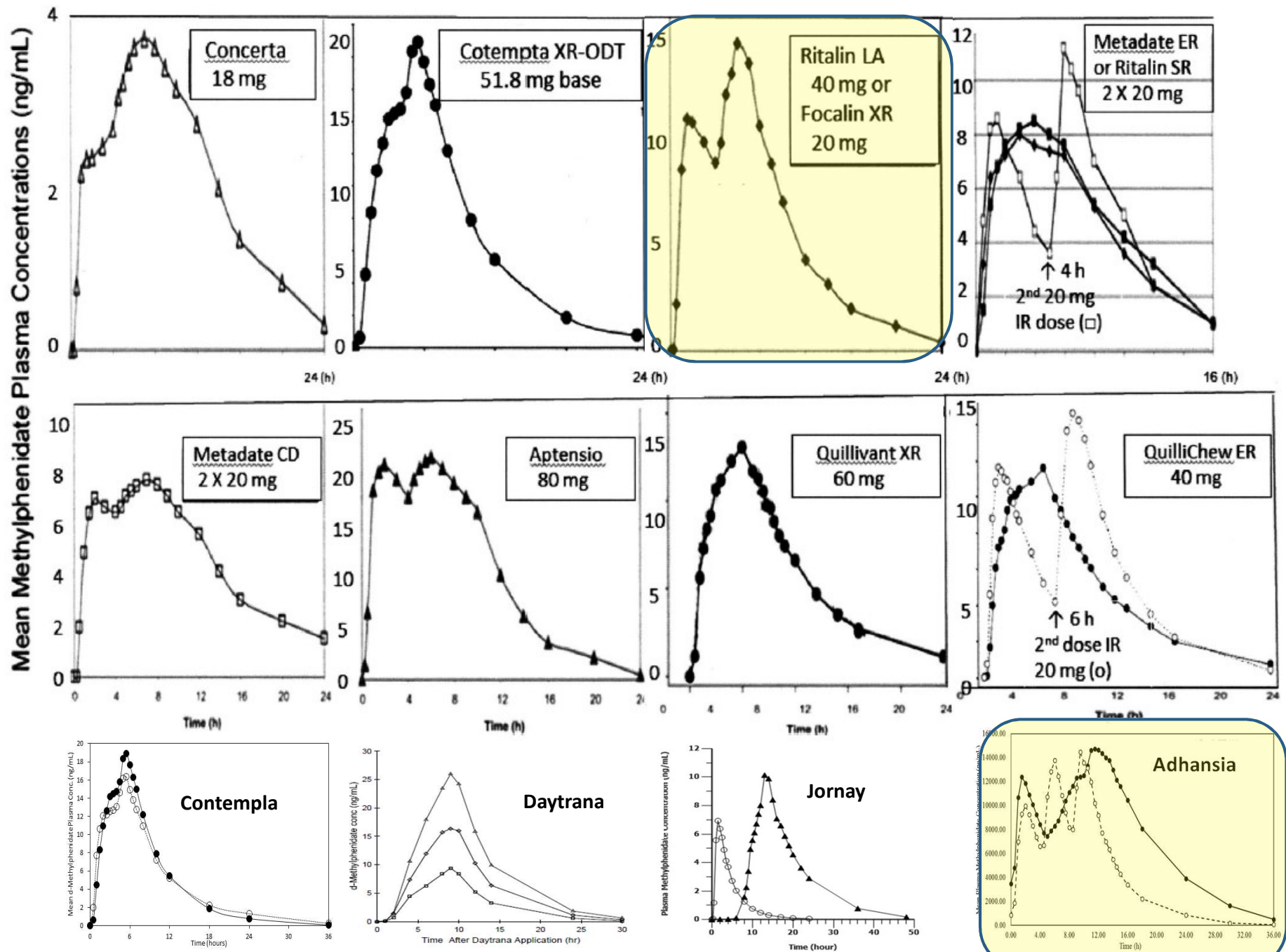
1 hour of instant
release

Concerta OROS (methylphenidate ER)



Concerta vs. Ritalin LA



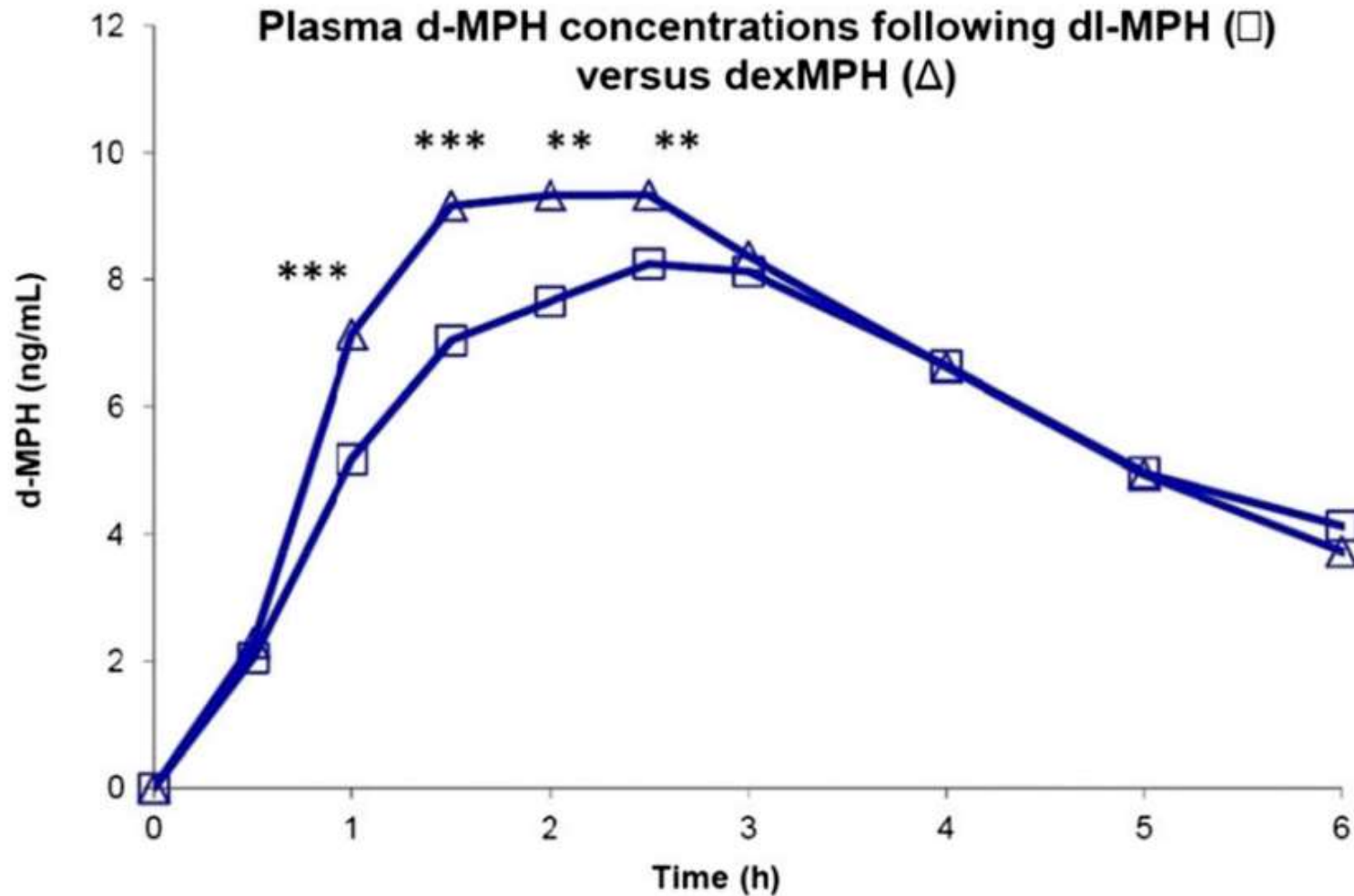


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Methylphenidates

Focalin etc

The dex- isomer peaks higher in dexamethylphenidate than in methylphenidate



Dexmethylphenidates 100% dex

Form	Dur	Max	Cost	Notes
Dexmethylphenidate (Focalin)	3-6 hr	20 child	\$20	Fast onset (15-30 min)
Dexmethylphenidate ER (Focalin XR)	8-12	30 child 40 adult	\$50	Fast onset (30 min), Biphasic (2 peaks)
Ser-Dex/Dexmethyl (Azstarys)	10-11	52.3/ 10.4 mg	\$390	Abuse deterrent prodrug (like Vyvanse) Duration 10 hr, fast onset (30 min)

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Amphetamines

Adderall, Vyvanse & Co

Amphetamine

50/50 Dextro/Levo

Evekeo 2014

Benzedrine 1935

Adderall & Co

75/50 Dextro/Levo

Adderall 1996

Adderall XR 2001

Adzenys XR ODT, Liquid 2016

Dyanavel XR liquid 2016

Mydayis 2017

100% Dextroamphetamine

Dexedrine, Zenzedi 1937

Dexedrine Spansules 1952

Vyvanse 2007



"...if the individual is depressed..."

"... if the individual is depressed or anhedonic . . . you can change his attitude . . . by physical means just as surely as you can change his digestion by distressing thought . . . In other words, drugs and physical therapeutics are just as much psychic agents as good advice and analysis and must be used together with these latter agents of cure."

Myerson, A.—*Anhedonia*—*Am. J. Psychiat.*, July, 1922.

When this was written—in 1922—the only stimulant drugs employed in the treatment of simple depression were of limited effectiveness.

Only in the last decade has there been available—in Benzedrine Sulfate—a therapeutic weapon capable of alleviating depression, overcoming "chronic fatigue" and breaking the vicious circle of anhedonia.



**BENZEDRINE
SULFATE TABLETS**

(racemic amphetamine sulfate)

Amphetamines 1:1 and 3:1 Dex/Levo

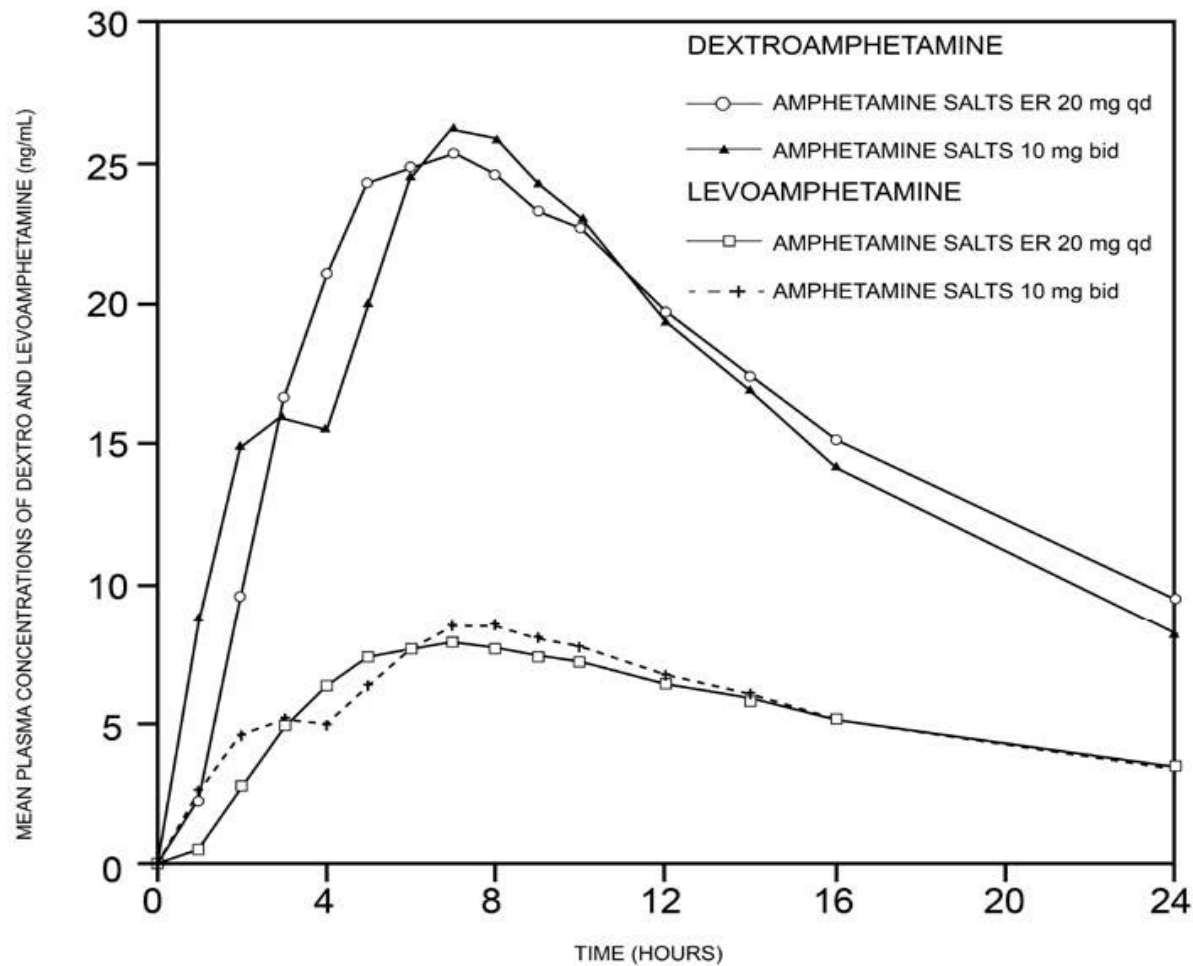
Ratio	Form	Dur	Max	Cost	Notes
1:1	Amphetamine (Evekeo IR, ODT)	9-10 hr	60mg	\$60	Less effective in most, more cardiac risks, less anorexia
3:1	Adderall IR	4-6	40mg	\$20	Slower onset than methylphenidate (1 Hr) Multiply by 1.3 to approximate Evekeo dose
3:1	Adderall XR	10-12	40mg	\$30	Taking with a high-fat meal can lower serum levels in the first half of the day
3:1	Mydayis	14-16	50mg	\$227	Long duration, but greater risk of insomnia
3:1	Adzenys XR-ODT Adzenys ER Liquid	10-12	18.8mg	\$326 ODT \$665 ER	Dissolves in the mouth with an orange flavor To convert to Adderall, multiply by 1.6
3:1	Dyanavel-XR Liquid	12	20mg	\$597	Onset is slower than other IR's (1 Hr)

Dextro-amphetamines

Form	Duration	Max	Cost	Notes
Dextroamphetamine	4-6 Hr	40mg	\$20	Multiply by 1.2 to approximate Adderall dose Liquid (ProCentra) lasts 6-10 Hr
Dextroamph ER (Dexedrine Spansules)	6-10 Hr	40mg	\$35	Multiply by 2.5 to convert to Vyvanse dose
Lisdexamfetamine (Vyvanse)	12-14 Hr	70mg	\$350	Abuse deterrent. Smooth levels. FDA-approved in <i>pure</i> binge eating (50-70 mg/d)

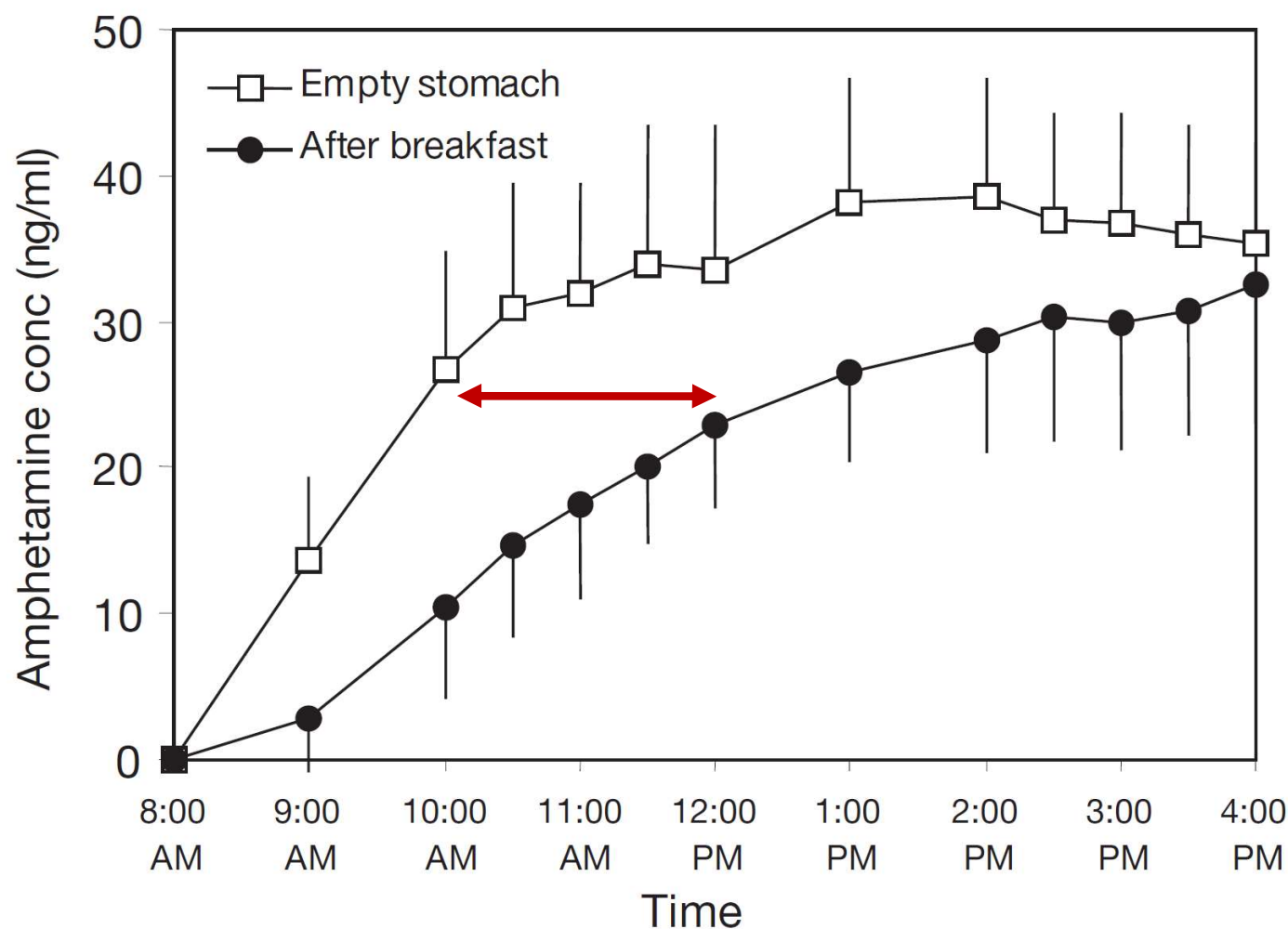
Adderall XR

10-12 hour duration vs. 4-6 for instant release



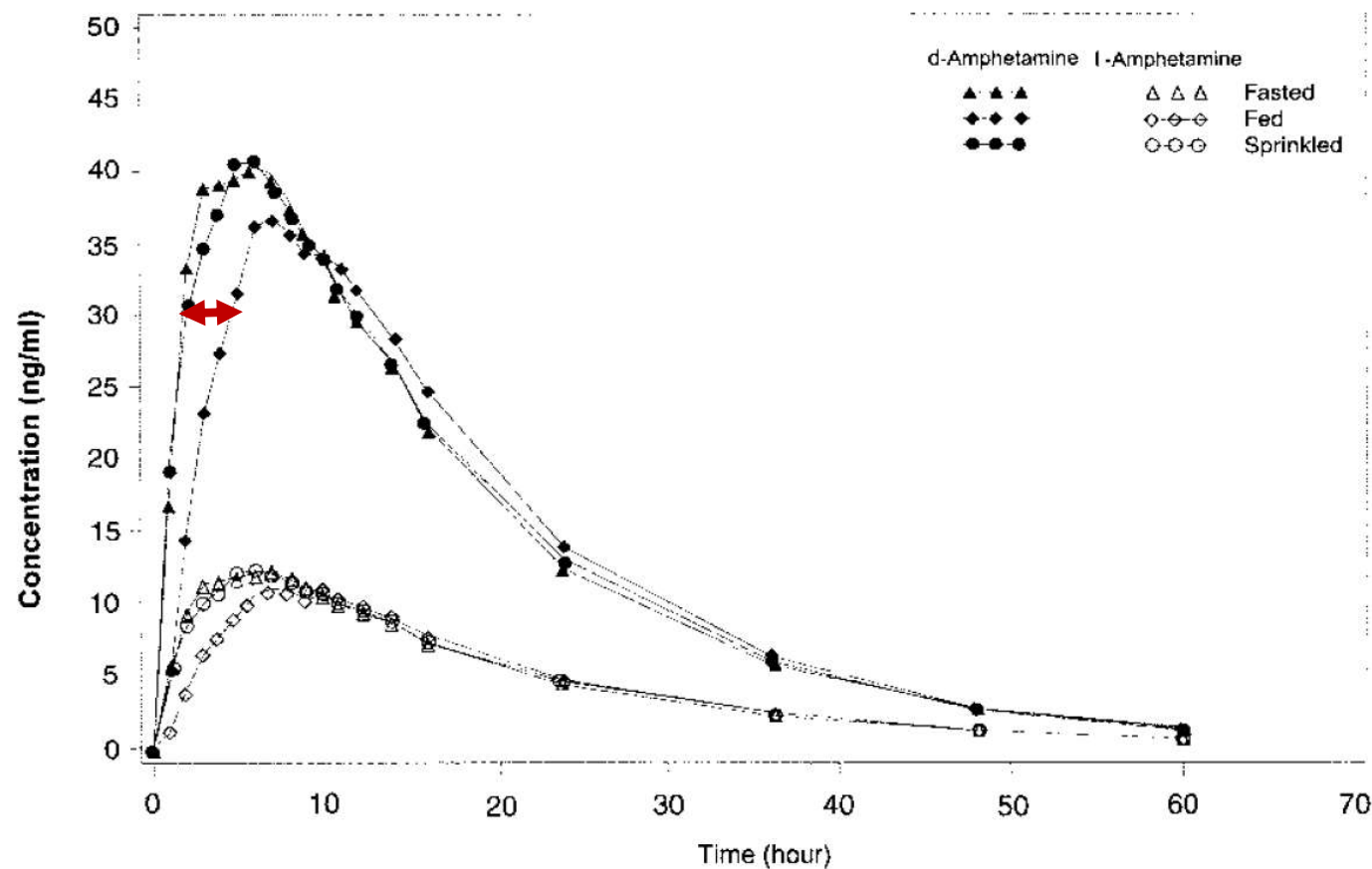
Adderall XR

Delayed by 2 hr with high-fat breakfast?



Adderall XR

Delayed by 2 hr with high-fat breakfast?



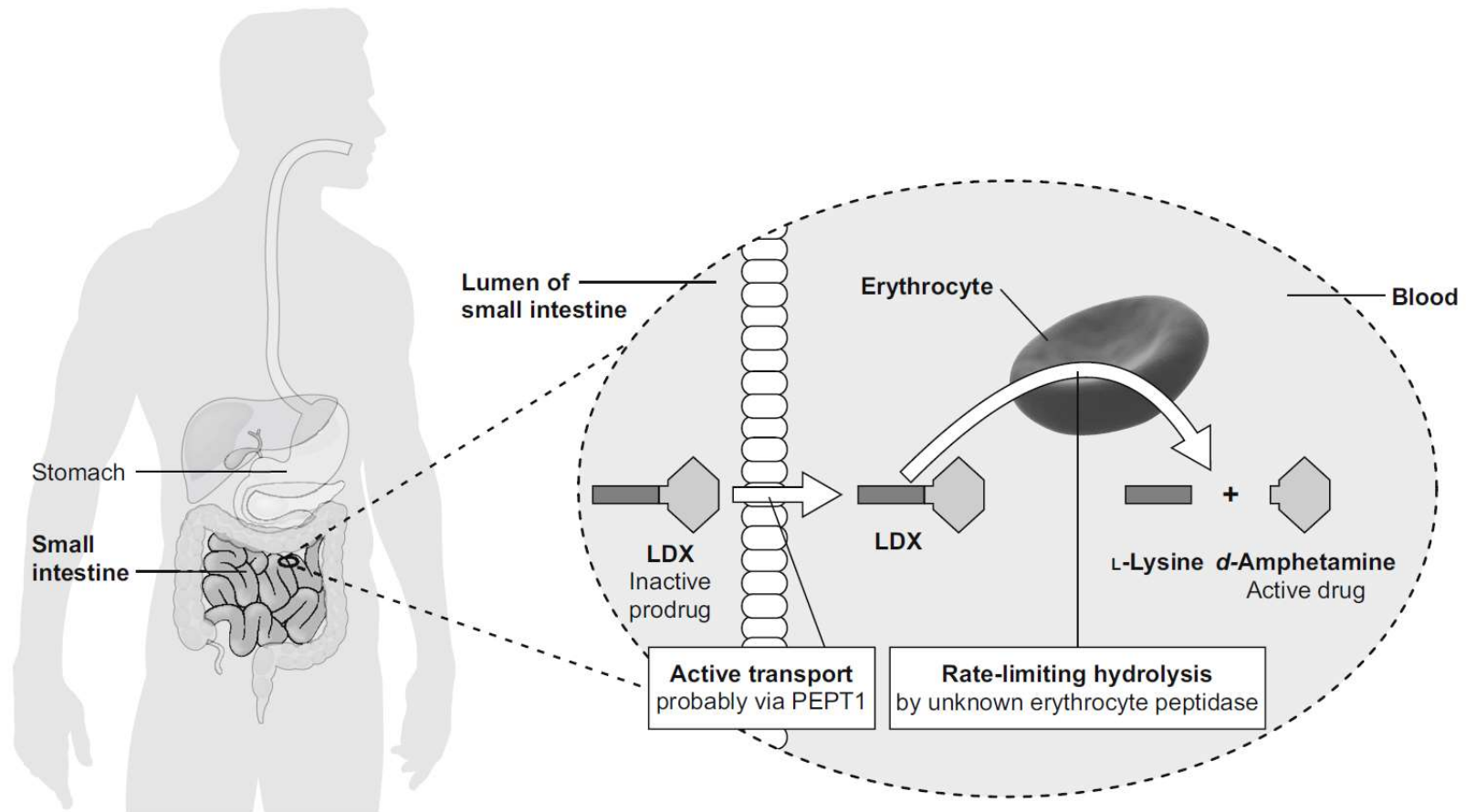
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Prodrugs

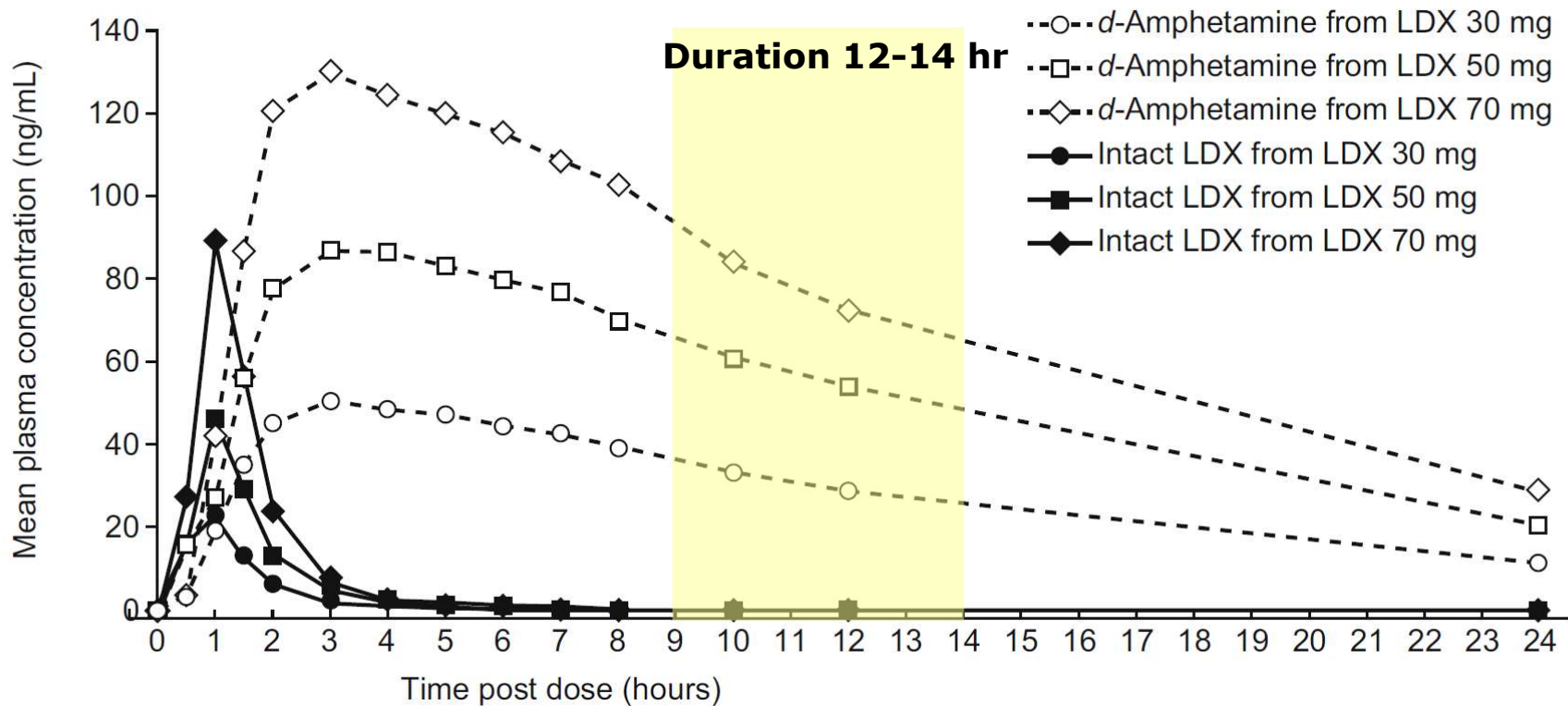
lis-dexamfetamine (*Vyvanse*)

ser-dexmethylphenidate *Azstarys*

Vyvanse (lis-dexamfetamine)

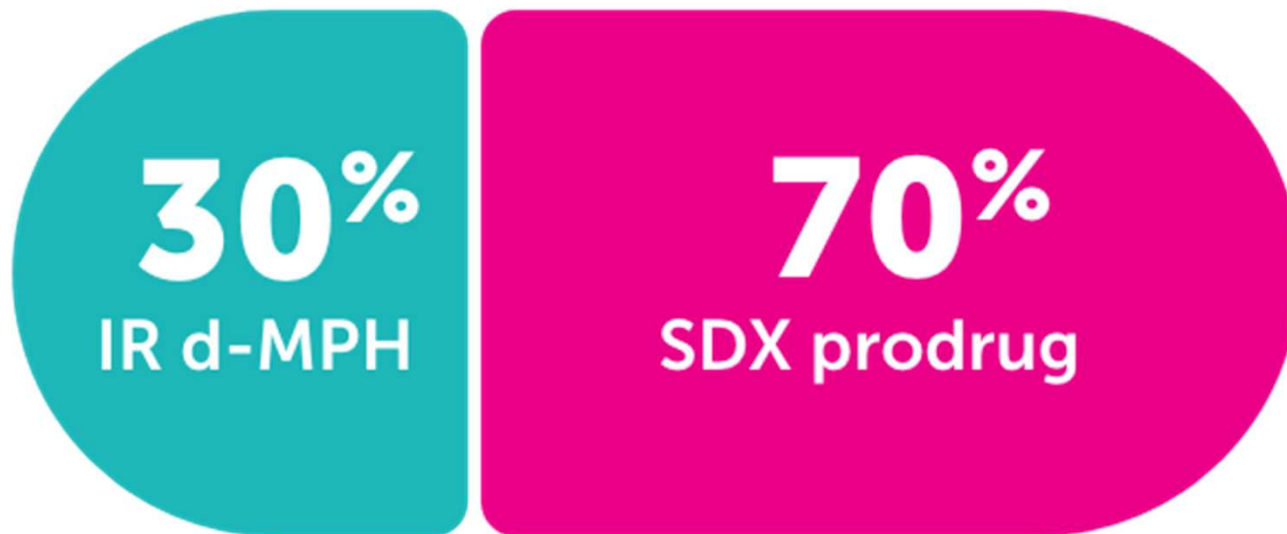


Lis-dexamfetamine (Vyvanse)

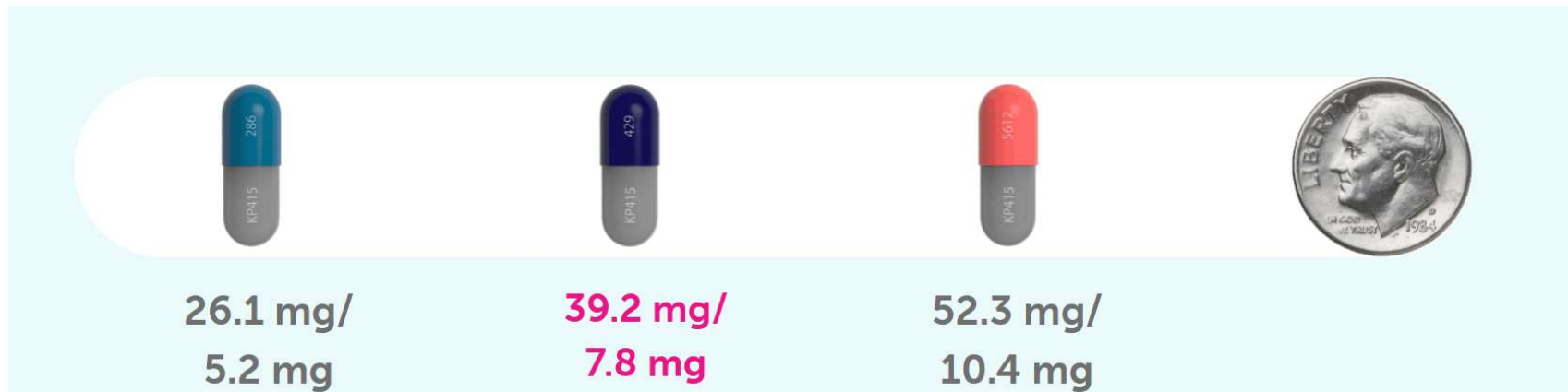


Azstarys

Prodrug is continuously converted in lower GI tract to extend the release



Azstarys



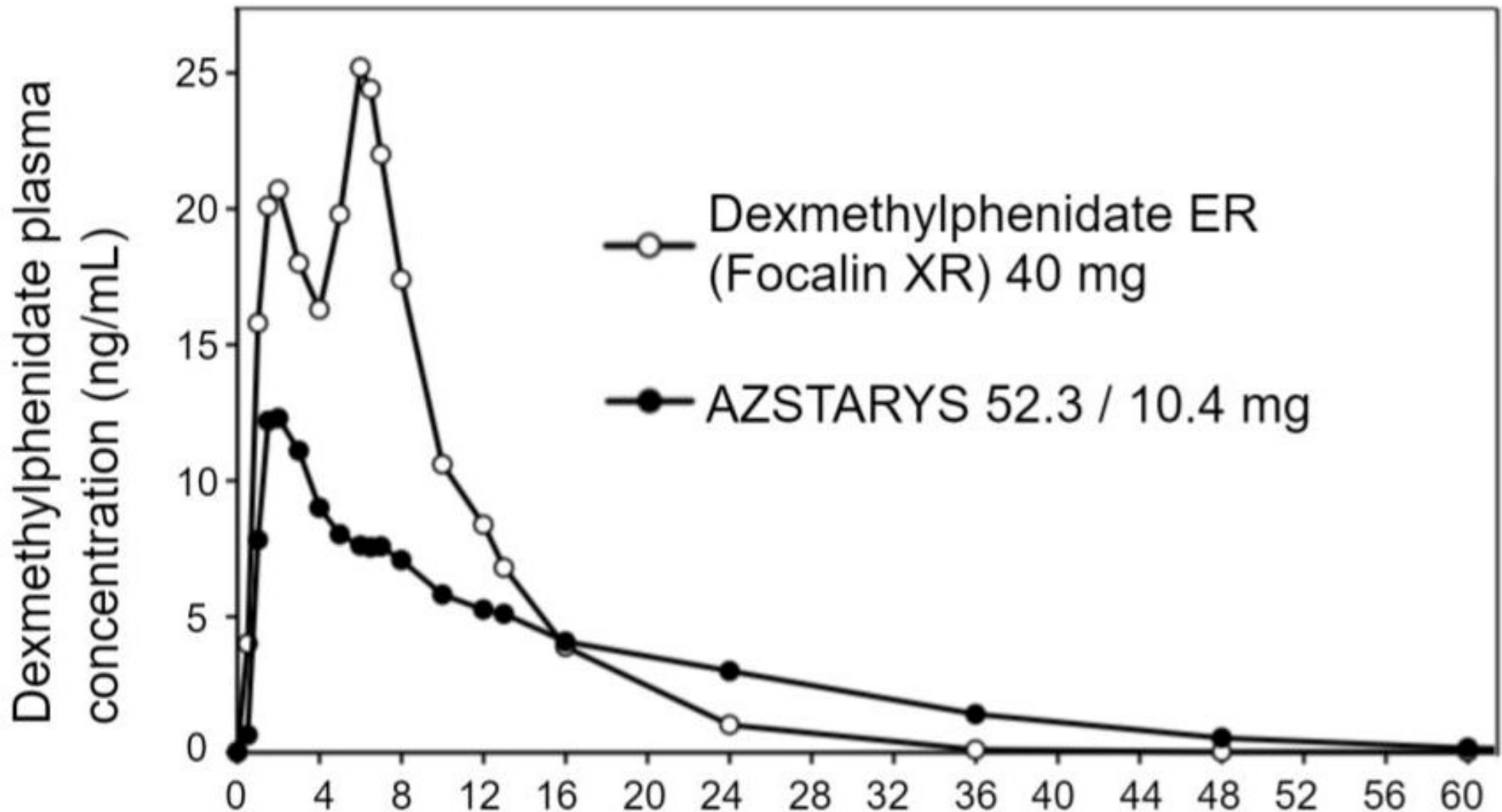
Equivalent to dexmethylphenidate (Focalin)

20mg

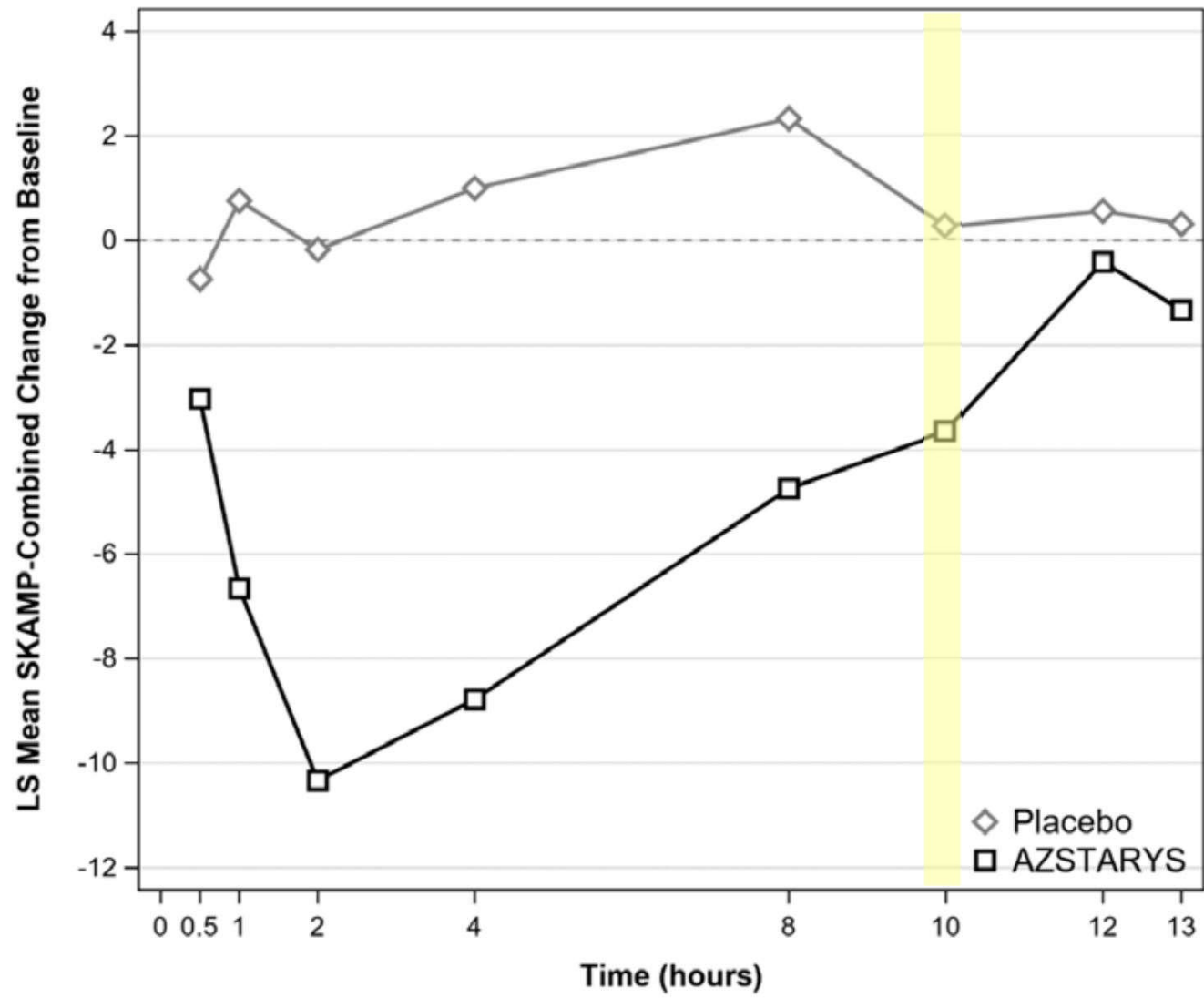
30mg

40mg

Is Azstarys 52/10 really equivalent to dexamethylphen 40?



Does Azstarys really last 13 hours?



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Converting

Converting Methylphenidate to Amphetamine

	Adderall	Evekeo	Dexedrine	Vyvanse
from methylphenidate	Methylphen x 0.5	Methylphen x 0.65	Methylphen x 0.4	Methylphen x 1.0
to methylphenidate	Adderall x 2	Evekeo x 1.5	Dexedrine x 2.5	Vyvanse x 1.0

Absorption Adjustments

These stimulants have unique bioavailability that requires special dosage adjustment

Cotempla ODT-XR	Jornay PM	Adzenys ODT
Methylphenidate x 0.86	Methylphenidate x 1.35	Adderall x 0.63

Transderma Daytrana has its own conversion table

Concerta	Ritalin LA or Metadate CD	Daytrana
18 mg/day	10-20 mg/d	10 mg/9 hr wear time
27 mg/day	30 mg/day	15 mg/9 hr wear time
36 mg/day	40 mg/day	20 mg/9 hr wear time
54 mg/day	50 mg/day	30 mg/9 hr wear time

Converting Amphetamines

	Adderall	Evekeo	Dexedrine	Vyvanse
Adderall Conversion	---	Adderall x 1.3	Adderall x 0.83	Adderall x 2.0
Dextroamphetamine Conversion	Dextro x 1.2	Dextro x 1.6	---	Dextro x 2.5

Here is how that looks for Adderall 20mg

Adderall XR	Evekeo	Dexedrine	Vyvanse
20 mg qam	26 mg qam	16 mg SR qam	40 mg qam

1952: Dexedrine Spansules

