



KemPharm

ADHD Investor Event

October 11, 2018

Cautionary Note Regarding Presentation Information

This presentation contains forward-looking statements, including statements about our plans to develop and commercialize our product candidates, our planned clinical trials for our prodrug product candidates, the timing of and our ability to obtain and maintain regulatory approvals for our product candidates, including expectations about our ability to use the 505(b)(2) pathway and expedited FDA review, the clinical utility of our product candidates and our intellectual property position. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this presentation. These and other risks concerning our business are described in additional detail in our Quarterly Report on Form 10-Q filed with the SEC on August 10, 2018, and our other Periodic and Current Reports filed with the SEC. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Further, the information contained in this presentation speaks only as the date hereof. While we may elect to update the information in this presentation in the future, we disclaim any obligation to do so except to the extent required by applicable law.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.



Welcome to KemPharm's ADHD Investor Event!

KOL and Prescriber Perspectives on the ADHD Treatment Landscape and Stimulant Abuse/Misuse

- **Travis C. Mickle, PhD**

President and Chief Executive Officer, KemPharm, Inc.



KemPharm ADHD Investor Event Key Opinion Leaders

- **Ann Childress, MD**

President of the Center for Psychiatry and Behavioral Medicine in Las Vegas; Adjunct Faculty Member at the University of Nevada School of Medicine and at Touro University Nevada; Board Certified in Psychiatry, with a subspecialty in Child and Adolescent Psychiatry; Education Director of the Nevada Psychiatric Association

- **Matthew Brams, MD**

Chief Medical Officer of Cingulate Therapeutics; Assistant Professor of Psychiatry at Baylor College of Medicine; Lead Investigator in several pivotal trials of drugs for the treatment of ADHD; Lifetime Board Certified in Adult, Adolescent and Child Psychiatry and Senior National Board Examiner for the American Board of Psychiatry and Neurology



KemPharm ADHD Investor Event Key Opinion Leaders

- **Timothy E. Wilens, MD**

Chief, Division of Child and Adolescent Psychiatry and Co-Director, Center for Addiction Medicine at the Massachusetts General Hospital; Associate Professor of Psychiatry at Harvard Medical School; Distinguished Fellow of the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry

Note: Drs. Childress, Brams and Wilens are not employees of KemPharm, and the views and opinions they may express in this presentation are their own, and shall not be construed as the views and opinions of KemPharm unless made by an authorized representative of KemPharm or are otherwise included in an official statement of KemPharm made in compliance with Regulation FD or otherwise filed with or furnished to the U.S. Securities and Exchange Commission in accordance with the Company's obligations under the Securities Exchange Act of 1934, as amended.



ADHD Investor Event Agenda

- Introduction (10 minutes)
Travis C. Mickle, PhD
- ADHD Treatment Landscape and Using the Laboratory Classroom to Determine Drug Effects (30 minutes)
Ann Childress, MD
- Prescribing ADHD Medications in a Large Outpatient Practice: The Good, The Bad, and the Ugly (20 minutes)
Matthew Brams, MD
- Nonmedical Use of Prescription Stimulants (20 minutes)
Timothy E. Wilens, MD
- Wrap-up/Q&A (30 minutes)
Travis C. Mickle, PhD



KemPharm Leverages its LAT™ Prodrug Technology to Improve the Attributes of Approved Drugs in Large Markets



- 1) Select FDA-approved and widely prescribed drug for improvement
- 2) Chemically modify using a ligand to create a prodrug
 - Ligands – GRAS or demonstrated to be safe
 - Prodrugs generate composition-based patents
- 3) Following ingestion, normal human metabolic processes cleave the ligand and release the active drug
 - Generates long-lived **composition-of-matter** patent protection
 - Proprietary to KemPharm and **applicable across many therapeutic areas**



The ADHD and ER Methylphenidate Market

- ~\$13 billion ADHD market with TRx growth of ~4% per year on average
- The branded portion of the ADHD market was ~\$6.1B in 2017 and more than 95% of these branded prescriptions are for extended release
- Methylphenidate (MPH) accounted for approximately 19.6 million TRx's and \$4.0 billion in sales in 2017
- Market research indicates prescribers see the following potential features of KP415 (KemPharm's investigational dexamethylphenidate prodrug product for ADHD) as key advantages
 - Duration of action (60%)
 - Lower abuse potential (52%)
 - Early onset of action (43%)
- Market research also indicates that prescribers estimate that MPH is given as the preferred first line of therapy for children under the age of 13 approximately 60% of the time

Source: Symphony Health, PHAST 2011-2017



The Adult ADHD Market

- More than 4% of U.S. adults (~10.5 million adults) have ADHD and are now the largest part of the ADHD market, comprising 53% of total TRx^{1,2}
- The adult ADHD market has grown at ~11% per year on average vs. 4% for the pediatric ADHD market for the last several years¹
- Vyvanse[®], the ADHD product known for its duration and abuse deterrent features has seen significant growth in the adult market averaging 22% year-over-year growth since 2009¹
- Shire's Mydayis[®] was recently approved as a super long-acting product in the amphetamine category (2-16 hour duration)
- Other potential market opportunities exist within indications where efficacy has been demonstrated by other stimulants or which remain as currently unmet medical needs

1. Symphony Health, PHAST 2011-2017

2. Ronald C. Kessler et al. (April 2006). The Prevalence and Correlates of Adult ADHD in the United States: Results From the National Comorbidity Survey Replication, American Journal of Psychiatry 163(5):71



KemPharm ADHD Clinical Product Pipeline

Category	Product Candidate	Parent Drug	Development Status	Next Milestone	Potential NDA Submission
ADHD	KP415	Methylphenidate (ER)	Clinical	NDA Submission	Q1 2019
	KP484	Methylphenidate (ER)	Clinical	Initiation of Efficacy Trial	2019



Key Opinion Leader Presentations:

KemPharm ADHD Investor Event



Ann Childress, MD

- Dr. Childress is President of the Center for Psychiatry and Behavioral Medicine, Inc., and has adjunct faculty appointments at the University of Nevada School of Medicine and at Touro University Nevada.
- She is an internationally recognized expert in the treatment of ADHD and is board certified in psychiatry, with a subspecialty in child and adolescent psychiatry.
- Dr. Childress has authored multiple articles in scientific journals. As a co-principal investigator, she has participated in more than 130 clinical trials. Her research has focused on treatment of children and adolescents and adults with mood disorders, post-traumatic stress disorder, schizophrenia, autism and ADHD.
- Dr. Childress is a board member of the American Professional Society of ADHD and Related Disorders (APSARD), a member of the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry. She is also Education Director for the Nevada Psychiatric Association.
- Dr. Childress earned her medical degree at the Medical University of South Carolina, Charleston, and her undergraduate degree at Washington University, St. Louis, Missouri.





CENTER FOR PSYCHIATRY

And Behavioral Medicine Inc.

ADHD Treatment Landscape and Using the Laboratory Classroom to Determine Drug Effects

Ann Childress, M.D.

Overview

- What is attention-deficit/hyperactivity disorder (ADHD)?
- Prevalence
- Human and monetary costs
- Treatment guidelines
- Approved and pipeline drugs
- What is a laboratory classroom?
- What data do we collect in the classroom?
 - SKAMP
 - PERMP (math test)
 - Examples

What is ADHD?

- ADHD is a common neurobehavioral disorder
- Symptoms include impairing levels of
 - Inattention and/or
 - Hyperactivity/impulsivity
 - Symptoms affect functioning and development

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Association, 2013.

Prevalence of ADHD

- 2016 National Survey of Children's Health
 - 9.4% or 6.1 million U.S. children ages 2-17 years ever diagnosed with ADHD
 - 8.4% or 5.4 million currently had the diagnosis
 - 89.4% of children ever diagnosed
 - 62% were taking medication
 - 46.7% had received behavioral treatment in the past year
 - 23.0% had not received either treatment in the past year

Danielson ML, Bitsko RH, Ghandour RM, et al. Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents, 2016. *J Clin Child Adolesc Psychol* 2018;47(2):199-212.

Prevalence of ADHD

- 2011 National Survey of Children's Health
 - 11% or 6.4 million U.S. children ages 4-17 years ever diagnosed with ADHD
 - 8.8% currently had the diagnosis
 - 6.2% were taking medication for ADHD

* Visser SN, Danielson ML, Bitsko RH, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *J Am Acad Child Adolesc Psychiatry* 2014;53(1):34-46 e2.

Duration of ADHD

- ADHD is a lifelong disorder
 - 75% persists into adolescence
 - 50% persists into adulthood
 - 4.4% of adults or an estimated 11 million

Wilens TE. *Psychiatr Clin North Am.* 2004;27:283-301.

Kessler et al. The Prevalence and Correlates of Adult ADHD in the United States: Results From the National Comorbidity Survey Replication *Am J Psychiatry* 2006; 163:716–723.

Cost of ADHD

- 2013 U.S. health care expenditures for ADHD
 - \$23 billion
- Annual societal costs \$38 billion to \$72 billion
 - Includes health care
 - Education
 - Reduced family productivity

Dieleman JL, Baral R, Birger M, et al. US Spending on Personal Health Care and Public Health, 1996-2013. *JAMA* 2016;316(24):2627-46.

Doshi JA, Hodgkins P, Kahle J, et al. Economic impact of childhood and adult attention-deficit/hyperactivity disorder in the United States. *J Am Acad Child Adolesc Psychiatry* 2012;51(10):990-1002 e2.

Impact of ADHD

- Can result in significant functional impairment
 - Grade retention
 - Lower standardized achievement scores & GPA
 - Failure to graduate high school
 - Legal problems
 - Higher teen pregnancy rates

Bussing R, Mason DM, Bell L, et al. Adolescent outcomes of childhood attention-deficit/hyperactivity disorder in a diverse community sample. *J Am Acad Child Adolesc Psychiatry* 2010;49(6):595-605.

Treatment of ADHD

American Academy of Pediatrics Guidelines

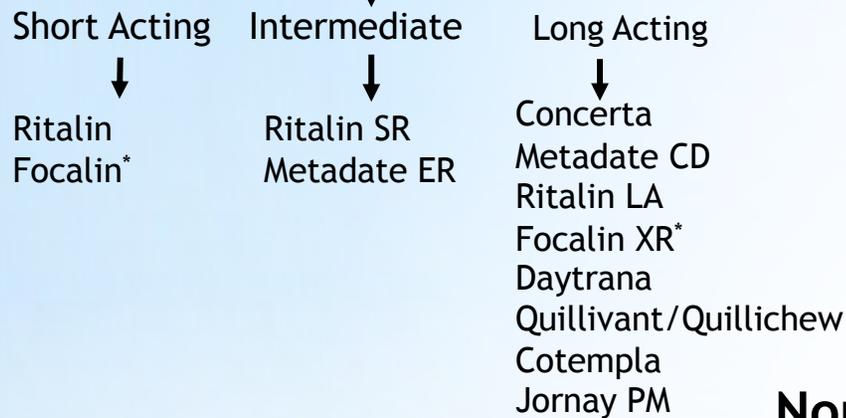
- 4-5 years: start with behavioral treatment
 - Methylphenidate recommended if symptoms are still moderate to severe or if behavioral treatment is not available
- 6-18 years: recommend both behavioral treatment and FDA approved medications
 - Stimulant > Atomoxetine > Guanfacine XR > Clonidine XR

Wolraich M, Brown L, Brown RT, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011;128(5):1007-22.

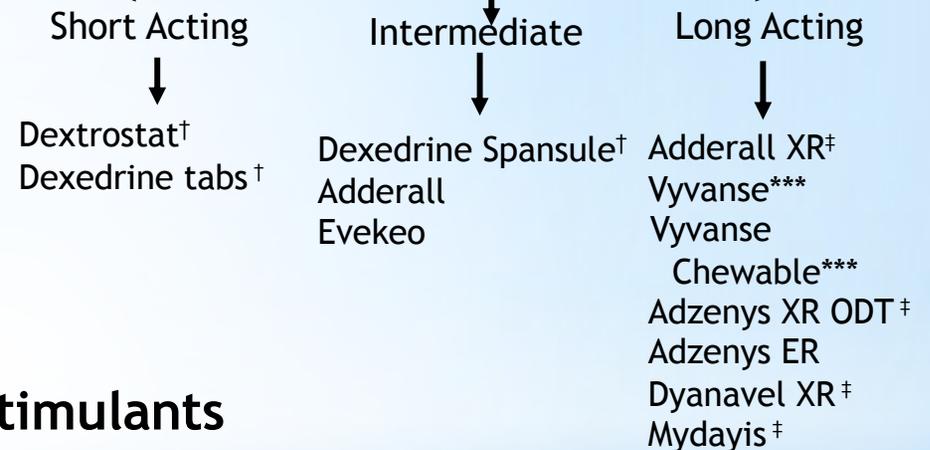
Medication Treatment for ADHD

Stimulants

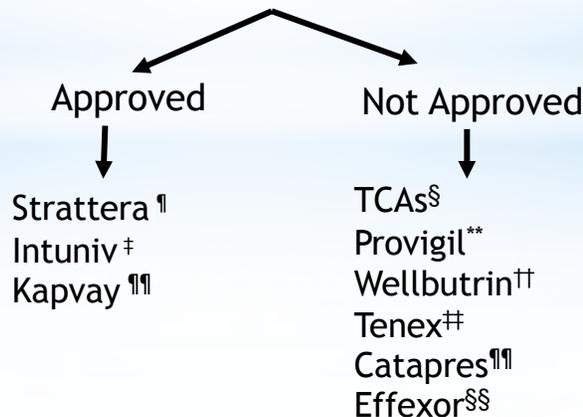
Methylphenidate



Amphetamine



Non-Stimulants



*dexamethylphenidate
 †dextroamphetamine sulfate
 ‡mixed amphetamine salts
 ¶atomoxetine
 ***lisdexamfetamine

§tricyclic antidepressants
 (many brands)
 **modafinil
 ††bupropion
 ‡‡guanfacine
 ¶¶clonidine
 §§venlafaxine

ADHD Drugs in the Pipeline

Stimulants

- KP415
- KP484
- PRC-063
- CTX 1301
- CTX 1302
- HLD-100
- Mazindol

Non Stimulants

- Dasotraline
- Viloxazine
- Fasroacetam
- Centanafadine

Other

- TRN-124

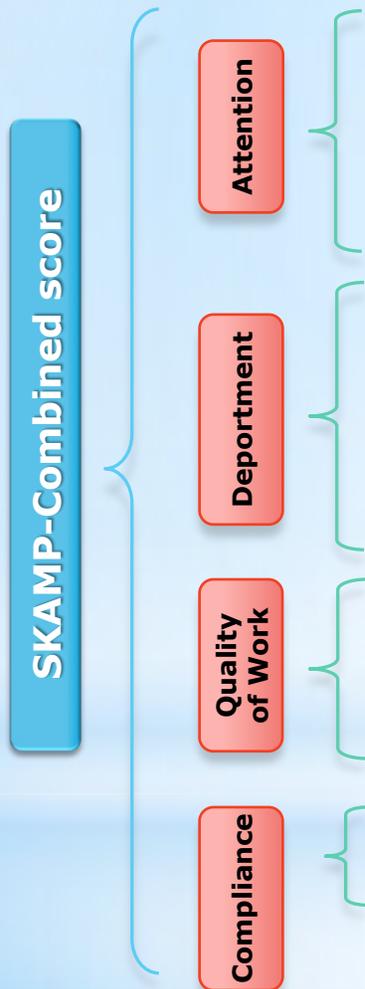
The Laboratory Classroom

- First laboratory school study can be traced to Bradley in 1937
- Swanson and Kinsbourne developed first version of current laboratory classroom procedures in 1977 in Toronto
- Further refined by Swanson et al. beginning in 1994 at University of California, Irvine

Greenhill LL, Osman BB. Ritalin : theory and practice. 2nd ed. Larchmont, NY: M.A. Liebert Publishers, 2000.



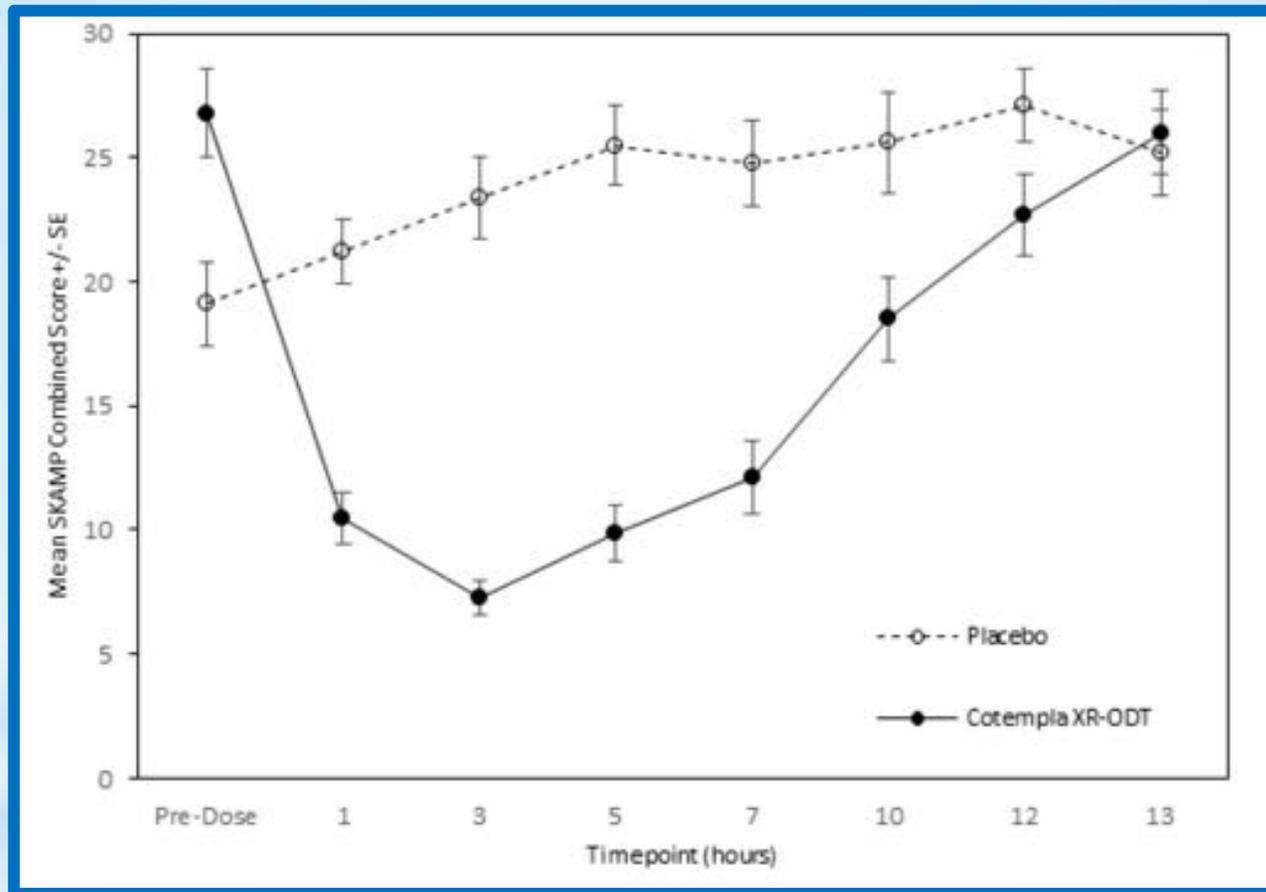
SKAMP Rating Scale



CLASSROOM BEHAVIOR	
1.	Getting started on assignments for classroom periods
2.	Sticking with tasks or activities for the allotted time
3.	Participating in an activity or classroom discussion
4.	Stopping and making transition to the next period
5.	Interacting with other children (eg, other students)
6.	Interacting with adults (eg, teacher or aide)
7.	Remaining quiet according to classroom rules
8.	Staying seated according to classroom rules
9.	Completing assigned work
10.	Performing work accurately
11.	Being careful and neat while writing or drawing
12.	Complying with teacher's usual requests or directions
13.	Following the rules established for the classroom

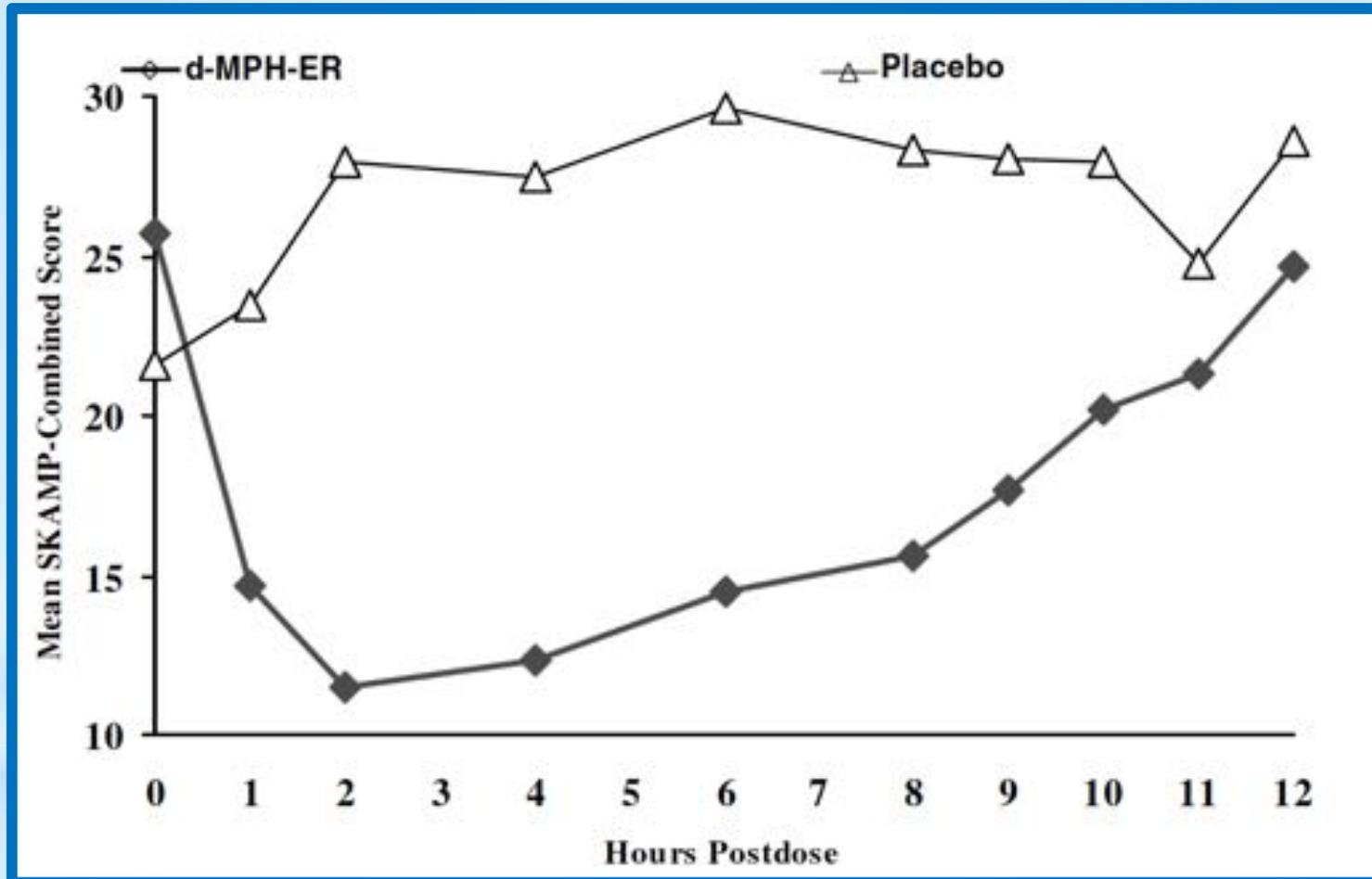
SKAMP, Swanson, Kotkin, Agler, M-Flynn, and Pelham rating scale. Wigal SB, Wigal TL. *J Atten Disord.* 2006;10(1):92-111.

Cotempla XR-ODT SKAMP-Combined



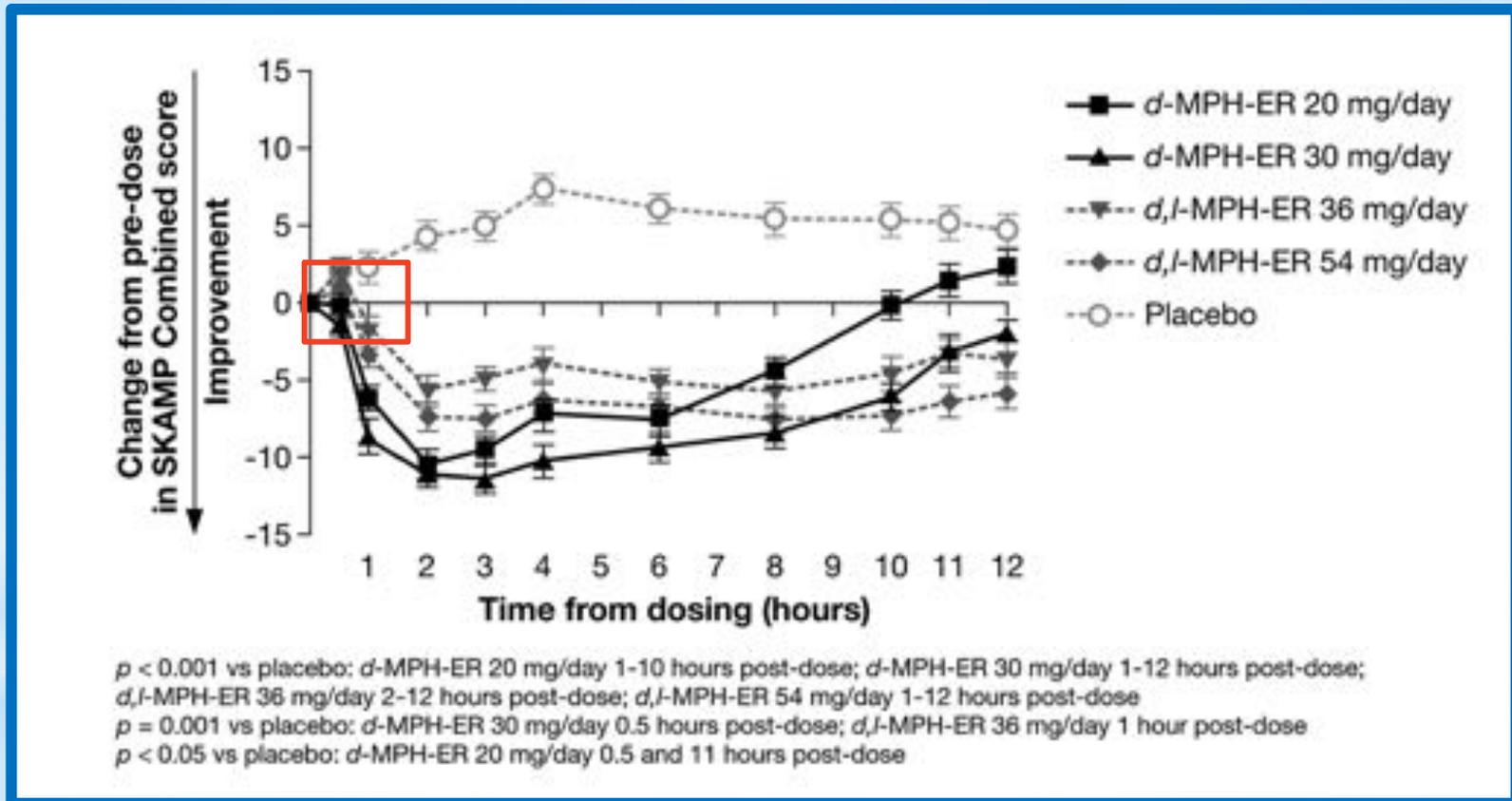
Childress AC, Kollins SH, Cutler AJ, et al. Efficacy, Safety, and Tolerability of an Extended-Release Orally Disintegrating Methylphenidate Tablet in Children 6-12 Years of Age with Attention-Deficit/Hyperactivity Disorder in the Laboratory Classroom Setting. *J Child Adolesc Psychopharmacol* 2017;27(1):66-74.

Focalin XR SKAMP-Combined



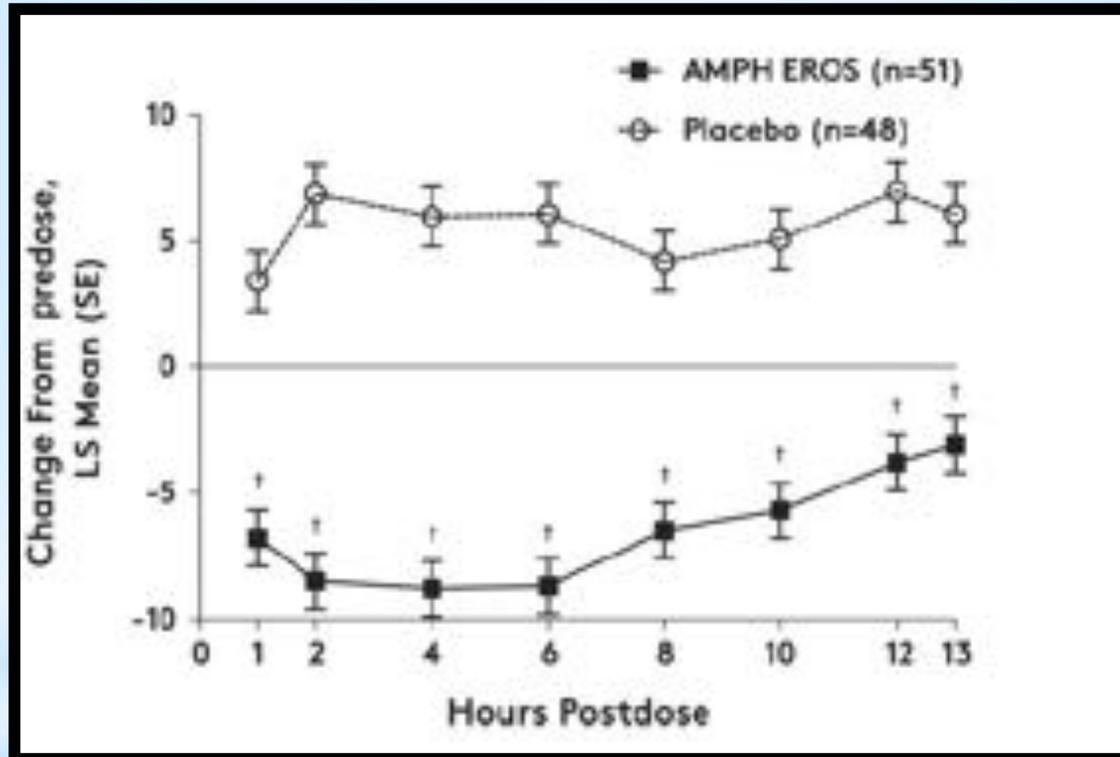
Silva RR, Muniz R, Pestreich L, et al. Efficacy and duration of effect of extended-release dexamethylphenidate versus placebo in schoolchildren with attention-deficit/hyperactivity disorder. *J Child Adolesc Psychopharmacol* 2006;16(3):239-51.

Focalin XR vs Concerta SKAMP-Combined



Muniz R, Brams M, Mao A, et al. Efficacy and safety of extended-release dexamethylphenidate compared with *d,l*-methylphenidate and placebo in the treatment of children with attention-deficit/hyperactivity disorder: a 12-hour laboratory classroom study. *J Child Adolesc Psychopharmacol* 2008;18(3):248-56.

SKAMP Dyanavel XR



Childress AC, Wigal SB, Brams MN, et al. Efficacy and Safety of Amphetamine Extended-Release Oral Suspension in Children with Attention-Deficit/Hyperactivity Disorder. *J Child Adolesc Psychopharmacol* 2018;28(5):306-13.

Permanent Product (PERMP)

- 400 problem math test
- 80 questions per page
- Subjects have 10 minutes to complete as many problems as they can
- 4 levels
 - Basic
 - Easy
 - Moderate
 - Difficult

KP415.E01 Pre-dose Math Test

NAME _____

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51 53 max 4/21/18
55 56

Val5 Hr-0.5 E p.1
 KomPrism KP415.E01

003-004
 27JAN2018

51 53 max 4/21/18
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KP415.E01 30 Minutes Post-dose Math Test

NAME _____

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$\begin{array}{r} 14 \\ - 13 \\ \hline 01 \end{array}$	$\begin{array}{r} 21 \\ - 10 \\ \hline 11 \end{array}$	$\begin{array}{r} 57 \\ - 13 \\ \hline 44 \end{array}$	$\begin{array}{r} 53 \\ - 40 \\ \hline 13 \end{array}$	$\begin{array}{r} 27 \\ - 26 \\ \hline 01 \end{array}$	$\begin{array}{r} 96 \\ - 15 \\ \hline 81 \end{array}$	$\begin{array}{r} 32 \\ - 20 \\ \hline 12 \end{array}$	$\begin{array}{r} 12 \\ - 10 \\ \hline 02 \end{array}$
$\begin{array}{r} 63 \\ + 15 \\ \hline 78 \end{array}$	$\begin{array}{r} 19 \\ + 50 \\ \hline 69 \end{array}$	$\begin{array}{r} 76 \\ + 21 \\ \hline 97 \end{array}$	$\begin{array}{r} 79 \\ + 10 \\ \hline 89 \end{array}$	$\begin{array}{r} 10 \\ + 17 \\ \hline 27 \end{array}$	$\begin{array}{r} 52 \\ + 33 \\ \hline 85 \end{array}$	$\begin{array}{r} 43 \\ + 43 \\ \hline 86 \end{array}$	$\begin{array}{r} 72 \\ + 11 \\ \hline 83 \end{array}$
$\begin{array}{r} 94 \\ - 11 \\ \hline 83 \end{array}$	$\begin{array}{r} 85 \\ - 15 \\ \hline 70 \end{array}$	$\begin{array}{r} 46 \\ - 12 \\ \hline 34 \end{array}$	$\begin{array}{r} 62 \\ - 62 \\ \hline 00 \end{array}$	$\begin{array}{r} 46 \\ - 34 \\ \hline 12 \end{array}$	$\begin{array}{r} 30 \\ - 20 \\ \hline 10 \end{array}$	$\begin{array}{r} 85 \\ - 63 \\ \hline 22 \end{array}$	$\begin{array}{r} 38 \\ - 12 \\ \hline 26 \end{array}$

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$\begin{array}{r} 85 \\ + 14 \\ \hline 99 \end{array}$	$\begin{array}{r} 39 \\ + 60 \\ \hline 99 \end{array}$	$\begin{array}{r} 37 \\ + 51 \\ \hline 88 \end{array}$	$\begin{array}{r} 33 \\ + 16 \\ \hline 49 \end{array}$	$\begin{array}{r} 33 \\ + 56 \\ \hline 89 \end{array}$	$\begin{array}{r} 12 \\ + 20 \\ \hline 32 \end{array}$	$\begin{array}{r} 12 \\ + 11 \\ \hline 23 \end{array}$	$\begin{array}{r} 65 \\ + 11 \\ \hline 76 \end{array}$
$\begin{array}{r} 41 \\ - 40 \\ \hline 01 \end{array}$	$\begin{array}{r} 24 \\ - 23 \\ \hline 01 \end{array}$	$\begin{array}{r} 75 \\ - 54 \\ \hline 21 \end{array}$	$\begin{array}{r} 23 \\ - 11 \\ \hline 12 \end{array}$	$\begin{array}{r} 57 \\ - 46 \\ \hline 11 \end{array}$	$\begin{array}{r} 98 \\ - 44 \\ \hline 54 \end{array}$	$\begin{array}{r} 51 \\ - 20 \\ \hline 31 \end{array}$	$\begin{array}{r} 36 \\ - 13 \\ \hline 23 \end{array}$
$\begin{array}{r} 84 \\ + 13 \\ \hline 97 \end{array}$	$\begin{array}{r} 24 \\ + 21 \\ \hline 45 \end{array}$	$\begin{array}{r} 21 \\ + 30 \\ \hline 51 \end{array}$	$\begin{array}{r} 38 \\ + 50 \\ \hline 88 \end{array}$	$\begin{array}{r} 72 \\ + 23 \\ \hline 95 \end{array}$	$\begin{array}{r} 79 \\ + 20 \\ \hline 99 \end{array}$	$\begin{array}{r} 63 \\ + 34 \\ \hline 97 \end{array}$	$\begin{array}{r} 10 \\ + 47 \\ \hline 57 \end{array}$
$\begin{array}{r} 33 \\ - 20 \\ \hline 13 \end{array}$	$\begin{array}{r} 72 \\ - 31 \\ \hline 41 \end{array}$	$\begin{array}{r} 18 \\ - 11 \\ \hline 07 \end{array}$	$\begin{array}{r} 13 \\ - 13 \\ \hline 00 \end{array}$	$\begin{array}{r} 64 \\ - 21 \\ \hline 43 \end{array}$	$\begin{array}{r} 51 \\ - 31 \\ \hline 20 \end{array}$	$\begin{array}{r} 44 \\ - 11 \\ \hline 33 \end{array}$	$\begin{array}{r} 67 \\ - 52 \\ \hline 15 \end{array}$
$\begin{array}{r} 67 \\ + 21 \\ \hline 88 \end{array}$	$\begin{array}{r} 24 \\ + 24 \\ \hline 48 \end{array}$	$\begin{array}{r} 47 \\ + 32 \\ \hline 79 \end{array}$	$\begin{array}{r} 12 \\ + 63 \\ \hline 75 \end{array}$	$\begin{array}{r} 14 \\ + 60 \\ \hline 74 \end{array}$	$\begin{array}{r} 33 \\ + 11 \\ \hline 44 \end{array}$	$\begin{array}{r} 82 \\ + 13 \\ \hline 95 \end{array}$	$\begin{array}{r} 77 \\ + 20 \\ \hline 97 \end{array}$
$\begin{array}{r} 72 \\ - 40 \\ \hline 32 \end{array}$	$\begin{array}{r} 88 \\ - 70 \\ \hline 18 \end{array}$	$\begin{array}{r} 27 \\ - 14 \\ \hline 13 \end{array}$	$\begin{array}{r} 84 \\ - 50 \\ \hline 34 \end{array}$	$\begin{array}{r} 34 \\ - 34 \\ \hline 00 \end{array}$	$\begin{array}{r} 87 \\ - 61 \\ \hline 26 \end{array}$	$\begin{array}{r} 84 \\ - 51 \\ \hline 33 \end{array}$	$\begin{array}{r} 20 \\ - 10 \\ \hline 10 \end{array}$
$\begin{array}{r} 75 \\ + 11 \\ \hline 86 \end{array}$	$\begin{array}{r} 48 \\ + 31 \\ \hline 79 \end{array}$	$\begin{array}{r} 44 \\ + 25 \\ \hline 69 \end{array}$	$\begin{array}{r} 72 \\ + 22 \\ \hline 94 \end{array}$	$\begin{array}{r} 59 \\ + 10 \\ \hline 69 \end{array}$	$\begin{array}{r} 89 \\ + 10 \\ \hline 99 \end{array}$	$\begin{array}{r} 15 \\ + 32 \\ \hline 47 \end{array}$	$\begin{array}{r} 50 \\ + 44 \\ \hline 94 \end{array}$
$\begin{array}{r} 65 \\ - 45 \\ \hline 20 \end{array}$	$\begin{array}{r} 17 \\ - 12 \\ \hline 05 \end{array}$	$\begin{array}{r} 13 \\ - 13 \\ \hline 00 \end{array}$	$\begin{array}{r} 88 \\ - 67 \\ \hline 21 \end{array}$	$\begin{array}{r} 56 \\ - 12 \\ \hline 44 \end{array}$	$\begin{array}{r} 99 \\ - 90 \\ \hline 09 \end{array}$	$\begin{array}{r} 99 \\ - 52 \\ \hline 47 \end{array}$	$\begin{array}{r} 64 \\ - 31 \\ \hline 33 \end{array}$
$\begin{array}{r} 17 \\ + 12 \\ \hline 29 \end{array}$	$\begin{array}{r} 25 \\ + 51 \\ \hline 76 \end{array}$	$\begin{array}{r} 13 \\ + 66 \\ \hline 79 \end{array}$	$\begin{array}{r} 38 \\ + 11 \\ \hline 49 \end{array}$	$\begin{array}{r} 25 \\ + 70 \\ \hline 95 \end{array}$	$\begin{array}{r} 70 \\ + 23 \\ \hline 93 \end{array}$	$\begin{array}{r} 59 \\ + 40 \\ \hline 99 \end{array}$	$\begin{array}{r} 84 \\ + 11 \\ \hline 95 \end{array}$
$\begin{array}{r} 79 \\ - 60 \\ \hline 19 \end{array}$	$\begin{array}{r} 45 \\ - 22 \\ \hline 23 \end{array}$	$\begin{array}{r} 58 \\ - 34 \\ \hline 24 \end{array}$	$\begin{array}{r} 61 \\ - 61 \\ \hline 00 \end{array}$	$\begin{array}{r} 55 \\ - 10 \\ \hline 45 \end{array}$	$\begin{array}{r} 93 \\ - 61 \\ \hline 32 \end{array}$	$\begin{array}{r} 21 \\ - 11 \\ \hline 10 \end{array}$	$\begin{array}{r} 49 \\ - 49 \\ \hline 00 \end{array}$

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$\begin{array}{r} 48 \\ +20 \\ \hline 68 \end{array}$	$\begin{array}{r} 13 \\ +16 \\ \hline 29 \end{array}$	$\begin{array}{r} 37 \\ +30 \\ \hline 67 \end{array}$	$\begin{array}{r} 48 \\ +30 \\ \hline 78 \end{array}$	$\begin{array}{r} 42 \\ +14 \\ \hline 56 \end{array}$	$\begin{array}{r} 87 \\ +11 \\ \hline 98 \end{array}$	$\begin{array}{r} 19 \\ +70 \\ \hline 89 \end{array}$	$\begin{array}{r} 26 \\ +31 \\ \hline 57 \end{array}$
$\begin{array}{r} 42 \\ -20 \\ \hline 22 \end{array}$	$\begin{array}{r} 82 \\ -51 \\ \hline 31 \end{array}$	$\begin{array}{r} 22 \\ -10 \\ \hline 12 \end{array}$	$\begin{array}{r} 64 \\ -42 \\ \hline 22 \end{array}$	$\begin{array}{r} 49 \\ -43 \\ \hline 06 \end{array}$	$\begin{array}{r} 31 \\ -30 \\ \hline 01 \end{array}$	$\begin{array}{r} 43 \\ -33 \\ \hline 10 \end{array}$	$\begin{array}{r} 40 \\ -30 \\ \hline 10 \end{array}$
$\begin{array}{r} 56 \\ +40 \\ \hline 96 \end{array}$	$\begin{array}{r} 58 \\ +31 \\ \hline 89 \end{array}$	$\begin{array}{r} 31 \\ +32 \\ \hline 63 \end{array}$	$\begin{array}{r} 15 \\ +34 \\ \hline 49 \end{array}$	$\begin{array}{r} 13 \\ +56 \\ \hline 69 \end{array}$	$\begin{array}{r} 43 \\ +15 \\ \hline 58 \end{array}$	$\begin{array}{r} 55 \\ +42 \\ \hline 97 \end{array}$	$\begin{array}{r} 80 \\ +17 \\ \hline 97 \end{array}$
$\begin{array}{r} 59 \\ -31 \\ \hline 28 \end{array}$	$\begin{array}{r} 96 \\ -50 \\ \hline 46 \end{array}$	$\begin{array}{r} 84 \\ -30 \\ \hline 54 \end{array}$	$\begin{array}{r} 52 \\ -22 \\ \hline 30 \end{array}$	$\begin{array}{r} 50 \\ -26 \\ \hline 24 \end{array}$	$\begin{array}{r} 79 \\ -69 \\ \hline 10 \end{array}$	$\begin{array}{r} 77 \\ -30 \\ \hline 47 \end{array}$	$\begin{array}{r} 86 \\ -21 \\ \hline 65 \end{array}$
$\begin{array}{r} 28 \\ +31 \\ \hline 59 \end{array}$	$\begin{array}{r} 76 \\ +10 \\ \hline 86 \end{array}$	$\begin{array}{r} 21 \\ +35 \\ \hline 56 \end{array}$	$\begin{array}{r} 34 \\ +61 \\ \hline 95 \end{array}$	$\begin{array}{r} 41 \\ +37 \\ \hline 78 \end{array}$	$\begin{array}{r} 54 \\ +45 \\ \hline 99 \end{array}$	$\begin{array}{r} 20 \\ +38 \\ \hline 58 \end{array}$	$\begin{array}{r} 46 \\ +22 \\ \hline 68 \end{array}$
$\begin{array}{r} 44 \\ -44 \\ \hline 00 \end{array}$	$\begin{array}{r} 93 \\ -31 \\ \hline 62 \end{array}$	$\begin{array}{r} 90 \\ -60 \\ \hline 30 \end{array}$	$\begin{array}{r} 98 \\ -10 \\ \hline 88 \end{array}$	$\begin{array}{r} 52 \\ -41 \\ \hline 11 \end{array}$	$\begin{array}{r} 77 \\ -67 \\ \hline 10 \end{array}$	$\begin{array}{r} 95 \\ -21 \\ \hline 74 \end{array}$	$\begin{array}{r} 31 \\ -30 \\ \hline 01 \end{array}$
$\begin{array}{r} 18 \\ +71 \\ \hline 89 \end{array}$	$\begin{array}{r} 76 \\ +11 \\ \hline 87 \end{array}$	$\begin{array}{r} 59 \\ +40 \\ \hline 99 \end{array}$	$\begin{array}{r} 85 \\ +12 \\ \hline 97 \end{array}$	$\begin{array}{r} 88 \\ +10 \\ \hline 98 \end{array}$	$\begin{array}{r} 18 \\ +21 \\ \hline 39 \end{array}$	$\begin{array}{r} 13 \\ +83 \\ \hline 96 \end{array}$	$\begin{array}{r} 89 \\ +10 \\ \hline 99 \end{array}$
$\begin{array}{r} 54 \\ -22 \\ \hline 32 \end{array}$	$\begin{array}{r} 41 \\ -40 \\ \hline 01 \end{array}$	$\begin{array}{r} 57 \\ -12 \\ \hline 45 \end{array}$	$\begin{array}{r} 49 \\ -37 \\ \hline 12 \end{array}$	$\begin{array}{r} 90 \\ -42 \\ \hline 48 \end{array}$	$\begin{array}{r} 21 \\ -10 \\ \hline 11 \end{array}$	$\begin{array}{r} 44 \\ -13 \\ \hline 31 \end{array}$	$\begin{array}{r} 53 \\ -23 \\ \hline 30 \end{array}$
$\begin{array}{r} 74 \\ +25 \\ \hline 99 \end{array}$	$\begin{array}{r} 65 \\ +13 \\ \hline 78 \end{array}$	$\begin{array}{r} 54 \\ +20 \\ \hline 74 \end{array}$	$\begin{array}{r} 38 \\ +41 \\ \hline 79 \end{array}$	$\begin{array}{r} 67 \\ +32 \\ \hline 99 \end{array}$	$\begin{array}{r} 51 \\ +41 \\ \hline 92 \end{array}$	$\begin{array}{r} 59 \\ +30 \\ \hline 89 \end{array}$	$\begin{array}{r} 29 \\ +40 \\ \hline 69 \end{array}$
$\begin{array}{r} 78 \\ -38 \\ \hline 40 \end{array}$	$\begin{array}{r} 93 \\ -43 \\ \hline 50 \end{array}$	$\begin{array}{r} 71 \\ -60 \\ \hline 11 \end{array}$	$\begin{array}{r} 60 \\ -40 \\ \hline 20 \end{array}$	$\begin{array}{r} 29 \\ -22 \\ \hline 07 \end{array}$	$\begin{array}{r} 29 \\ -19 \\ \hline 10 \end{array}$	$\begin{array}{r} 78 \\ -33 \\ \hline 45 \end{array}$	$\begin{array}{r} 19 \\ -15 \\ \hline 04 \end{array}$

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$\begin{array}{r} 27 \\ +22 \\ \hline 49 \end{array}$	$\begin{array}{r} 70 \\ +18 \\ \hline 88 \end{array}$	$\begin{array}{r} 46 \\ +42 \\ \hline 88 \end{array}$	$\begin{array}{r} 50 \\ +39 \\ \hline 89 \end{array}$	$\begin{array}{r} 82 \\ +10 \\ \hline 92 \end{array}$	$\begin{array}{r} 13 \\ +41 \\ \hline 54 \end{array}$	$\begin{array}{r} 43 \\ +43 \\ \hline 86 \end{array}$	$\begin{array}{r} 78 \\ +20 \\ \hline 98 \end{array}$
$\begin{array}{r} 50 \\ -40 \\ \hline 10 \end{array}$	$\begin{array}{r} 90 \\ -40 \\ \hline 50 \end{array}$	$\begin{array}{r} 42 \\ -20 \\ \hline 22 \end{array}$	$\begin{array}{r} 75 \\ -15 \\ \hline 60 \end{array}$	$\begin{array}{r} 31 \\ -21 \\ \hline 10 \end{array}$	$\begin{array}{r} 69 \\ -48 \\ \hline 21 \end{array}$	$\begin{array}{r} 30 \\ -30 \\ \hline 00 \end{array}$	$\begin{array}{r} 34 \\ -23 \\ \hline 11 \end{array}$
$\begin{array}{r} 89 \\ +10 \\ \hline 99 \end{array}$	$\begin{array}{r} 14 \\ +61 \\ \hline 75 \end{array}$	$\begin{array}{r} 11 \\ +14 \\ \hline 25 \end{array}$	$\begin{array}{r} 76 \\ +21 \\ \hline 97 \end{array}$	$\begin{array}{r} 58 \\ +11 \\ \hline 69 \end{array}$	$\begin{array}{r} 34 \\ +53 \\ \hline 87 \end{array}$	$\begin{array}{r} 58 \\ +11 \\ \hline 69 \end{array}$	$\begin{array}{r} 18 \\ +10 \\ \hline 28 \end{array}$
$\begin{array}{r} 87 \\ -81 \\ \hline 06 \end{array}$	$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 76 \\ -62 \\ \hline 14 \end{array}$	$\begin{array}{r} 44 \\ -34 \\ \hline 10 \end{array}$	$\begin{array}{r} 69 \\ -39 \\ \hline 30 \end{array}$	$\begin{array}{r} 43 \\ -13 \\ \hline 30 \end{array}$	$\begin{array}{r} 23 \\ -11 \\ \hline 12 \end{array}$	$\begin{array}{r} 67 \\ -45 \\ \hline 22 \end{array}$
$\begin{array}{r} 11 \\ +87 \\ \hline 98 \end{array}$	$\begin{array}{r} 10 \\ +55 \\ \hline 65 \end{array}$	$\begin{array}{r} 52 \\ +11 \\ \hline 63 \end{array}$	$\begin{array}{r} 35 \\ +14 \\ \hline 49 \end{array}$	$\begin{array}{r} 20 \\ +61 \\ \hline 81 \end{array}$	$\begin{array}{r} 53 \\ +45 \\ \hline 98 \end{array}$	$\begin{array}{r} 30 \\ +69 \\ \hline 99 \end{array}$	$\begin{array}{r} 86 \\ +12 \\ \hline 98 \end{array}$
$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 58 \\ -51 \\ \hline 07 \end{array}$	$\begin{array}{r} 73 \\ -40 \\ \hline 33 \end{array}$	$\begin{array}{r} 67 \\ -13 \\ \hline 54 \end{array}$	$\begin{array}{r} 76 \\ -54 \\ \hline 22 \end{array}$	$\begin{array}{r} 19 \\ -15 \\ \hline 04 \end{array}$	$\begin{array}{r} 26 \\ -26 \\ \hline 00 \end{array}$	$\begin{array}{r} 93 \\ -62 \\ \hline 31 \end{array}$
$\begin{array}{r} 39 \\ +30 \\ \hline 69 \end{array}$	$\begin{array}{r} 32 \\ +12 \\ \hline 44 \end{array}$	$\begin{array}{r} 10 \\ +34 \\ \hline 44 \end{array}$	$\begin{array}{r} 42 \\ +53 \\ \hline 95 \end{array}$	$\begin{array}{r} 72 \\ +14 \\ \hline 86 \end{array}$	$\begin{array}{r} 85 \\ +13 \\ \hline 98 \end{array}$	$\begin{array}{r} 53 \\ +44 \\ \hline 97 \end{array}$	$\begin{array}{r} 82 \\ +12 \\ \hline 94 \end{array}$
$\begin{array}{r} 42 \\ -40 \\ \hline 02 \end{array}$	$\begin{array}{r} 88 \\ -15 \\ \hline 73 \end{array}$	$\begin{array}{r} 57 \\ -26 \\ \hline 31 \end{array}$	$\begin{array}{r} 99 \\ -62 \\ \hline 37 \end{array}$	$\begin{array}{r} 32 \\ -20 \\ \hline 12 \end{array}$	$\begin{array}{r} 72 \\ -50 \\ \hline 22 \end{array}$	$\begin{array}{r} 57 \\ -47 \\ \hline 10 \end{array}$	$\begin{array}{r} 91 \\ -61 \\ \hline 30 \end{array}$
$\begin{array}{r} 57 \\ +21 \\ \hline 78 \end{array}$	$\begin{array}{r} 50 \\ +32 \\ \hline 82 \end{array}$	$\begin{array}{r} 33 \\ +15 \\ \hline 48 \end{array}$	$\begin{array}{r} 88 \\ +10 \\ \hline 98 \end{array}$	$\begin{array}{r} 54 \\ +40 \\ \hline 94 \end{array}$	$\begin{array}{r} 44 \\ +11 \\ \hline 55 \end{array}$	$\begin{array}{r} 12 \\ +73 \\ \hline 85 \end{array}$	$\begin{array}{r} 65 \\ +21 \\ \hline 86 \end{array}$
$\begin{array}{r} 71 \\ -60 \\ \hline 11 \end{array}$	$\begin{array}{r} 68 \\ -65 \\ \hline 03 \end{array}$	$\begin{array}{r} 65 \\ -35 \\ \hline 30 \end{array}$	$\begin{array}{r} 29 \\ -17 \\ \hline 12 \end{array}$	$\begin{array}{r} 74 \\ -70 \\ \hline 04 \end{array}$	$\begin{array}{r} 64 \\ -32 \\ \hline 32 \end{array}$	$\begin{array}{r} 30 \\ -30 \\ \hline 00 \end{array}$	$\begin{array}{r} 92 \\ -11 \\ \hline 81 \end{array}$

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$\begin{array}{r} 14 \\ +55 \\ \hline 69 \end{array}$	$\begin{array}{r} 78 \\ +11 \\ \hline 89 \end{array}$	$\begin{array}{r} 43 \\ +46 \\ \hline 89 \end{array}$	$\begin{array}{r} 21 \\ +63 \\ \hline 84 \end{array}$	$\begin{array}{r} 29 \\ +60 \\ \hline 89 \end{array}$	$\begin{array}{r} 76 \\ +21 \\ \hline 97 \end{array}$	$\begin{array}{r} 66 \\ +22 \\ \hline 88 \end{array}$	$\begin{array}{r} 21 \\ +61 \\ \hline 82 \end{array}$
$\begin{array}{r} 55 \\ -11 \\ \hline 44 \end{array}$	$\begin{array}{r} 17 \\ -16 \\ \hline 01 \end{array}$	$\begin{array}{r} 57 \\ -51 \\ \hline 06 \end{array}$	$\begin{array}{r} 64 \\ -30 \\ \hline 34 \end{array}$	$\begin{array}{r} 98 \\ -37 \\ \hline 61 \end{array}$	$\begin{array}{r} 89 \\ -80 \\ \hline 09 \end{array}$	$\begin{array}{r} 91 \\ -50 \\ \hline 41 \end{array}$	$\begin{array}{r} 98 \\ -56 \\ \hline 42 \end{array}$
$\begin{array}{r} 28 \\ +70 \\ \hline 98 \end{array}$	$\begin{array}{r} 64 \\ +33 \\ \hline 97 \end{array}$	$\begin{array}{r} 59 \\ +40 \\ \hline 99 \end{array}$	$\begin{array}{r} 87 \\ +12 \\ \hline 99 \end{array}$	$\begin{array}{r} 14 \\ +20 \\ \hline 34 \end{array}$	$\begin{array}{r} 19 \\ +40 \\ \hline 59 \end{array}$	$\begin{array}{r} 61 \\ +14 \\ \hline 75 \end{array}$	$\begin{array}{r} 61 \\ +17 \\ \hline 78 \end{array}$
$\begin{array}{r} 87 \\ -32 \\ \hline 55 \end{array}$	$\begin{array}{r} 73 \\ -21 \\ \hline 52 \end{array}$	$\begin{array}{r} 17 \\ -17 \\ \hline 00 \end{array}$	$\begin{array}{r} 99 \\ -47 \\ \hline 52 \end{array}$	$\begin{array}{r} 26 \\ -25 \\ \hline 01 \end{array}$	$\begin{array}{r} 52 \\ -41 \\ \hline 11 \end{array}$	$\begin{array}{r} 44 \\ -41 \\ \hline 03 \end{array}$	$\begin{array}{r} 84 \\ -21 \\ \hline 63 \end{array}$
$\begin{array}{r} 10 \\ +55 \\ \hline 65 \end{array}$	$\begin{array}{r} 71 \\ +16 \\ \hline 87 \end{array}$	$\begin{array}{r} 24 \\ +74 \\ \hline 98 \end{array}$	$\begin{array}{r} 27 \\ +11 \\ \hline 38 \end{array}$	$\begin{array}{r} 40 \\ +15 \\ \hline 55 \end{array}$	$\begin{array}{r} 74 \\ +12 \\ \hline 86 \end{array}$	$\begin{array}{r} 76 \\ +11 \\ \hline 87 \end{array}$	$\begin{array}{r} 13 \\ +12 \\ \hline 25 \end{array}$
$\begin{array}{r} 76 \\ -13 \\ \hline 63 \end{array}$	$\begin{array}{r} 86 \\ -86 \\ \hline 00 \end{array}$	$\begin{array}{r} 27 \\ -24 \\ \hline 03 \end{array}$	$\begin{array}{r} 86 \\ -55 \\ \hline 31 \end{array}$	$\begin{array}{r} 91 \\ -81 \\ \hline 10 \end{array}$	$\begin{array}{r} 13 \\ -12 \\ \hline 01 \end{array}$	$\begin{array}{r} 58 \\ -28 \\ \hline 30 \end{array}$	$\begin{array}{r} 17 \\ -13 \\ \hline 04 \end{array}$
$\begin{array}{r} 13 \\ +85 \\ \hline 98 \end{array}$	$\begin{array}{r} 14 \\ +72 \\ \hline 86 \end{array}$	$\begin{array}{r} 54 \\ +12 \\ \hline 66 \end{array}$	$\begin{array}{r} 35 \\ +41 \\ \hline 76 \end{array}$	$\begin{array}{r} 47 \\ +51 \\ \hline 98 \end{array}$	$\begin{array}{r} 26 \\ +13 \\ \hline 39 \end{array}$	$\begin{array}{r} 88 \\ +11 \\ \hline 99 \end{array}$	$\begin{array}{r} 67 \\ +10 \\ \hline 77 \end{array}$
$\begin{array}{r} 27 \\ -17 \\ \hline 10 \end{array}$	$\begin{array}{r} 92 \\ -22 \\ \hline 70 \end{array}$	$\begin{array}{r} 97 \\ -46 \\ \hline 51 \end{array}$	$\begin{array}{r} 26 \\ -20 \\ \hline 06 \end{array}$	$\begin{array}{r} 76 \\ -35 \\ \hline 41 \end{array}$	$\begin{array}{r} 81 \\ -41 \\ \hline 40 \end{array}$	$\begin{array}{r} 96 \\ -53 \\ \hline 43 \end{array}$	$\begin{array}{r} 78 \\ -74 \\ \hline 04 \end{array}$
$\begin{array}{r} 52 \\ +45 \\ \hline 97 \end{array}$	$\begin{array}{r} 73 \\ +26 \\ \hline 99 \end{array}$	$\begin{array}{r} 69 \\ +10 \\ \hline 79 \end{array}$	$\begin{array}{r} 47 \\ +50 \\ \hline 97 \end{array}$	$\begin{array}{r} 81 \\ +12 \\ \hline 93 \end{array}$	$\begin{array}{r} 14 \\ +85 \\ \hline 99 \end{array}$	$\begin{array}{r} 46 \\ +22 \\ \hline 68 \end{array}$	$\begin{array}{r} 38 \\ +50 \\ \hline 88 \end{array}$
$\begin{array}{r} 94 \\ -11 \\ \hline 83 \end{array}$	$\begin{array}{r} 19 \\ -14 \\ \hline 05 \end{array}$	$\begin{array}{r} 99 \\ -36 \\ \hline 63 \end{array}$	$\begin{array}{r} 70 \\ -60 \\ \hline 10 \end{array}$	$\begin{array}{r} 49 \\ -38 \\ \hline 11 \end{array}$	$\begin{array}{r} 16 \\ -13 \\ \hline 03 \end{array}$	$\begin{array}{r} 92 \\ -12 \\ \hline 80 \end{array}$	$\begin{array}{r} 26 \\ -15 \\ \hline 11 \end{array}$

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$\begin{array}{r} 79 \\ +10 \\ \hline 89 \end{array}$	$\begin{array}{r} 49 \\ +10 \\ \hline 59 \end{array}$	$\begin{array}{r} 44 \\ +12 \\ \hline 56 \end{array}$	$\begin{array}{r} 88 \\ +11 \\ \hline 99 \end{array}$	$\begin{array}{r} 62 \\ +11 \\ \hline 73 \end{array}$	$\begin{array}{r} 45 \\ +42 \\ \hline 87 \end{array}$	$\begin{array}{r} 83 \\ +12 \\ \hline 95 \end{array}$	$\begin{array}{r} 82 \\ +11 \\ \hline 93 \end{array}$
$\begin{array}{r} 11 \\ -10 \\ \hline 01 \end{array}$	$\begin{array}{r} 35 \\ -10 \\ \hline 25 \end{array}$	$\begin{array}{r} 76 \\ -30 \\ \hline 46 \end{array}$	$\begin{array}{r} 79 \\ -17 \\ \hline 62 \end{array}$	$\begin{array}{r} 78 \\ -56 \\ \hline 22 \end{array}$	$\begin{array}{r} 11 \\ -11 \\ \hline 00 \end{array}$	$\begin{array}{r} 54 \\ -42 \\ \hline 12 \end{array}$	$\begin{array}{r} 65 \\ -63 \\ \hline 02 \end{array}$
$\begin{array}{r} 24 \\ +74 \\ \hline 98 \end{array}$	$\begin{array}{r} 59 \\ +10 \\ \hline 69 \end{array}$	$\begin{array}{r} 46 \\ +43 \\ \hline 89 \end{array}$	$\begin{array}{r} 30 \\ +33 \\ \hline 63 \end{array}$	$\begin{array}{r} 23 \\ +13 \\ \hline 36 \end{array}$	$\begin{array}{r} 83 \\ +13 \\ \hline 96 \end{array}$	$\begin{array}{r} 11 \\ +67 \\ \hline 78 \end{array}$	$\begin{array}{r} 38 \\ +41 \\ \hline 79 \end{array}$
$\begin{array}{r} 54 \\ -34 \\ \hline 20 \end{array}$	$\begin{array}{r} 59 \\ -55 \\ \hline 04 \end{array}$	$\begin{array}{r} 41 \\ -41 \\ \hline 00 \end{array}$	$\begin{array}{r} 83 \\ -11 \\ \hline 72 \end{array}$	$\begin{array}{r} 64 \\ -62 \\ \hline 02 \end{array}$	$\begin{array}{r} 38 \\ -23 \\ \hline 15 \end{array}$	$\begin{array}{r} 56 \\ -13 \\ \hline 43 \end{array}$	$\begin{array}{r} 67 \\ -54 \\ \hline 13 \end{array}$
$\begin{array}{r} 69 \\ +30 \\ \hline 99 \end{array}$	$\begin{array}{r} 42 \\ +26 \\ \hline 68 \end{array}$	$\begin{array}{r} 44 \\ +24 \\ \hline 68 \end{array}$	$\begin{array}{r} 52 \\ +17 \\ \hline 69 \end{array}$	$\begin{array}{r} 31 \\ +34 \\ \hline 65 \end{array}$	$\begin{array}{r} 69 \\ +10 \\ \hline 79 \end{array}$	$\begin{array}{r} 43 \\ +54 \\ \hline 97 \end{array}$	$\begin{array}{r} 59 \\ +20 \\ \hline 79 \end{array}$
$\begin{array}{r} 53 \\ -42 \\ \hline 11 \end{array}$	$\begin{array}{r} 66 \\ -22 \\ \hline 44 \end{array}$	$\begin{array}{r} 41 \\ -40 \\ \hline 01 \end{array}$	$\begin{array}{r} 96 \\ -31 \\ \hline 65 \end{array}$	$\begin{array}{r} 95 \\ -53 \\ \hline 42 \end{array}$	$\begin{array}{r} 12 \\ -11 \\ \hline 01 \end{array}$	$\begin{array}{r} 47 \\ -35 \\ \hline 12 \end{array}$	$\begin{array}{r} 84 \\ -21 \\ \hline 63 \end{array}$
$\begin{array}{r} 29 \\ +50 \\ \hline 79 \end{array}$	$\begin{array}{r} 50 \\ +14 \\ \hline 64 \end{array}$	$\begin{array}{r} 25 \\ +14 \\ \hline 39 \end{array}$	$\begin{array}{r} 80 \\ +18 \\ \hline 98 \end{array}$	$\begin{array}{r} 26 \\ +70 \\ \hline 96 \end{array}$	$\begin{array}{r} 63 \\ +15 \\ \hline 78 \end{array}$	$\begin{array}{r} 67 \\ +21 \\ \hline 88 \end{array}$	$\begin{array}{r} 82 \\ +13 \\ \hline 95 \end{array}$
$\begin{array}{r} 16 \\ -15 \\ \hline 01 \end{array}$	$\begin{array}{r} 21 \\ -21 \\ \hline 00 \end{array}$	$\begin{array}{r} 84 \\ -62 \\ \hline 22 \end{array}$	$\begin{array}{r} 27 \\ -21 \\ \hline 06 \end{array}$	$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 13 \\ -11 \\ \hline 02 \end{array}$	$\begin{array}{r} 15 \\ -14 \\ \hline 01 \end{array}$	$\begin{array}{r} 55 \\ -45 \\ \hline 10 \end{array}$
$\begin{array}{r} 48 \\ +11 \\ \hline 59 \end{array}$	$\begin{array}{r} 27 \\ +31 \\ \hline 58 \end{array}$	$\begin{array}{r} 55 \\ +44 \\ \hline 99 \end{array}$	$\begin{array}{r} 17 \\ +31 \\ \hline 48 \end{array}$	$\begin{array}{r} 14 \\ +75 \\ \hline 89 \end{array}$	$\begin{array}{r} 31 \\ +20 \\ \hline 51 \end{array}$	$\begin{array}{r} 19 \\ +60 \\ \hline 79 \end{array}$	$\begin{array}{r} 25 \\ +14 \\ \hline 39 \end{array}$
$\begin{array}{r} 29 \\ -24 \\ \hline 05 \end{array}$	$\begin{array}{r} 35 \\ -25 \\ \hline 10 \end{array}$	$\begin{array}{r} 51 \\ -21 \\ \hline 30 \end{array}$	$\begin{array}{r} 40 \\ -30 \\ \hline 10 \end{array}$	$\begin{array}{r} 92 \\ -92 \\ \hline 00 \end{array}$	$\begin{array}{r} 26 \\ -20 \\ \hline 06 \end{array}$	$\begin{array}{r} 58 \\ -48 \\ \hline 10 \end{array}$	$\begin{array}{r} 87 \\ -20 \\ \hline 67 \end{array}$

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$\begin{array}{r} 89 \\ + 10 \\ \hline 99 \end{array}$	$\begin{array}{r} 43 \\ + 52 \\ \hline 95 \end{array}$	$\begin{array}{r} 23 \\ + 34 \\ \hline 57 \end{array}$	$\begin{array}{r} 31 \\ + 21 \\ \hline 52 \end{array}$	$\begin{array}{r} 79 \\ + 10 \\ \hline 89 \end{array}$	$\begin{array}{r} 69 \\ + 10 \\ \hline 79 \end{array}$	$\begin{array}{r} 57 \\ + 42 \\ \hline 99 \end{array}$	$\begin{array}{r} 74 \\ + 10 \\ \hline 84 \end{array}$
$\begin{array}{r} 76 \\ - 34 \\ \hline 42 \end{array}$	$\begin{array}{r} 64 \\ - 63 \\ \hline 01 \end{array}$	$\begin{array}{r} 67 \\ - 27 \\ \hline 40 \end{array}$	$\begin{array}{r} 56 \\ - 40 \\ \hline 16 \end{array}$	$\begin{array}{r} 79 \\ - 71 \\ \hline 08 \end{array}$	$\begin{array}{r} 29 \\ - 18 \\ \hline 11 \end{array}$	$\begin{array}{r} 31 \\ - 21 \\ \hline 10 \end{array}$	$\begin{array}{r} 59 \\ - 48 \\ \hline 11 \end{array}$
$\begin{array}{r} 71 \\ + 10 \\ \hline 81 \end{array}$	$\begin{array}{r} 45 \\ + 41 \\ \hline 86 \end{array}$	$\begin{array}{r} 39 \\ + 60 \\ \hline 99 \end{array}$	$\begin{array}{r} 17 \\ + 81 \\ \hline 98 \end{array}$	$\begin{array}{r} 13 \\ + 43 \\ \hline 56 \end{array}$	$\begin{array}{r} 57 \\ + 22 \\ \hline 79 \end{array}$	$\begin{array}{r} 45 \\ + 42 \\ \hline 87 \end{array}$	$\begin{array}{r} 12 \\ + 57 \\ \hline 69 \end{array}$
$\begin{array}{r} 43 \\ - 11 \\ \hline 32 \end{array}$	$\begin{array}{r} 55 \\ - 51 \\ \hline 04 \end{array}$	$\begin{array}{r} 90 \\ - 77 \\ \hline 13 \end{array}$	$\begin{array}{r} 56 \\ - 21 \\ \hline 35 \end{array}$	$\begin{array}{r} 75 \\ - 33 \\ \hline 42 \end{array}$	$\begin{array}{r} 48 \\ - 24 \\ \hline 24 \end{array}$	$\begin{array}{r} 18 \\ - 15 \\ \hline 03 \end{array}$	$\begin{array}{r} 36 \\ - 36 \\ \hline 00 \end{array}$
$\begin{array}{r} 47 \\ + 30 \\ \hline 77 \end{array}$	$\begin{array}{r} 82 \\ + 16 \\ \hline 98 \end{array}$	$\begin{array}{r} 89 \\ + 10 \\ \hline 99 \end{array}$	$\begin{array}{r} 84 \\ + 13 \\ \hline 97 \end{array}$	$\begin{array}{r} 22 \\ + 24 \\ \hline 46 \end{array}$	$\begin{array}{r} 45 \\ + 50 \\ \hline 95 \end{array}$	$\begin{array}{r} 20 \\ + 59 \\ \hline 79 \end{array}$	$\begin{array}{r} 11 \\ + 33 \\ \hline 44 \end{array}$
$\begin{array}{r} 17 \\ - 16 \\ \hline 01 \end{array}$	$\begin{array}{r} 66 \\ - 21 \\ \hline 45 \end{array}$	$\begin{array}{r} 69 \\ - 26 \\ \hline 43 \end{array}$	$\begin{array}{r} 98 \\ - 90 \\ \hline 08 \end{array}$	$\begin{array}{r} 60 \\ - 20 \\ \hline 40 \end{array}$	$\begin{array}{r} 21 \\ - 21 \\ \hline 00 \end{array}$	$\begin{array}{r} 53 \\ - 21 \\ \hline 32 \end{array}$	$\begin{array}{r} 50 \\ - 30 \\ \hline 20 \end{array}$
$\begin{array}{r} 50 \\ + 13 \\ \hline 63 \end{array}$	$\begin{array}{r} 76 \\ + 23 \\ \hline 99 \end{array}$	$\begin{array}{r} 52 \\ + 25 \\ \hline 77 \end{array}$	$\begin{array}{r} 92 \\ + 73 \\ \hline 165 \end{array}$	$\begin{array}{r} 72 \\ + 13 \\ \hline 85 \end{array}$	$\begin{array}{r} 38 \\ + 11 \\ \hline 49 \end{array}$	$\begin{array}{r} 62 \\ + 22 \\ \hline 84 \end{array}$	$\begin{array}{r} 65 \\ + 31 \\ \hline 96 \end{array}$
$\begin{array}{r} 39 \\ - 17 \\ \hline 22 \end{array}$	$\begin{array}{r} 50 \\ - 50 \\ \hline 00 \end{array}$	$\begin{array}{r} 68 \\ - 24 \\ \hline 44 \end{array}$	$\begin{array}{r} 92 \\ - 60 \\ \hline 32 \end{array}$	$\begin{array}{r} 33 \\ - 32 \\ \hline 01 \end{array}$	$\begin{array}{r} 78 \\ - 24 \\ \hline 54 \end{array}$	$\begin{array}{r} 94 \\ - 30 \\ \hline 64 \end{array}$	$\begin{array}{r} 28 \\ - 26 \\ \hline 02 \end{array}$
$\begin{array}{r} 89 \\ + 10 \\ \hline 99 \end{array}$	$\begin{array}{r} 24 \\ + 11 \\ \hline 35 \end{array}$	$\begin{array}{r} 84 \\ + 15 \\ \hline 99 \end{array}$	$\begin{array}{r} 86 \\ + 11 \\ \hline 97 \end{array}$	$\begin{array}{r} 65 \\ + 20 \\ \hline 85 \end{array}$	$\begin{array}{r} 67 \\ + 32 \\ \hline 99 \end{array}$	$\begin{array}{r} 36 \\ + 63 \\ \hline 99 \end{array}$	$\begin{array}{r} 80 \\ + 18 \\ \hline 98 \end{array}$
$\begin{array}{r} 36 \\ - 14 \\ \hline 22 \end{array}$	$\begin{array}{r} 11 \\ - 10 \\ \hline 01 \end{array}$	$\begin{array}{r} 46 \\ - 25 \\ \hline 21 \end{array}$	$\begin{array}{r} 87 \\ - 67 \\ \hline 20 \end{array}$	$\begin{array}{r} 55 \\ - 35 \\ \hline 20 \end{array}$	$\begin{array}{r} 89 \\ - 77 \\ \hline 12 \end{array}$	$\begin{array}{r} 14 \\ - 10 \\ \hline 04 \end{array}$	$\begin{array}{r} 11 \\ - 10 \\ \hline 01 \end{array}$

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$\begin{array}{r} 11 \\ +10 \\ \hline 21 \end{array}$	$\begin{array}{r} 62 \\ +10 \\ \hline 72 \end{array}$	$\begin{array}{r} 69 \\ +20 \\ \hline 89 \end{array}$	$\begin{array}{r} 71 \\ +27 \\ \hline 98 \end{array}$	$\begin{array}{r} 50 \\ +22 \\ \hline 72 \end{array}$	$\begin{array}{r} 70 \\ +18 \\ \hline 88 \end{array}$	$\begin{array}{r} 68 \\ +20 \\ \hline 88 \end{array}$	$\begin{array}{r} 72 \\ +17 \\ \hline 89 \end{array}$
$\begin{array}{r} 60 \\ -30 \\ \hline 30 \end{array}$	$\begin{array}{r} 81 \\ -21 \\ \hline 60 \end{array}$	$\begin{array}{r} 34 \\ -14 \\ \hline 20 \end{array}$	$\begin{array}{r} 81 \\ -30 \\ \hline 51 \end{array}$	$\begin{array}{r} 18 \\ -11 \\ \hline 07 \end{array}$	$\begin{array}{r} 21 \\ -11 \\ \hline 10 \end{array}$	$\begin{array}{r} 58 \\ -22 \\ \hline 36 \end{array}$	$\begin{array}{r} 97 \\ -12 \\ \hline 85 \end{array}$
$\begin{array}{r} 33 \\ +65 \\ \hline 98 \end{array}$	$\begin{array}{r} 83 \\ +10 \\ \hline 93 \end{array}$	$\begin{array}{r} 33 \\ +53 \\ \hline 86 \end{array}$	$\begin{array}{r} 83 \\ +14 \\ \hline 97 \end{array}$	$\begin{array}{r} 82 \\ +13 \\ \hline 95 \end{array}$	$\begin{array}{r} 11 \\ +25 \\ \hline 36 \end{array}$	$\begin{array}{r} 30 \\ +35 \\ \hline 65 \end{array}$	$\begin{array}{r} 88 \\ +11 \\ \hline 99 \end{array}$
$\begin{array}{r} 84 \\ -74 \\ \hline 10 \end{array}$	$\begin{array}{r} 91 \\ -70 \\ \hline 21 \end{array}$	$\begin{array}{r} 50 \\ -40 \\ \hline 10 \end{array}$	$\begin{array}{r} 37 \\ -12 \\ \hline 25 \end{array}$	$\begin{array}{r} 28 \\ -10 \\ \hline 18 \end{array}$	$\begin{array}{r} 51 \\ -40 \\ \hline 11 \end{array}$	$\begin{array}{r} 24 \\ -20 \\ \hline 04 \end{array}$	$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$
$\begin{array}{r} 57 \\ +22 \\ \hline 79 \end{array}$	$\begin{array}{r} 74 \\ +15 \\ \hline 89 \end{array}$	$\begin{array}{r} 41 \\ +47 \\ \hline 88 \end{array}$	$\begin{array}{r} 37 \\ +20 \\ \hline 57 \end{array}$	$\begin{array}{r} 30 \\ +41 \\ \hline 71 \end{array}$	$\begin{array}{r} 55 \\ +12 \\ \hline 67 \end{array}$	$\begin{array}{r} 45 \\ +14 \\ \hline 59 \end{array}$	$\begin{array}{r} 83 \\ +10 \\ \hline 93 \end{array}$
$\begin{array}{r} 22 \\ -11 \\ \hline 11 \end{array}$	$\begin{array}{r} 97 \\ -41 \\ \hline 56 \end{array}$	$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 62 \\ -60 \\ \hline 02 \end{array}$	$\begin{array}{r} 21 \\ -20 \\ \hline 01 \end{array}$	$\begin{array}{r} 96 \\ -93 \\ \hline 03 \end{array}$	$\begin{array}{r} 90 \\ -80 \\ \hline 10 \end{array}$	$\begin{array}{r} 98 \\ -58 \\ \hline 40 \end{array}$
$\begin{array}{r} 12 \\ +52 \\ \hline 64 \end{array}$	$\begin{array}{r} 20 \\ +15 \\ \hline 35 \end{array}$	$\begin{array}{r} 51 \\ +21 \\ \hline 72 \end{array}$	$\begin{array}{r} 88 \\ +11 \\ \hline 99 \end{array}$	$\begin{array}{r} 27 \\ +72 \\ \hline 99 \end{array}$	$\begin{array}{r} 60 \\ +27 \\ \hline 87 \end{array}$	$\begin{array}{r} 39 \\ +10 \\ \hline 49 \end{array}$	$\begin{array}{r} 33 \\ +26 \\ \hline 59 \end{array}$
$\begin{array}{r} 14 \\ -13 \\ \hline 01 \end{array}$	$\begin{array}{r} 21 \\ -10 \\ \hline 11 \end{array}$	$\begin{array}{r} 57 \\ -13 \\ \hline 44 \end{array}$	$\begin{array}{r} 53 \\ -40 \\ \hline 13 \end{array}$	$\begin{array}{r} 27 \\ -26 \\ \hline 01 \end{array}$	$\begin{array}{r} 96 \\ -15 \\ \hline 81 \end{array}$	$\begin{array}{r} 32 \\ -20 \\ \hline 12 \end{array}$	$\begin{array}{r} 12 \\ -10 \\ \hline 02 \end{array}$
$\begin{array}{r} 63 \\ +15 \\ \hline 78 \end{array}$	$\begin{array}{r} 19 \\ +50 \\ \hline 69 \end{array}$	$\begin{array}{r} 76 \\ +21 \\ \hline 97 \end{array}$	$\begin{array}{r} 79 \\ +10 \\ \hline 89 \end{array}$	$\begin{array}{r} 10 \\ +17 \\ \hline 27 \end{array}$	$\begin{array}{r} 52 \\ +33 \\ \hline 85 \end{array}$	$\begin{array}{r} 43 \\ +43 \\ \hline 86 \end{array}$	$\begin{array}{r} 72 \\ +11 \\ \hline 83 \end{array}$
$\begin{array}{r} 94 \\ -11 \\ \hline 83 \end{array}$	$\begin{array}{r} 85 \\ -15 \\ \hline 70 \end{array}$	$\begin{array}{r} 46 \\ -12 \\ \hline 34 \end{array}$	$\begin{array}{r} 62 \\ -62 \\ \hline 00 \end{array}$	$\begin{array}{r} 46 \\ -34 \\ \hline 12 \end{array}$	$\begin{array}{r} 30 \\ -20 \\ \hline 10 \end{array}$	$\begin{array}{r} 85 \\ -63 \\ \hline 22 \end{array}$	$\begin{array}{r} 38 \\ -12 \\ \hline 26 \end{array}$

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$\begin{array}{r} 85 \\ +14 \\ \hline 99 \end{array}$	$\begin{array}{r} 39 \\ +60 \\ \hline 99 \end{array}$	$\begin{array}{r} 37 \\ +51 \\ \hline 88 \end{array}$	$\begin{array}{r} 33 \\ +18 \\ \hline 49 \end{array}$	$\begin{array}{r} 33 \\ +56 \\ \hline 89 \end{array}$	$\begin{array}{r} 12 \\ +20 \\ \hline 32 \end{array}$	$\begin{array}{r} 12 \\ +11 \\ \hline 23 \end{array}$	$\begin{array}{r} 65 \\ +11 \\ \hline 76 \end{array}$
$\begin{array}{r} 41 \\ -40 \\ \hline 01 \end{array}$	$\begin{array}{r} 24 \\ -23 \\ \hline 01 \end{array}$	$\begin{array}{r} 75 \\ -54 \\ \hline 21 \end{array}$	$\begin{array}{r} 23 \\ -11 \\ \hline 12 \end{array}$	$\begin{array}{r} 57 \\ -46 \\ \hline 11 \end{array}$	$\begin{array}{r} 98 \\ -44 \\ \hline 54 \end{array}$	$\begin{array}{r} 51 \\ -20 \\ \hline 31 \end{array}$	$\begin{array}{r} 36 \\ -13 \\ \hline 23 \end{array}$
$\begin{array}{r} 84 \\ +13 \\ \hline 97 \end{array}$	$\begin{array}{r} 24 \\ +21 \\ \hline 45 \end{array}$	$\begin{array}{r} 21 \\ +30 \\ \hline 51 \end{array}$	$\begin{array}{r} 38 \\ +50 \\ \hline 88 \end{array}$	$\begin{array}{r} 72 \\ +23 \\ \hline 95 \end{array}$	$\begin{array}{r} 79 \\ +20 \\ \hline 99 \end{array}$	$\begin{array}{r} 63 \\ +34 \\ \hline 97 \end{array}$	$\begin{array}{r} 10 \\ +47 \\ \hline 57 \end{array}$
$\begin{array}{r} 33 \\ -20 \\ \hline 13 \end{array}$	$\begin{array}{r} 72 \\ -31 \\ \hline 41 \end{array}$	$\begin{array}{r} 18 \\ -11 \\ \hline 07 \end{array}$	$\begin{array}{r} 13 \\ -13 \\ \hline 00 \end{array}$	$\begin{array}{r} 64 \\ -21 \\ \hline 43 \end{array}$	$\begin{array}{r} 51 \\ -31 \\ \hline 20 \end{array}$	$\begin{array}{r} 24 \\ -11 \\ \hline 00 \end{array}$	$\begin{array}{r} 67 \\ -52 \\ \hline 15 \end{array}$
$\begin{array}{r} 67 \\ +21 \\ \hline 88 \end{array}$	$\begin{array}{r} 24 \\ +51 \\ \hline 75 \end{array}$	$\begin{array}{r} 47 \\ +32 \\ \hline 79 \end{array}$	$\begin{array}{r} 12 \\ +63 \\ \hline 75 \end{array}$	$\begin{array}{r} 14 \\ +60 \\ \hline 74 \end{array}$	$\begin{array}{r} 33 \\ +11 \\ \hline 44 \end{array}$	$\begin{array}{r} 82 \\ +13 \\ \hline 95 \end{array}$	$\begin{array}{r} 77 \\ +20 \\ \hline 97 \end{array}$
$\begin{array}{r} 72 \\ -40 \\ \hline 32 \end{array}$	$\begin{array}{r} 88 \\ -70 \\ \hline 18 \end{array}$	$\begin{array}{r} 27 \\ -14 \\ \hline 13 \end{array}$	$\begin{array}{r} 84 \\ -50 \\ \hline 34 \end{array}$	$\begin{array}{r} 34 \\ -34 \\ \hline 00 \end{array}$	$\begin{array}{r} 87 \\ -61 \\ \hline 26 \end{array}$	$\begin{array}{r} 84 \\ -51 \\ \hline 33 \end{array}$	$\begin{array}{r} 20 \\ -10 \\ \hline 10 \end{array}$
$\begin{array}{r} 75 \\ +11 \\ \hline 86 \end{array}$	$\begin{array}{r} 48 \\ +31 \\ \hline 79 \end{array}$	$\begin{array}{r} 44 \\ +25 \\ \hline 69 \end{array}$	$\begin{array}{r} 72 \\ +22 \\ \hline 94 \end{array}$	$\begin{array}{r} 59 \\ +10 \\ \hline 69 \end{array}$	$\begin{array}{r} 89 \\ +10 \\ \hline 99 \end{array}$	$\begin{array}{r} 15 \\ +32 \\ \hline 47 \end{array}$	$\begin{array}{r} 50 \\ +44 \\ \hline 94 \end{array}$
$\begin{array}{r} 65 \\ -45 \\ \hline 20 \end{array}$	$\begin{array}{r} 17 \\ -12 \\ \hline 05 \end{array}$	$\begin{array}{r} 13 \\ -13 \\ \hline 00 \end{array}$	$\begin{array}{r} 88 \\ -67 \\ \hline 21 \end{array}$	$\begin{array}{r} 56 \\ -12 \\ \hline 44 \end{array}$	$\begin{array}{r} 99 \\ -90 \\ \hline 09 \end{array}$	$\begin{array}{r} 99 \\ -52 \\ \hline 47 \end{array}$	$\begin{array}{r} 64 \\ -31 \\ \hline 33 \end{array}$
$\begin{array}{r} 17 \\ +12 \\ \hline 29 \end{array}$	$\begin{array}{r} 25 \\ +51 \\ \hline 76 \end{array}$	$\begin{array}{r} 13 \\ +66 \\ \hline 79 \end{array}$	$\begin{array}{r} 38 \\ +11 \\ \hline 49 \end{array}$	$\begin{array}{r} 25 \\ +70 \\ \hline 95 \end{array}$	$\begin{array}{r} 70 \\ +23 \\ \hline 93 \end{array}$	$\begin{array}{r} 59 \\ +40 \\ \hline 99 \end{array}$	$\begin{array}{r} 84 \\ +11 \\ \hline 95 \end{array}$
$\begin{array}{r} 79 \\ -60 \\ \hline 19 \end{array}$	$\begin{array}{r} 45 \\ -22 \\ \hline 23 \end{array}$	$\begin{array}{r} 58 \\ -34 \\ \hline 24 \end{array}$	$\begin{array}{r} 61 \\ -61 \\ \hline 00 \end{array}$	$\begin{array}{r} 55 \\ -10 \\ \hline 45 \end{array}$	$\begin{array}{r} 93 \\ -61 \\ \hline 32 \end{array}$	$\begin{array}{r} 21 \\ -11 \\ \hline 10 \end{array}$	$\begin{array}{r} 49 \\ -49 \\ \hline 00 \end{array}$

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$\begin{array}{r} 48 \\ +20 \\ \hline 68 \end{array}$	$\begin{array}{r} 13 \\ +16 \\ \hline 29 \end{array}$	$\begin{array}{r} 37 \\ +30 \\ \hline 67 \end{array}$	$\begin{array}{r} 48 \\ +30 \\ \hline 78 \end{array}$	$\begin{array}{r} 42 \\ +14 \\ \hline 56 \end{array}$	$\begin{array}{r} 87 \\ +11 \\ \hline 98 \end{array}$	$\begin{array}{r} 19 \\ +70 \\ \hline 89 \end{array}$	$\begin{array}{r} 26 \\ +31 \\ \hline 57 \end{array}$
$\begin{array}{r} 42 \\ -20 \\ \hline 22 \end{array}$	$\begin{array}{r} 82 \\ -51 \\ \hline 31 \end{array}$	$\begin{array}{r} 22 \\ -10 \\ \hline 12 \end{array}$	$\begin{array}{r} 64 \\ -42 \\ \hline 22 \end{array}$	$\begin{array}{r} 49 \\ -43 \\ \hline 6 \end{array}$	$\begin{array}{r} 31 \\ -30 \\ \hline 1 \end{array}$	$\begin{array}{r} 43 \\ -33 \\ \hline 10 \end{array}$	$\begin{array}{r} 40 \\ -30 \\ \hline 10 \end{array}$
$\begin{array}{r} 56 \\ +40 \\ \hline 96 \end{array}$	$\begin{array}{r} 58 \\ +31 \\ \hline 89 \end{array}$	$\begin{array}{r} 31 \\ +32 \\ \hline 63 \end{array}$	$\begin{array}{r} 15 \\ +34 \\ \hline 49 \end{array}$	$\begin{array}{r} 13 \\ +56 \\ \hline 69 \end{array}$	$\begin{array}{r} 43 \\ +15 \\ \hline 58 \end{array}$	$\begin{array}{r} 55 \\ +42 \\ \hline 97 \end{array}$	$\begin{array}{r} 80 \\ +17 \\ \hline 97 \end{array}$
$\begin{array}{r} 59 \\ -31 \\ \hline 28 \end{array}$	$\begin{array}{r} 96 \\ -50 \\ \hline 46 \end{array}$	$\begin{array}{r} 84 \\ -30 \\ \hline 54 \end{array}$	$\begin{array}{r} 52 \\ -22 \\ \hline 30 \end{array}$	$\begin{array}{r} 59 \\ -26 \\ \hline 33 \end{array}$	$\begin{array}{r} 79 \\ -69 \\ \hline 10 \end{array}$	$\begin{array}{r} 77 \\ -30 \\ \hline 47 \end{array}$	$\begin{array}{r} 86 \\ -21 \\ \hline 65 \end{array}$
$\begin{array}{r} 28 \\ +31 \\ \hline 59 \end{array}$	$\begin{array}{r} 76 \\ +10 \\ \hline 86 \end{array}$	$\begin{array}{r} 21 \\ +35 \\ \hline 56 \end{array}$	$\begin{array}{r} 34 \\ +61 \\ \hline 95 \end{array}$	$\begin{array}{r} 41 \\ +37 \\ \hline 78 \end{array}$	$\begin{array}{r} 54 \\ +45 \\ \hline 99 \end{array}$	$\begin{array}{r} 20 \\ +38 \\ \hline 58 \end{array}$	$\begin{array}{r} 46 \\ +22 \\ \hline 68 \end{array}$
$\begin{array}{r} 44 \\ -44 \\ \hline 00 \end{array}$	$\begin{array}{r} 93 \\ -31 \\ \hline 62 \end{array}$	$\begin{array}{r} 99 \\ -60 \\ \hline 39 \end{array}$	$\begin{array}{r} 98 \\ -10 \\ \hline 88 \end{array}$	$\begin{array}{r} 52 \\ -41 \\ \hline 11 \end{array}$	$\begin{array}{r} 77 \\ -67 \\ \hline 10 \end{array}$	$\begin{array}{r} 95 \\ -21 \\ \hline 74 \end{array}$	$\begin{array}{r} 31 \\ -30 \\ \hline 01 \end{array}$
$\begin{array}{r} 18 \\ +71 \\ \hline 89 \end{array}$	$\begin{array}{r} 76 \\ +11 \\ \hline 87 \end{array}$	$\begin{array}{r} 59 \\ +40 \\ \hline 99 \end{array}$	$\begin{array}{r} 85 \\ +12 \\ \hline 97 \end{array}$	$\begin{array}{r} 88 \\ +10 \\ \hline 98 \end{array}$	$\begin{array}{r} 18 \\ +21 \\ \hline 39 \end{array}$	$\begin{array}{r} 13 \\ +83 \\ \hline 96 \end{array}$	$\begin{array}{r} 89 \\ +10 \\ \hline 99 \end{array}$
$\begin{array}{r} 54 \\ -22 \\ \hline 32 \end{array}$	$\begin{array}{r} 41 \\ -40 \\ \hline 01 \end{array}$	$\begin{array}{r} 57 \\ -12 \\ \hline 45 \end{array}$	$\begin{array}{r} 49 \\ -37 \\ \hline 12 \end{array}$	$\begin{array}{r} 98 \\ -22 \\ \hline 76 \end{array}$	$\begin{array}{r} 21 \\ -10 \\ \hline 11 \end{array}$	$\begin{array}{r} 44 \\ -13 \\ \hline 31 \end{array}$	$\begin{array}{r} 53 \\ -23 \\ \hline 30 \end{array}$
$\begin{array}{r} 74 \\ +25 \\ \hline 99 \end{array}$	$\begin{array}{r} 65 \\ +13 \\ \hline 78 \end{array}$	$\begin{array}{r} 54 \\ +20 \\ \hline 74 \end{array}$	$\begin{array}{r} 38 \\ +41 \\ \hline 79 \end{array}$	$\begin{array}{r} 67 \\ +32 \\ \hline 99 \end{array}$	$\begin{array}{r} 51 \\ +41 \\ \hline 92 \end{array}$	$\begin{array}{r} 59 \\ +30 \\ \hline 89 \end{array}$	$\begin{array}{r} 29 \\ +40 \\ \hline 69 \end{array}$
$\begin{array}{r} 78 \\ -38 \\ \hline 40 \end{array}$	$\begin{array}{r} 93 \\ -43 \\ \hline 50 \end{array}$	$\begin{array}{r} 71 \\ -60 \\ \hline 11 \end{array}$	$\begin{array}{r} 60 \\ -40 \\ \hline 20 \end{array}$	$\begin{array}{r} 29 \\ -22 \\ \hline 07 \end{array}$	$\begin{array}{r} 29 \\ -19 \\ \hline 10 \end{array}$	$\begin{array}{r} 78 \\ -33 \\ \hline 45 \end{array}$	$\begin{array}{r} 19 \\ -15 \\ \hline 04 \end{array}$

150
150

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$\begin{array}{r} 27 \\ +22 \\ \hline 49 \end{array}$	$\begin{array}{r} 70 \\ +18 \\ \hline 88 \end{array}$	$\begin{array}{r} 46 \\ +42 \\ \hline 88 \end{array}$	$\begin{array}{r} 50 \\ +39 \\ \hline 89 \end{array}$	$\begin{array}{r} 82 \\ +10 \\ \hline 92 \end{array}$	$\begin{array}{r} 13 \\ +41 \\ \hline 54 \end{array}$	$\begin{array}{r} 43 \\ +43 \\ \hline 86 \end{array}$	$\begin{array}{r} 78 \\ +20 \\ \hline 98 \end{array}$
$\begin{array}{r} 50 \\ -40 \\ \hline 10 \end{array}$	$\begin{array}{r} 90 \\ -40 \\ \hline 50 \end{array}$	$\begin{array}{r} 42 \\ -20 \\ \hline 22 \end{array}$	$\begin{array}{r} 75 \\ -15 \\ \hline 60 \end{array}$	$\begin{array}{r} 31 \\ -21 \\ \hline 10 \end{array}$	$\begin{array}{r} 69 \\ -48 \\ \hline 21 \end{array}$	$\begin{array}{r} 30 \\ -30 \\ \hline 00 \end{array}$	$\begin{array}{r} 34 \\ -23 \\ \hline 11 \end{array}$
$\begin{array}{r} 89 \\ +10 \\ \hline 99 \end{array}$	$\begin{array}{r} 14 \\ +61 \\ \hline 75 \end{array}$	$\begin{array}{r} 11 \\ +14 \\ \hline 25 \end{array}$	$\begin{array}{r} 76 \\ +21 \\ \hline 97 \end{array}$	$\begin{array}{r} 58 \\ +11 \\ \hline 69 \end{array}$	$\begin{array}{r} 34 \\ +53 \\ \hline 87 \end{array}$	$\begin{array}{r} 58 \\ +11 \\ \hline 69 \end{array}$	$\begin{array}{r} 18 \\ +10 \\ \hline 28 \end{array}$
$\begin{array}{r} 87 \\ -81 \\ \hline 06 \end{array}$	$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 76 \\ -62 \\ \hline 14 \end{array}$	$\begin{array}{r} 44 \\ -34 \\ \hline 10 \end{array}$	$\begin{array}{r} 69 \\ -39 \\ \hline 30 \end{array}$	$\begin{array}{r} 43 \\ -13 \\ \hline 30 \end{array}$	$\begin{array}{r} 23 \\ -11 \\ \hline 12 \end{array}$	$\begin{array}{r} 67 \\ -45 \\ \hline 22 \end{array}$
$\begin{array}{r} 11 \\ +87 \\ \hline 98 \end{array}$	$\begin{array}{r} 10 \\ +55 \\ \hline 65 \end{array}$	$\begin{array}{r} 52 \\ +11 \\ \hline 63 \end{array}$	$\begin{array}{r} 35 \\ +14 \\ \hline 49 \end{array}$	$\begin{array}{r} 20 \\ +61 \\ \hline 81 \end{array}$	$\begin{array}{r} 53 \\ +45 \\ \hline 98 \end{array}$	$\begin{array}{r} 30 \\ +69 \\ \hline 99 \end{array}$	$\begin{array}{r} 86 \\ +12 \\ \hline 98 \end{array}$
$\begin{array}{r} 10 \\ -10 \\ \hline 00 \end{array}$	$\begin{array}{r} 58 \\ -51 \\ \hline 07 \end{array}$	$\begin{array}{r} 73 \\ -40 \\ \hline 33 \end{array}$	$\begin{array}{r} 67 \\ -13 \\ \hline 54 \end{array}$	$\begin{array}{r} 76 \\ -54 \\ \hline 22 \end{array}$	$\begin{array}{r} 19 \\ -15 \\ \hline 04 \end{array}$	$\begin{array}{r} 26 \\ -26 \\ \hline 00 \end{array}$	$\begin{array}{r} 93 \\ -62 \\ \hline 31 \end{array}$
$\begin{array}{r} 39 \\ +30 \\ \hline 69 \end{array}$	$\begin{array}{r} 32 \\ +12 \\ \hline 44 \end{array}$	$\begin{array}{r} 10 \\ +34 \\ \hline 44 \end{array}$	$\begin{array}{r} 42 \\ +53 \\ \hline 95 \end{array}$	$\begin{array}{r} 72 \\ +14 \\ \hline 86 \end{array}$	$\begin{array}{r} 85 \\ +13 \\ \hline 98 \end{array}$	$\begin{array}{r} 53 \\ +44 \\ \hline 97 \end{array}$	$\begin{array}{r} 82 \\ +12 \\ \hline 94 \end{array}$
$\begin{array}{r} 42 \\ -40 \\ \hline 02 \end{array}$	$\begin{array}{r} 88 \\ -15 \\ \hline 73 \end{array}$	$\begin{array}{r} 57 \\ -26 \\ \hline 31 \end{array}$	$\begin{array}{r} 99 \\ -62 \\ \hline 37 \end{array}$	$\begin{array}{r} 32 \\ -20 \\ \hline 12 \end{array}$	$\begin{array}{r} 72 \\ -50 \\ \hline 22 \end{array}$	$\begin{array}{r} 57 \\ -47 \\ \hline 10 \end{array}$	$\begin{array}{r} 91 \\ -61 \\ \hline 30 \end{array}$
$\begin{array}{r} 57 \\ +21 \\ \hline 78 \end{array}$	$\begin{array}{r} 50 \\ +32 \\ \hline 82 \end{array}$	$\begin{array}{r} 33 \\ +15 \\ \hline 48 \end{array}$	$\begin{array}{r} 88 \\ +10 \\ \hline 98 \end{array}$	$\begin{array}{r} 54 \\ +40 \\ \hline 94 \end{array}$	$\begin{array}{r} 44 \\ +11 \\ \hline 55 \end{array}$	$\begin{array}{r} 12 \\ +73 \\ \hline 85 \end{array}$	$\begin{array}{r} 65 \\ +21 \\ \hline 86 \end{array}$
$\begin{array}{r} 71 \\ -60 \\ \hline 11 \end{array}$	$\begin{array}{r} 68 \\ -65 \\ \hline 03 \end{array}$	$\begin{array}{r} 65 \\ -35 \\ \hline 30 \end{array}$	$\begin{array}{r} 29 \\ -17 \\ \hline 12 \end{array}$	$\begin{array}{r} 74 \\ -70 \\ \hline 04 \end{array}$	$\begin{array}{r} 64 \\ -32 \\ \hline 32 \end{array}$	$\begin{array}{r} 30 \\ -30 \\ \hline 00 \end{array}$	$\begin{array}{r} 92 \\ -11 \\ \hline 81 \end{array}$

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70
70

KP415.E01 2 Hours Post-dose Math Test

NAME _____							
82	58	49	50	70	43	72	48
+14	+10	+30	+38	+17	+32	+10	+30
96	68	79	88	87	75	82	78
91	72	43	53	12	82	53	15
-80	-61	-31	-12	-12	-61	-12	-10
11	11	12	41	00	21	41	65
28	76	15	27	62	72	71	18
+62	+23	+51	+12	+13	+14	+14	+30
69	49	64	39	75	86	85	40
33	46	29	40	80	77	66	35
-12	-30	-11	-30	-60	-35	-41	-12
21	10	18	10	20	42	25	27
79	87	63	28	47	89	39	56
+20	+12	+10	+11	+22	+10	+50	+32
79	99	73	39	69	74	89	68
94	97	95	31	67	35	37	71
-33	-96	-35	-11	-61	-24	-13	-31
61	01	66	26	06	11	24	40
87	89	75	76	73	65	72	41
+10	+10	+21	+22	+25	+23	+20	+53
97	99	96	98	98	87	92	94
32	37	85	93	90	81	25	62
-31	-33	-40	-91	-50	-30	-10	-32
01	04	45	02	40	51	15	30
56	77	56	20	45	79	56	80
+40	+10	+43	+56	+14	+10	+12	+15
14	87	91	76	59	81	62	95
31	82	57	39	30	70	39	22
-31	-72	-47	-31	-20	-30	-19	-21
00	10	10	08	10	40	20	01

178/180

15	23	71	50	24	78	55	84
+62	+51	+12	+31	+31	+11	+13	+12
77	74	83	81	53	81	68	96
88	98	79	65	97	83	88	34
-84	-12	-26	-54	-61	-12	-67	-34
29	10	53	11	39	71	27	00
85	30	85	73	69	49	45	52
+14	+17	+13	+21	+20	+30	+14	+17
99	47	98	91	89	70	59	69
66	23	37	39	54	78	55	69
-51	-23	-12	-22	-31	-42	-15	-29
15	00	25	17	23	16	40	70
57	48	87	19	70	28	67	89
+21	+50	+12	+70	+10	+41	+20	+10
73	98	94	82	30	69	87	94
37	37	99	86	77	79	10	37
-37	-12	-50	-76	-17	-12	-10	-27
00	25	99	10	60	67	00	10
14	74	43	58	49	47	77	13
+24	+12	+51	+31	+40	+11	+21	+22
38	86	99	89	89	58	98	55
60	14	62	53	52	31	13	93
-40	-13	-12	-32	-21	-10	-13	-21
20	01	50	21	31	21	00	72
40	63	69	43	81	13	71	75
+15	+26	+20	+34	+15	+34	+16	+14
55	89	89	77	96	47	82	59
30	47	53	32	81	14	43	38
-30	-34	-23	-31	-60	-11	-22	-38
08	13	30	01	21	03	21	00

180/180

12	29	47	18	76	40	55	31
+33	+40	+40	+41	+12	+18	+34	+43
45	69	87	59	88	58	87	79
59	42	61	58	99	58	26	19
-17	-21	-51	-46	-18	-47	-25	-13
72	23	10	12	81	11	01	00
19	78	45	66	25	50	80	17
+50	+10	+21	+12	+63	+15	+14	+70
69	88	60	73	63	15	14	70
60	76	85	69	37	90	43	80
-20	-25	-63	-66	-21	-10	-40	-50
82	31	24	34	69	27	41	46
+12	+52	+12	+31	+20	+21	+52	+10
77	78	34	76	21	51	58	50
-77	-45	-34	-12	-20	-10	-55	-40
67	64	19	68	50	38	35	11
+31	+25	+80	+30	+19	+31	+22	+33
89	96	72	63	86	62	64	91
-32	-22	-51	-22	-66	-42	-20	-91
53	42	86	82	17	79	84	76
+42	+44	+11	+16	+22	+20	+13	+21
62	62	96	49	47	91	10	86
-11	-32	-72	-49	-47	-50	-10	-72

181/200

Pre-dose: 54/55
 30 mins: 144/145
 1 hour: 150/150
 2 hour: 178/180

Parent-Reported Comments

KP415.E01 Study

- **Subject DSS on 40 mg KP415**
- **Comments from subject's parent:**
 - **Getting A's in Math, Science & Computer Literacy**
 - **C's in Chorus and English**
 - **No complaints from the teachers**
 - **Last year was getting C's, D's and F's**

Matthew Brams, MD

- Dr. Brams serves as the Chief Medical Officer of Cingulate Therapeutics, a development-stage company bringing two ADHD assets to market in 2020. He is an Assistant Professor of Psychiatry at Baylor College of Medicine and contributes lectures to their core curriculum. In addition, he has been an invited speaker to numerous medical conferences, both regionally, nationally and internationally.
- He is the Founder of Bayou City Research and has been an investigator in over 200 Phase 1-4 clinical trials in all areas of psychiatry, specializing in ADHD.
- In addition to having lifetime board certification in Adult, Adolescent, and Child Psychiatry, Dr. Brams currently serves as a Senior National Board Examiner for the American Board of Psychiatry and Neurology. He is also a member of the American Academy of Child and Adolescent Psychiatry.
- Dr. Brams completed his medical training at The University of Texas Health Science Center in Houston and his residency and Child Fellowship and Baylor College of Medicine.



Prescribing ADHD Medications in a Large Outpatient Practice: The Good, The Bad, and the Ugly

Matthew Brams, MD

Practice Overview

- Opened in 1992
- 3 Board Certified Adult and Child Psychiatrists
- 7 Mid Levels
- 12,000 Active Patients
- 25% Medicaid/Medicare, 75% Managed Care/Self Pay
- Over 10,000 Stimulant Prescriptions Annually
- 1 Full Time Employee Just Doing Prior Authorizations

Research Experience

- Bayou City Research opened in 1999
- Involved in over 200 clinical trials
- Contributed to development of almost every ADHD product on market
- On many advisory boards of ADHD pharma companies
- Testify in front of several state Medicaid panels

Complaints of ADHD Patients and Families

- “Medications don’t last the full day”
- “In morning, it takes too long to start working”
- “I don’t want to take a dose at school”
- “In the afternoon, it seems that the medicine wears off and my child is behaving worse than even before he took his medicine” (rebound)
- “In the afternoon, I notice the medicine wearing off and I am really irritable” (crash)

Generic ADHD Meds

- Adderall, Adderall XR – Shorter-acting, very high abuse potential, still very expensive
- Dexedrine tabs and spansules – Short-acting, high abusability
- Ritalin LA – Short-acting, often twice-daily medication
- Focalin, Focalin XR – Active isomer of methylphenidate (dexmethylphenidate); XR formulation has fast onset (30 minutes) BUT shorter duration, needs booster or twice daily
- Concerta – First-line drug, slow onset but good afternoon efficacy, can't sprinkle
- Metadate CD, ER – Shorter duration, possibly less efficacious in afternoon

Brand Name ADHD Medications Are Preferred

(But not easily accessed)

Barriers to Prescribing Branded Meds

- Expensive
- Some not on drug formularies
- Most not on Medicaid formularies
- Most not preferred on Medicaid
- Many “me too” meds that have no real clinical improvement from generics
- Need prior approvals - very labor intensive at times

Accessible Branded Meds

- Vyvanse, Vyvanse Chew - Prodrug, longer duration, “smoother”, first of its kind, less likeability in terms of abuse potential
- Dyanavel XR - First long-acting amphetamine in oral suspension, fast onset, long duration, ability to titrate slowly or rapidly and microtitrate
- Quillivant XR - First longer-acting methylphenidate in oral suspension, has production issues

Qualities of Inaccessible Meds

- “Me too” meds
- Expensive
- Do not address unmet needs
- Non-traditional delivery systems that are not routinely prescribed by clinicians, especially Pediatricians and more conservative providers (i.e., dissolvable tablet versus traditional tablet)
- Niche meds (mainly for children who cant swallow pills)

Inaccessible Branded Meds (combined market share of less than 5%)

- Aptensio XR – methylphenidate preparation, intermediate duration, no unmet clinical need
- Evekeo – d,l amphetamine preparation, intermediate duration, may need twice daily, no unmet clinical needs
- Zenzedi – branded amphetamine, can be split four ways (double scored) but no greater efficacy than generic dexedrine
- Cotelpla – oral dissolving tablet (ODT) methylphenidate, faster onset, longer duration but ODT
- Adzenys XR – Bioequivalent to Adderall, ODT technology but no real unmet clinical needs
- Quillichew – chewable version of Quillivant. Do we really want to cannibalize Quillivant?

Qualities of Accessible Branded Meds

- Address unmet needs – MAKES CLINICAL SENSE to prescribe!
- Fast onset
- Long duration
- Improved tolerability
- Once daily preferred, with little use of afternoon boosters
- First-line usage (pharmacist will stock more readily, etc.)
- Cost
- Preferred on Medicaid

First-Line ADHD Drugs Have The Following

- Tablets or capsules (oral suspensions can be used in any age but relegated to the younger population)
- Not niched to a small segment of the ADHD population
- PREFERRED ON MEDICAID – clinicians do not like prior authorizations
 - Will use generics for convenience unless the branded meds do NOT require a prior approval in most cases and is on the drug formularies
- Meets clinical unmet needs - fast onset, true once-daily duration, favorable tolerability, at least as effective as other stimulants
- Low co-pays, effective discount cards

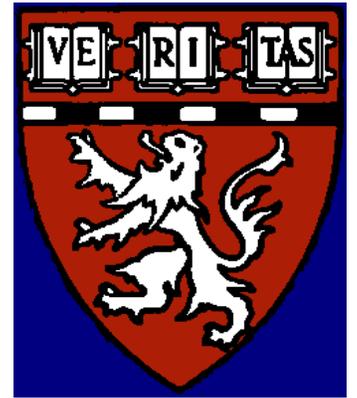
Timothy Edwin Wilens, MD

- Dr. Timothy Wilens is Chief, Division of Child and Adolescent Psychiatry and Co-Director, Center for Addiction Medicine at the Massachusetts General Hospital. He is also Associate Professor of Psychiatry at Harvard Medical School in Boston, Massachusetts.
- Dr. Wilens' research interests include the relationship among ADHD, bipolar disorder, and substance use disorders; and the pharmacotherapy of ADHD and juvenile bipolar disorder across the lifespan.
- Dr. Wilens is a Distinguished Fellow of the American Psychiatric Association and the American Academy of Child and Adolescent Psychiatry, serves as a scientific reviewer for 25 journals, and is active in a number of other local and national professional societies.
- Dr. Wilens is a consultant to the National Football League, Major/Minor League Baseball, Bay Cove Human Services and Phoenix/Gavin House and is consistently named one of the Best Doctors in Boston and in America for psychiatry.
- Dr. Wilens earned his BS in Literature, Science, and Arts at the University of Michigan Honors College and his MD at the University of Michigan Medical School in Ann Arbor.





Nonmedical Use of Prescription Stimulants



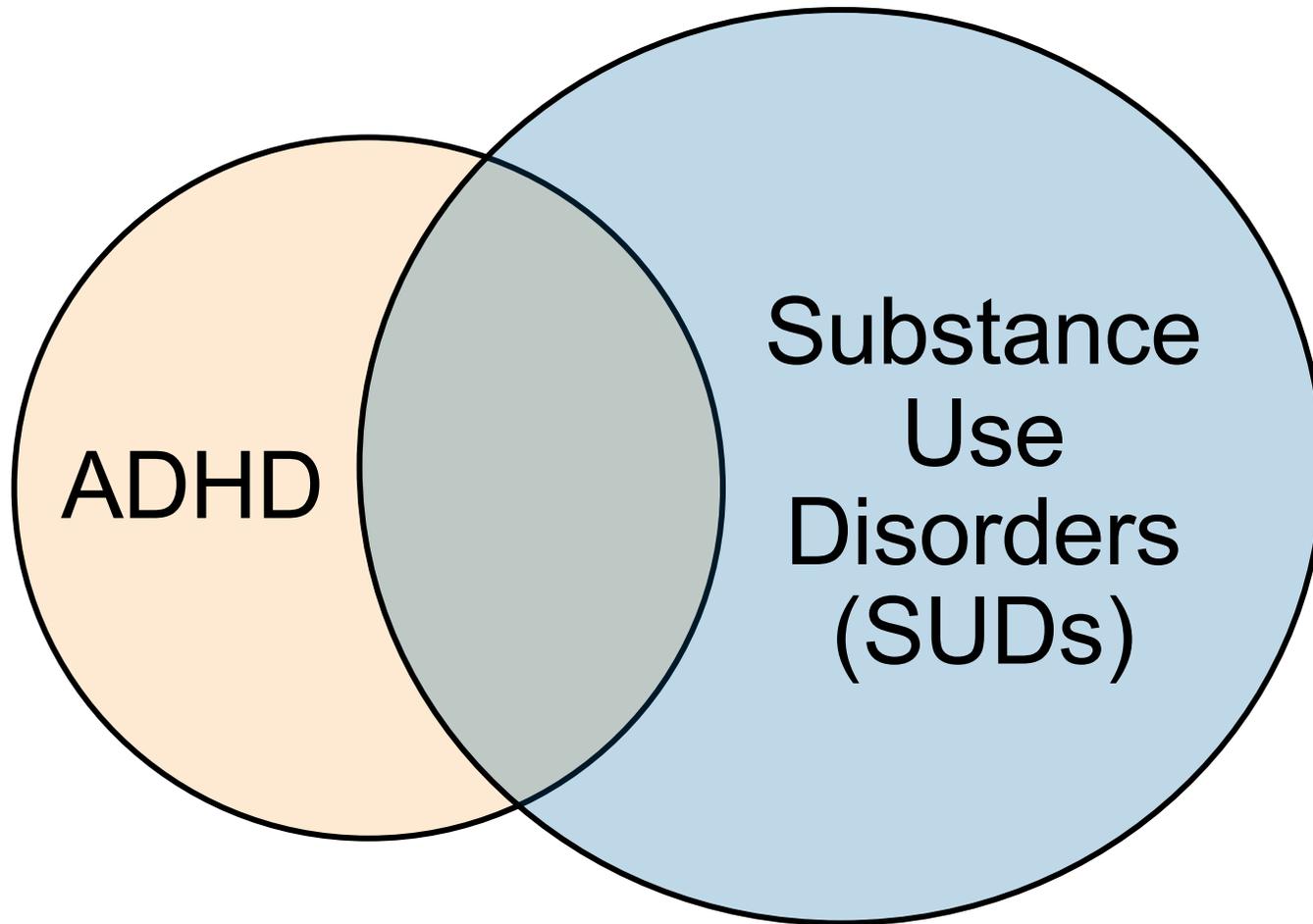
Timothy E. Wilens, M.D.

Chief, Division of Child & Adolescent Psychiatry;
(Co) Director, Center for Addiction Medicine

Massachusetts General Hospital
Harvard Medical School



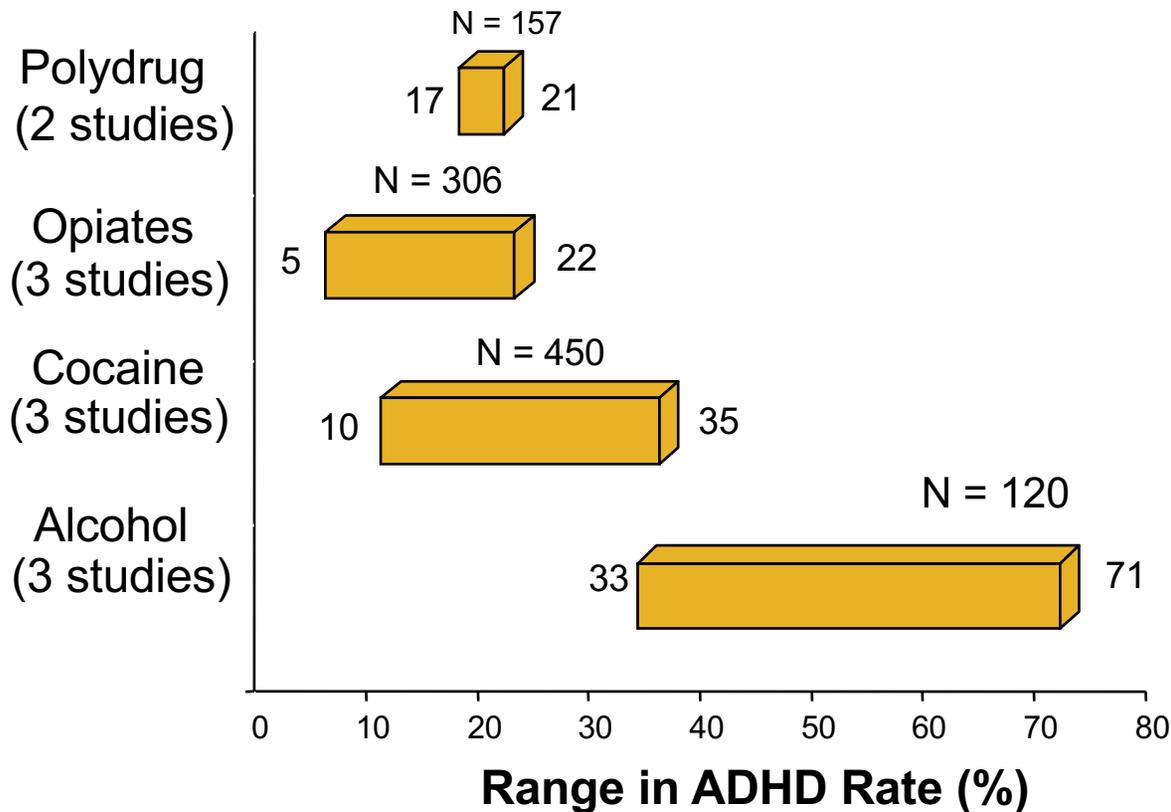
Overlap between ADHD and SUDs



Wilens TE. *Psychiatr Clin North Am.* 2004;27(2):283-301.

van Emmerik-van Oortmerssen K et al. *Drug Alcohol Depend.* 2012;122(1-2):11-19.

SUD is a Risk Factor for ADHD: Illustrative Overlap of ADHD in Adults with SUD

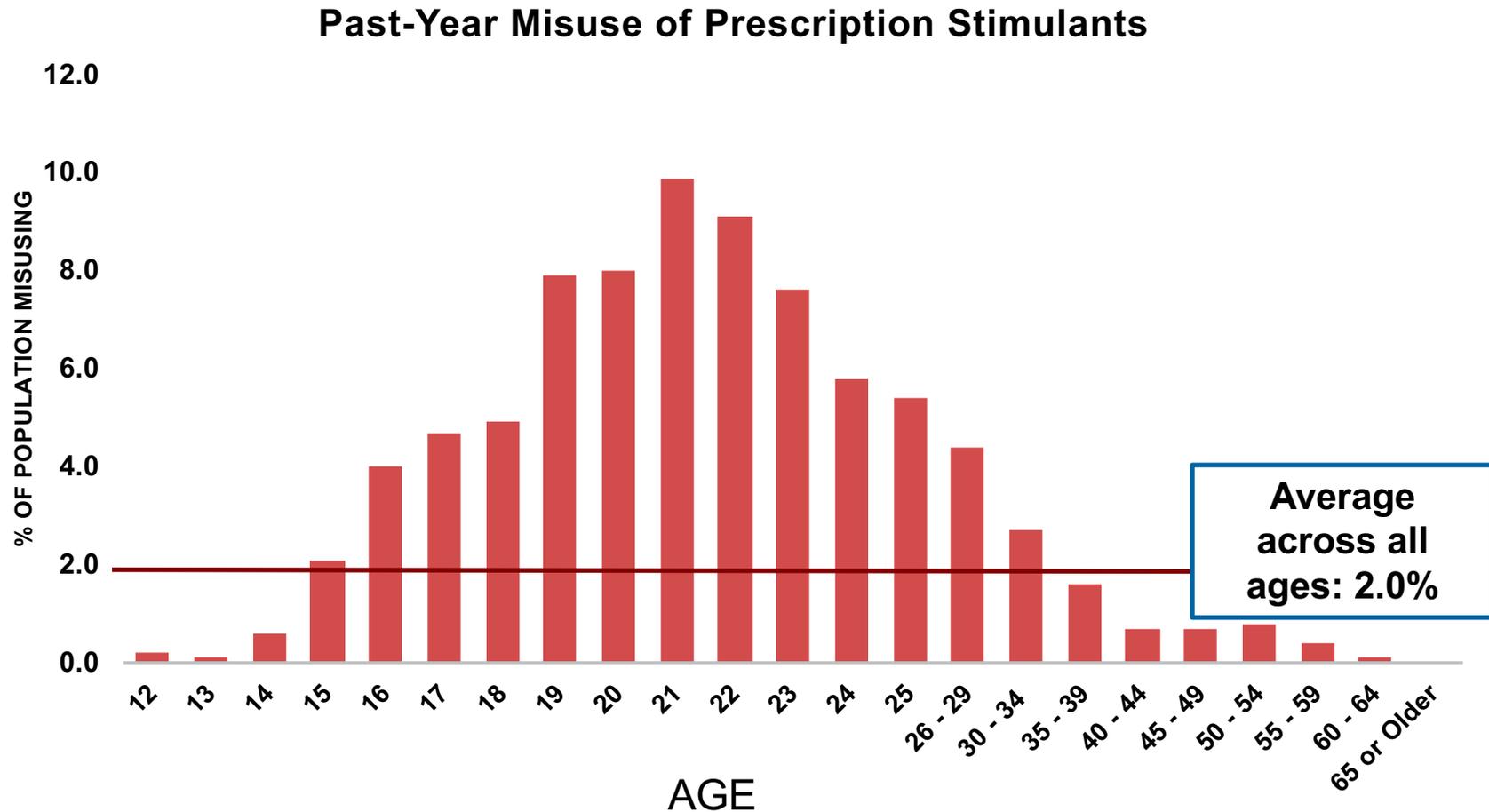


Overall, 23% of adults with SUD have ADHD (N = 29 studies)*.

Wilens TE. *Psychiatr Clin North Am.* 2004;27(2):283-301.

*van Emmerik-van Oortmerssen K et al. *Drug Alcohol Depend.* 2012;122(1-2):11-19.

Misuse Peaks at Age 21, with 10% of the Population Reporting Lifetime Misuse of Stimulants



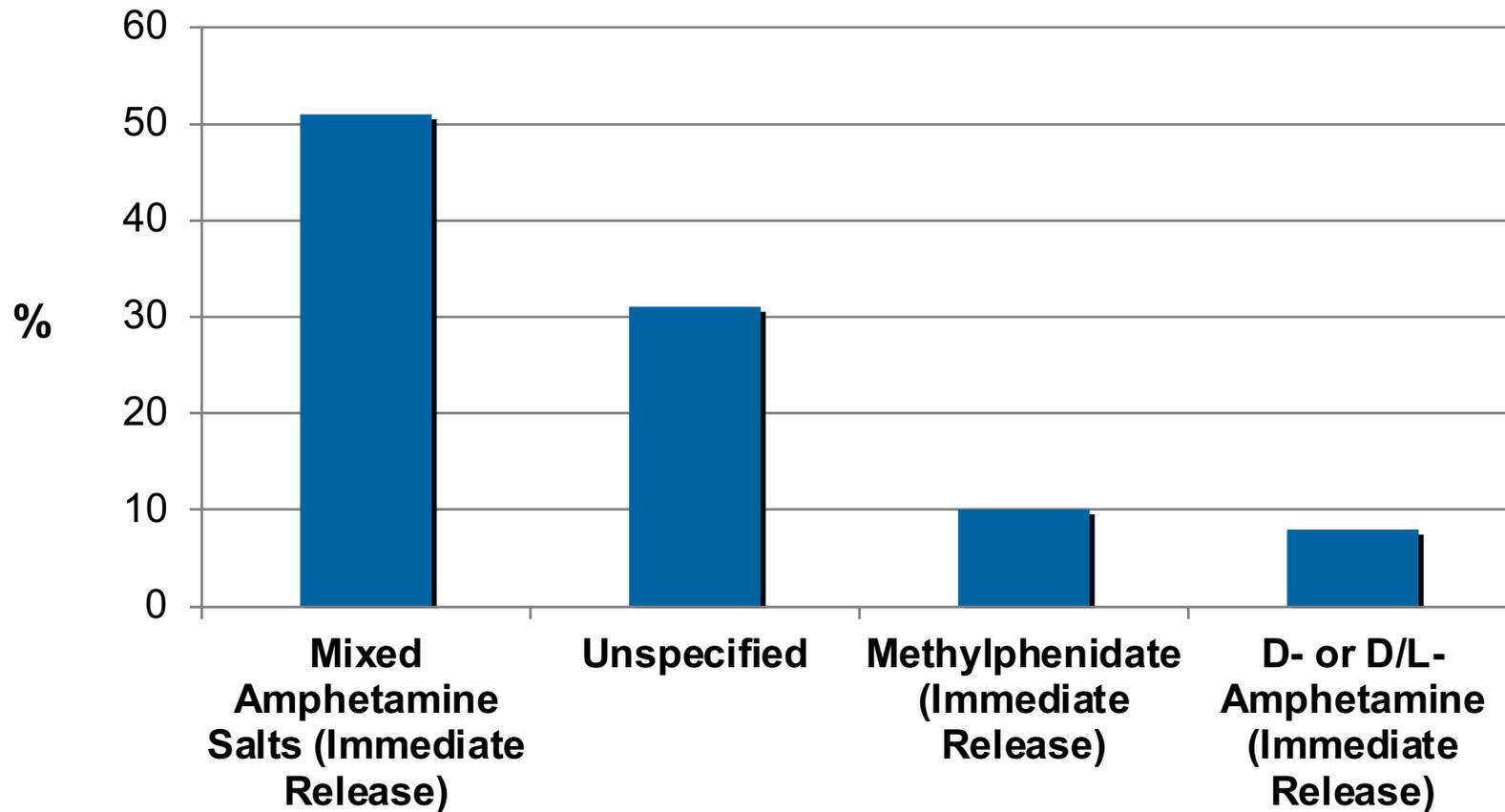
Source: SAMHSA, Center for Behavioral Health Statistics & Quality, National Survey on Drug Use and Health, 2015

Stimulant Misuse and Diversion

- N = 22 studies (N > 113,000 participants); mostly survey studies in college students (80%)
- 10% to 20% prevalence of nonmedical use of stimulants
- 65% to 85% of stimulants diverted from “friends”
 - Majority not “scamming” local doctors
 - Not seen as potentially dangerous
- Motivation typically for concentration/alertness > getting “high”
- Appears to be occurring in substance (ab)users during academic decline
- High rates of full or subthreshold stimulant use disorder in misusers
- High rates of ADHD and neuropsychological dysfunction in stimulant misusers
- More misuse of immediate- vs extended-release stimulant preparations

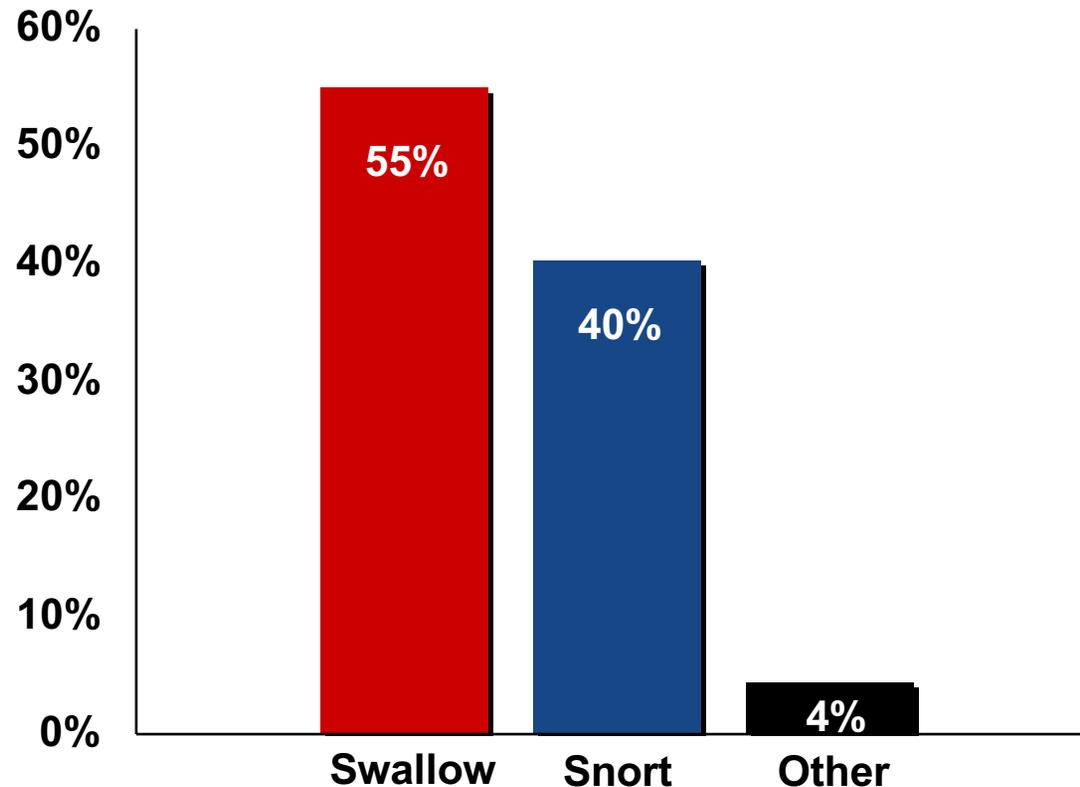
Immediate-Release Stimulants are Misused by College Students with a Stimulant Use Disorder

N = 100



Misuse by Alternative Routes is Common: Snorting is Frequently Reported

Method of Stimulant Misuse by College Students (n = 1025)

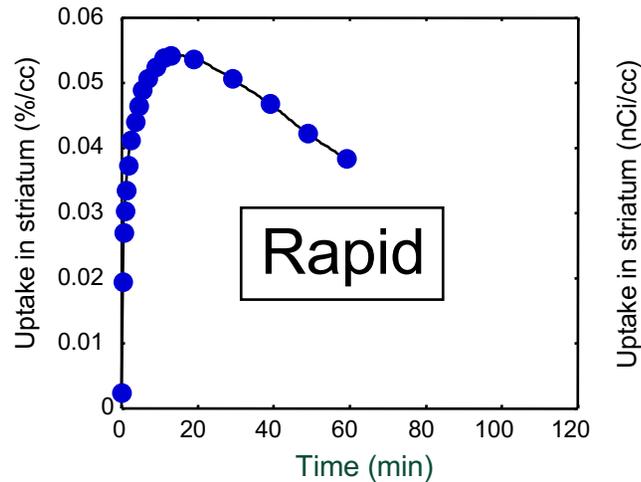


Random sample: Anonymous surveys at the University of New Hampshire administered via e-mail and paper, 1025 received out of 5000 distributed, 6.6% diagnosed with ADHD, over 16% of students abuse stimulants.

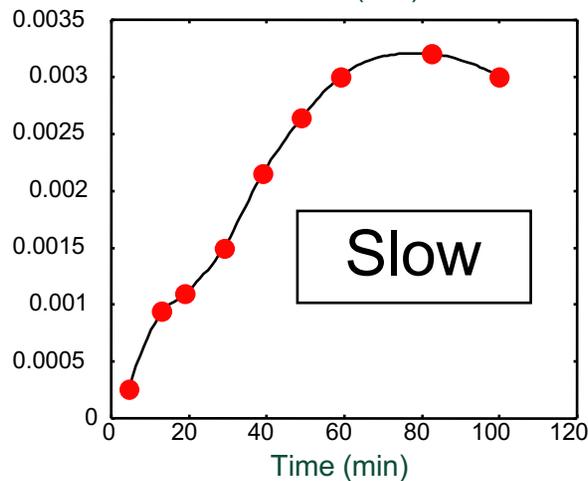
White BP, et al. *J Am Coll Health*. 2006;54(5):261-268.

Rapidity of Brain Dopaminergic Uptake Drives Euphoric Effects of Stimulants

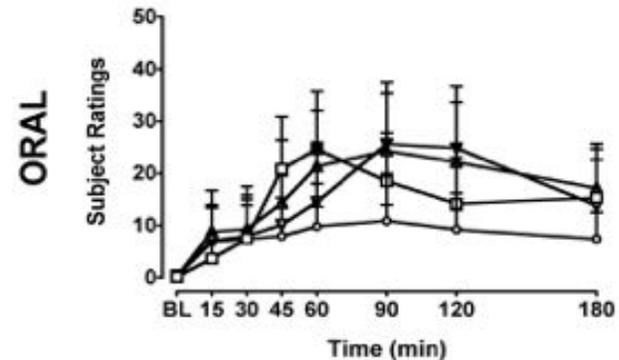
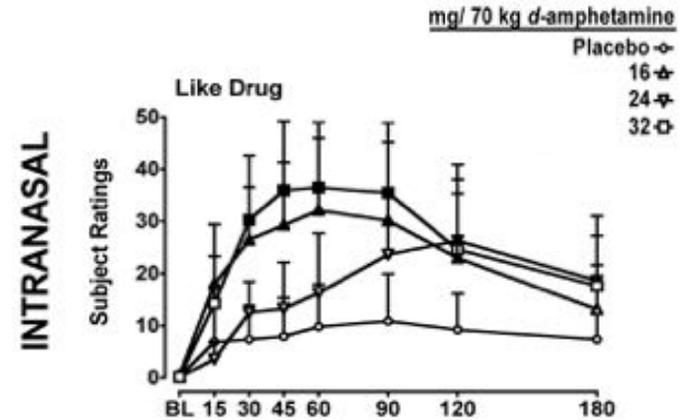
iv
MPH



oral
MPH

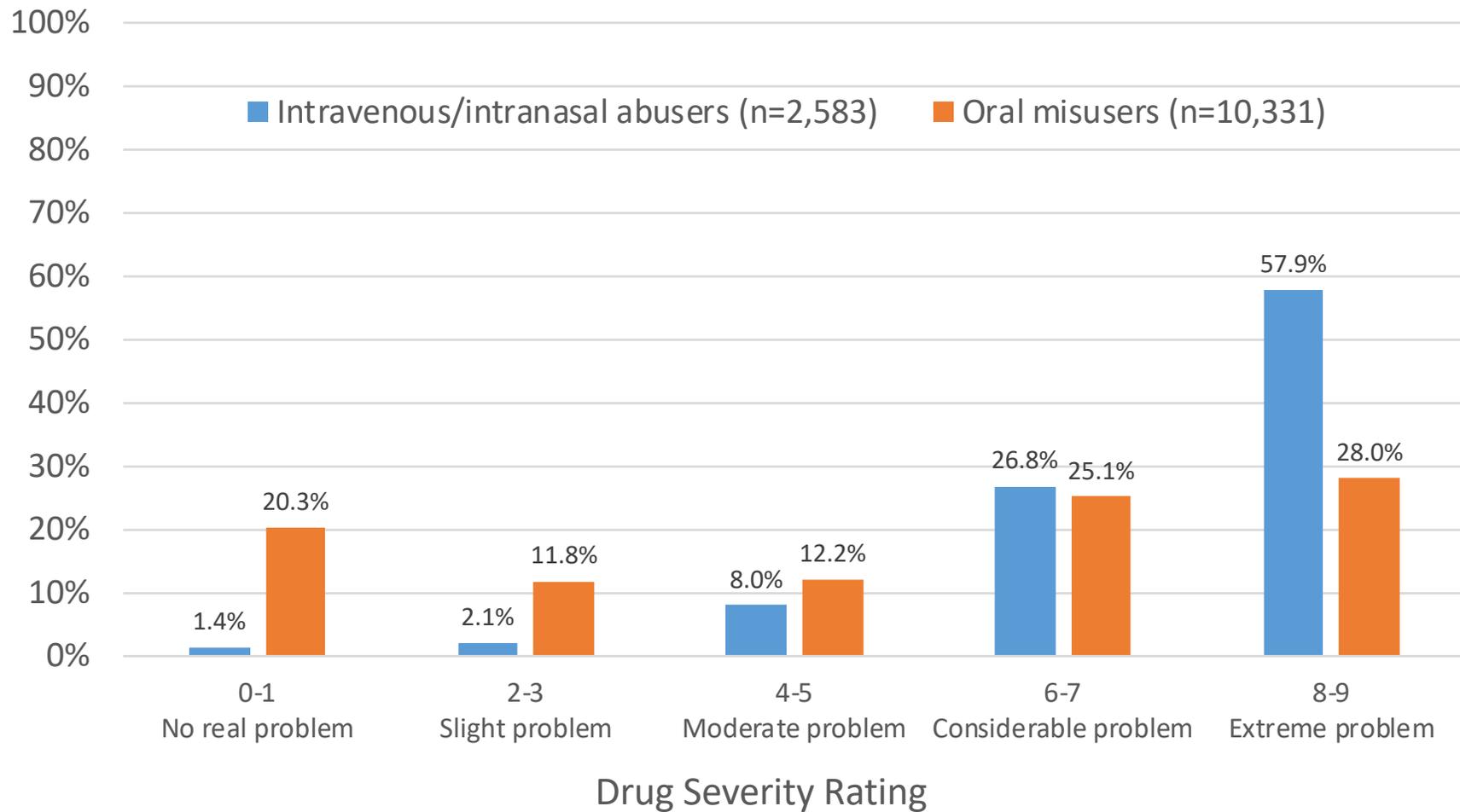


Intravenous (IV) methylphenidate leads to stronger rewarding effects (euphoria) than oral methylphenidate

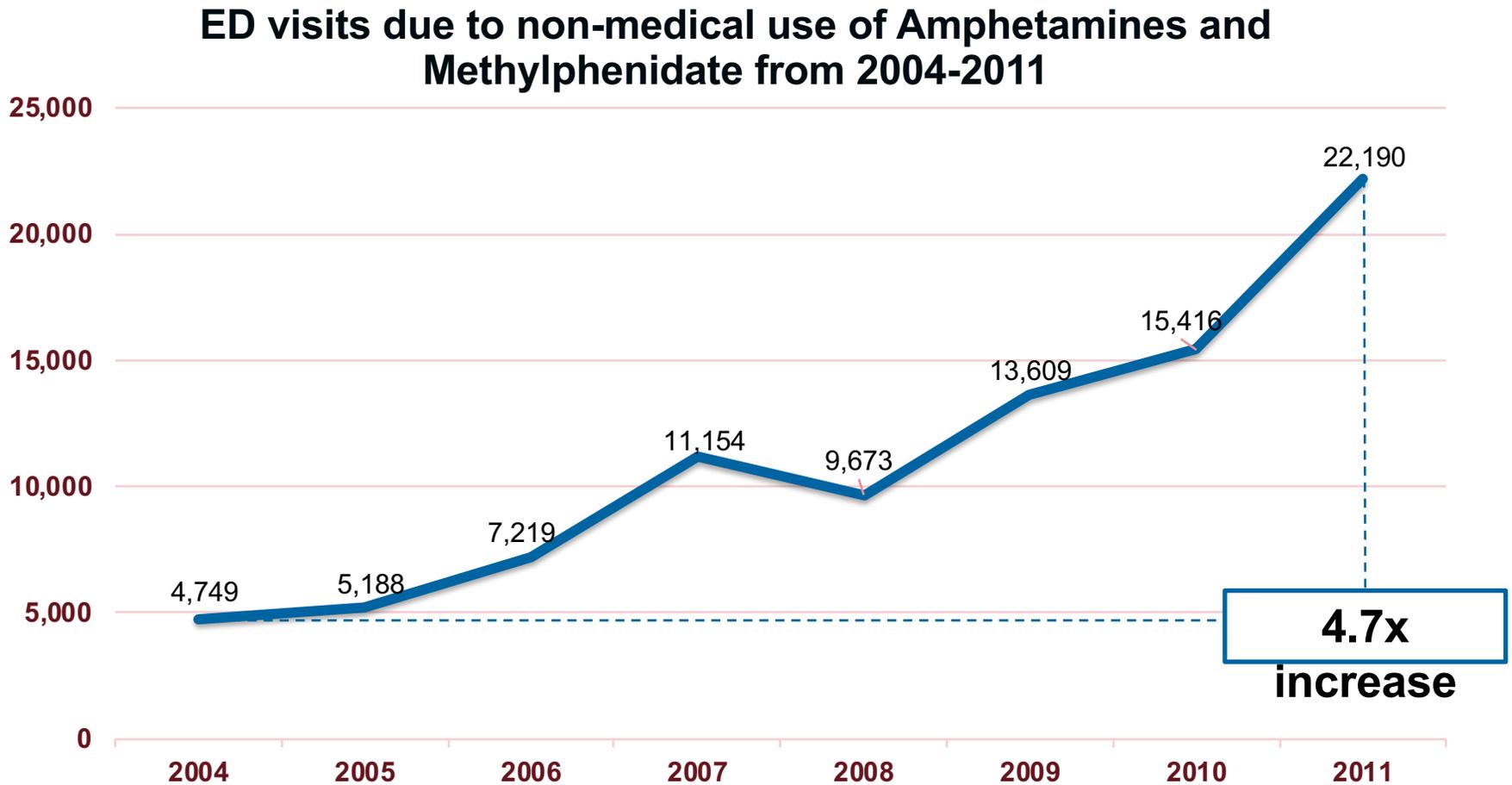


Intranasal abuse of dextro-amphetamine is associated with increased "Liking" ratings over oral abuse

More Severe Problems Linked to Substance Use are Found with Intranasal/Intravenous vs. Oral Misuse



Emergency Department Visits Due to Non-Medical Use of Stimulants More Than Quadrupled (2004-11)



Drug Abuse Warning Network Report, 2011, pg 21, table 5.2, CNS Stimulants, amphetamine/dextro-amphetamine and methylphenidate only (excluded caffeine)

Note: DAWN was discontinued in 2011 and will be re-established in mid-2019 as a smaller-scale, sentinel surveillance system

Associated Medical Complications of Chronic Stimulant Abuse / Dependence / Overdose* / Withdrawal

Snorting or injecting stimulants is especially concerning due to higher risk of serious events with quick entry into the bloodstream

- **Neurological complications**
(e.g., seizures, strokes, hemorrhages, cerebral atrophy and brain lesions, neurological deficiencies, cognitive deficits)
- **Psychological/Behavioral**
(e.g., psychosis, depression, suicidal thoughts, impaired judgment, violence)
- **Cardiovascular system effects**
(e.g., cardiovascular damage, rapid and erratic heart beat, hypertension, every form of heart disease, fatal reactions)
- **Respiratory/pulmonary effects**
(e.g., respiratory depression, hemorrhage, death from respiratory failure)
- **Muscular and renal toxicity**
(e.g., skeletal muscle destruction that may cause kidney failure)
- **Gastrointestinal complaints**
(e.g., weight loss and anorexia, severe bowel infarction)
- **Reproductive function and fetal/neonatal effects**
(e.g., low birth weight, spontaneous abortion, impotence, infertility)
- **Other: Infections (HIV, Hepatitis), blood clots and perforation/necrosis of nasal septum**

*The amount needed to produce a toxic dose varies widely and is not related to body weight.

UM football student manager dies from an overdose at 22

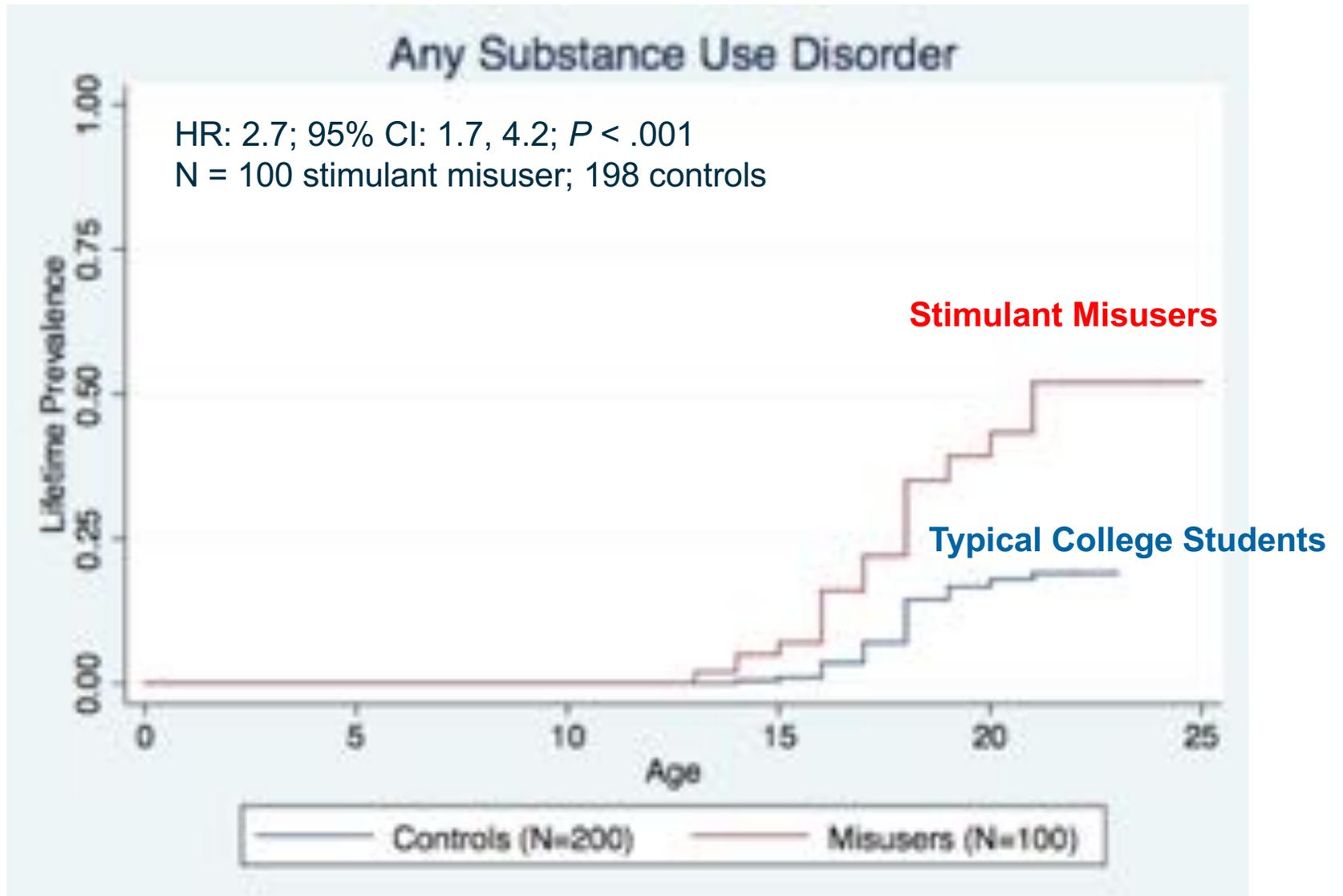
PUBLISHED [SEPTEMBER 16, 2014](#)



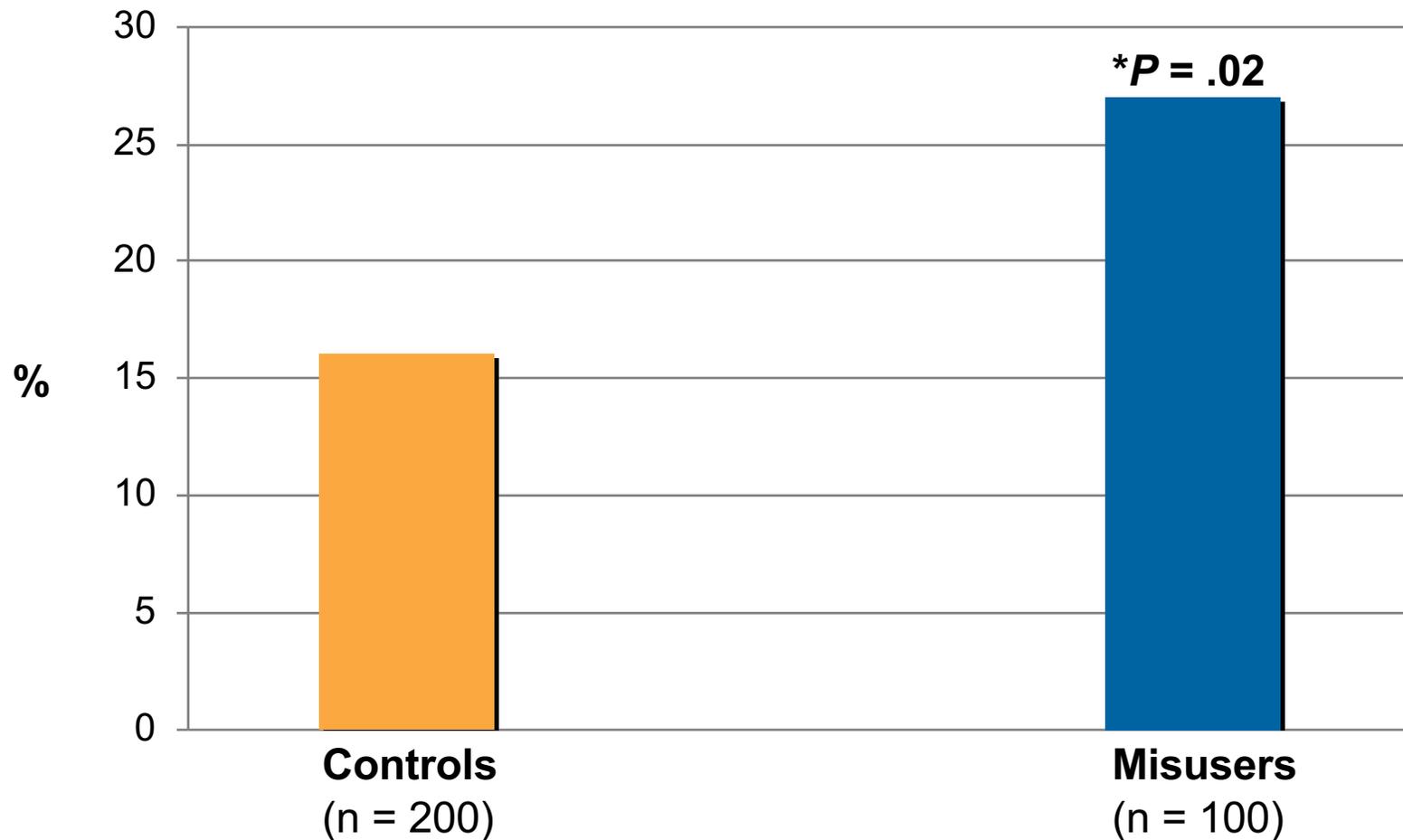
On the morning of July 20, Levine was found unconscious on a sidewalk in the neighborhood of Wicker Park, in Chicago. He spent the previous Saturday night pushing his body to limits through binge drinking and snorting crushed Adderall. This was enough to stop his heart. He was taken to the hospital where he was put on life support in intensive care. The ventilator was turned off the next day.

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College Stimulant Misusers Have High Rates of SUD

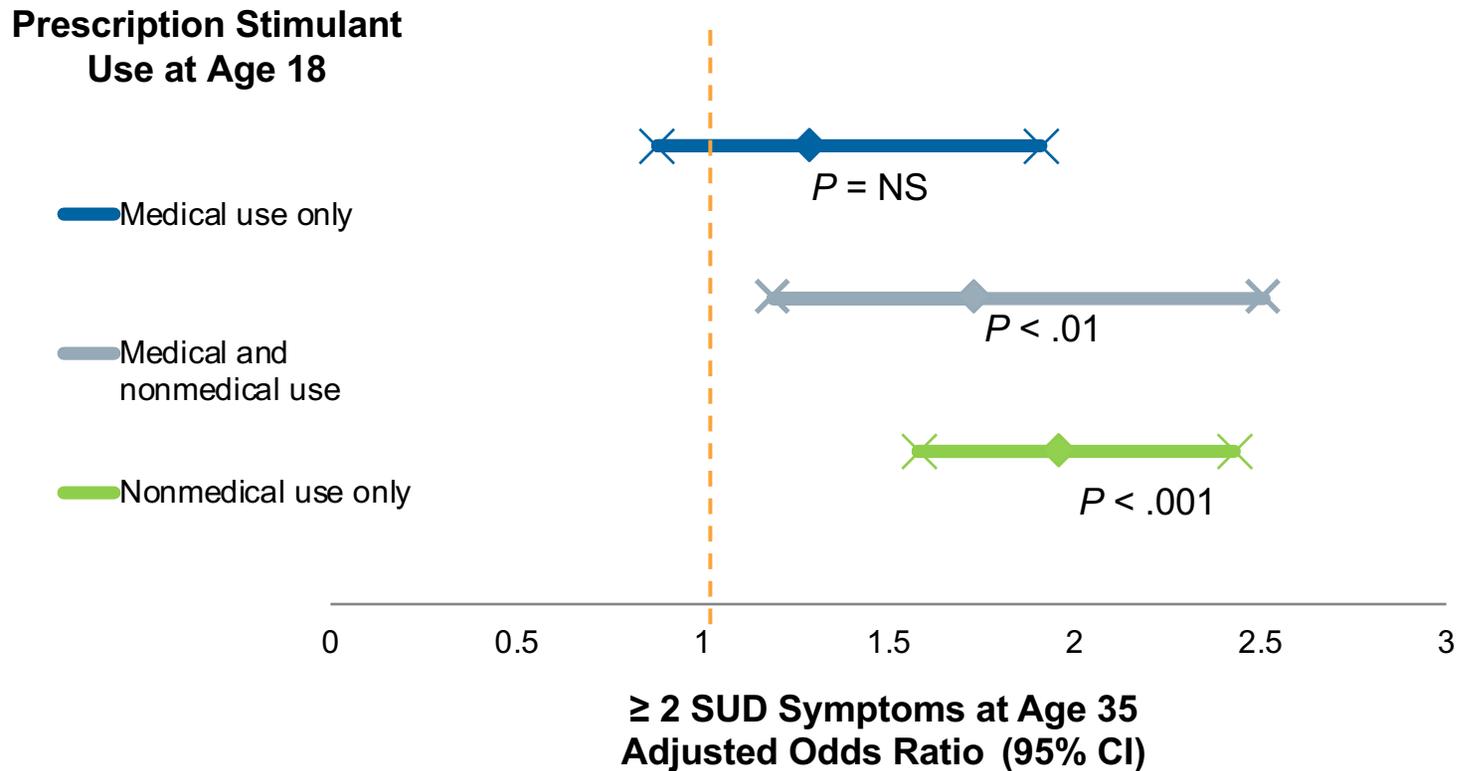


Rates of ADHD are Higher in College Students Who Misuse Stimulants Compared to Controls



N = 300. Subthreshold + full diagnosis of ADHD.
Wilens TE et al. *J Clin Psychiatry*. 2016;77(7):940-947.

SUD Symptoms at Age 35 Years as a Function of Medical and Nonmedical Use of Prescription Stimulants at Age 18 Years



All analyses control for race/ethnicity, sex, truancy, average grade during high school, parental education, geographical region, metropolitan statistical area, cohort year at baseline, annual alcohol use at baseline, annual cannabis use at baseline, and annual other drug use at baseline.

N = 8362

McCabe SE et al. *J Am Acad Child Adolesc Psychiatry*. 2017;56(3):226-233.e4

Summary

- Stimulants are frequently misused
- Amphetamines are the most commonly misused stimulant
- Stimulant misuse is more common with immediate- vs. extended-release preparations
- Snorting and intravenous use is common in stimulant misusers: many develop a stimulant use disorder as a result
- Myths: “It is benign” and “it is really just kids taking it orally to study for exams...”
- There are short- and long-term adverse medical/psychological risks associated with stimulant misuse and that risk increases with intranasal and intravenous use

Closing Remarks:

KemPharm ADHD Investor Event

KP415 Product Overview

- Prodrug of d-MPH (serdexmethylphenidate) with extended release properties, co-formulated with immediate release d-MPH
- Potential KP415 features and benefits
 - Once-daily dosing
 - Earlier onset and longer duration of therapeutic effect
 - Active metabolism may offer more predictable therapeutic effect
 - Lower abuse potential
 - Patient-friendly dosage form
 - Small capsule size (same as Vyvanse®), easily swallowed
 - May be opened and contents sprinkled on food or mixed into liquids for easier ingestion
- May be the first MPH product approved for pre-school patients (4-5 yrs old)
- No generic equivalent product
- Composition-based patent expires in 2032; pending applications, if granted, may potentially expire in 2037; potentially NCE eligible



KP484 Product Overview

- Prodrug of d-MPH (serdexmethylphenidate) with extended release properties
- Potential KP484 features and benefits
 - Once-daily dosing
 - Longer duration than other super-extended release ADHD products
 - Active metabolism may offer more predictable therapeutic effect
 - Lower abuse potential
 - Patient-friendly dosage form
 - Capsule may be opened and contents sprinkled on food or mixed into liquids for easier ingestion
- No generic equivalent product
- Composition-based patent expires in 2032; pending applications, if granted, may potentially expire in 2037; potentially NCE eligible



Corporate Update and Next Steps

- Completed a \$25MM follow-on offering on October 10, 2018, increasing total cash and security-related items¹ to approximately \$39MM immediately following the offering
- Offering was strategically timed to improve our balance sheet which we believe may strengthen our negotiating position with potential KP415 and KP484 strategic partners
- KP415 NDA remains on track for submission in Q1 2019
- KP484 NDA submission expected to follow later in 2019
- Strategic partnering discussions for KP415 and KP484 continue based on:
 - Significant, near-term ADHD prodrug commercial opportunity
 - Differentiated onset and duration efficacy profile
 - Differentiated oral, IV and IN HAP data for serdexmethylphenidate
 - Long patent life and potential NCE status

1 - Includes estimated cash, cash equivalents, restricted cash, marketable securities, and trade date receivables as of September 30, 2018



Q & A Session:

KemPharm ADHD Investor Event





KemPharm

ADHD Investor Event

October 11, 2018