Treatments for Stimulant Use Disorders: Pharmacotherapy and Future Directions

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Center for Depression Research and Clinical Care
Demystifying depression through discovery

Disclosure Information

Pharmacological Treatments for Stimulant Use Disorders

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Consulting:

- Axsome Therapeutics, BasePoint Health Management LLC, Biogen MA Inc., Cerebral Inc., Circular Genomics Inc, Compass Pathfinder Limited, Daiichi Sankyo Inc, GH Research Limited, Heading Health Inc, Janssen, Legion Health Inc, Merck Sharp & Dohme Corp., Mind Medicine (MindMed) Inc, Naki Health, Ltd., Neurocrine Biosciences Inc, Otsuka American Pharmaceutical Inc, Otsuka Pharmaceutical Development & Commercialization Inc, Praxis Precision Medicines Inc, PureTech LYT, Relmada Therapeutics, Inc, SAGE Therapeutics, Sparian Biosciences Inc, Takeda Pharmaceutical Company Ltd, WebMD

Scientific Advisory:

- Alto Neuroscience Inc, BasePoint Health Management LLC, Cerebral Inc., Compass Pathfinder Limited, Heading Health, Legion Health Inc, Merck Sharp & Dohme Corp, Signant Health

Stockholder:

- Alto Neuroscience Inc, BasePoint Health Management LLC, Cerebral Inc, GreenLight VitalSign6 Inc, Legion Health Inc

Research:

- NIMH, NIDA, NCATS, American Foundation for Suicide Prevention, Patient-Centered Outcomes Research Institute (PCORI), and Blue Cross Blue Shield of Texas

Editorial Compensation:

- American Psychiatric Association, Oxford University Press

American Society of Addiction Medicine Founded 1954 ASAM

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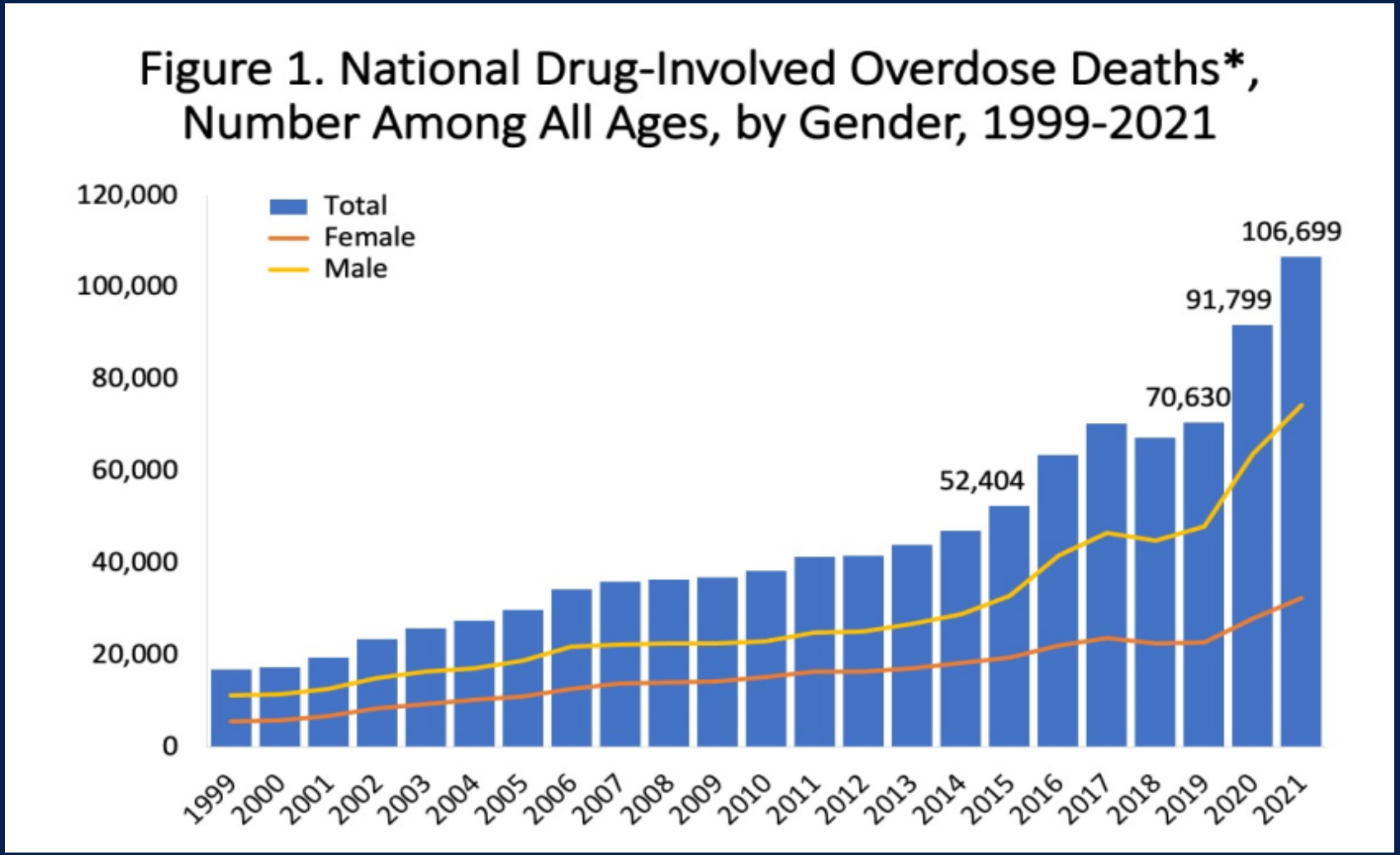
Learning Objectives

Upon completion of the session, the participant will be able to…

1. …recognize the need for stimulant use disorder research as well as the newest work regarding possible treatment options.
2. …demonstrate an awareness of novel pharmacotherapy options for the treatment of stimulant use disorders.
3. …elucidate potential obstacles and solutions to stimulant use disorder treatment.
4. …describe the benefits that biomarker research may have on the future of pharmacotherapy for stimulant use disorders.

Overdose Deaths are Reaching an All-Time High



Centers for Disease Control and Prevention, National Center for Health Statistics. (2023).

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No Pharmacological Treatments for Stimulant Use Disorders

The National Institute on Drug Abuse says that for people with addictions to drugs like stimulants, no medications are currently available for treatment

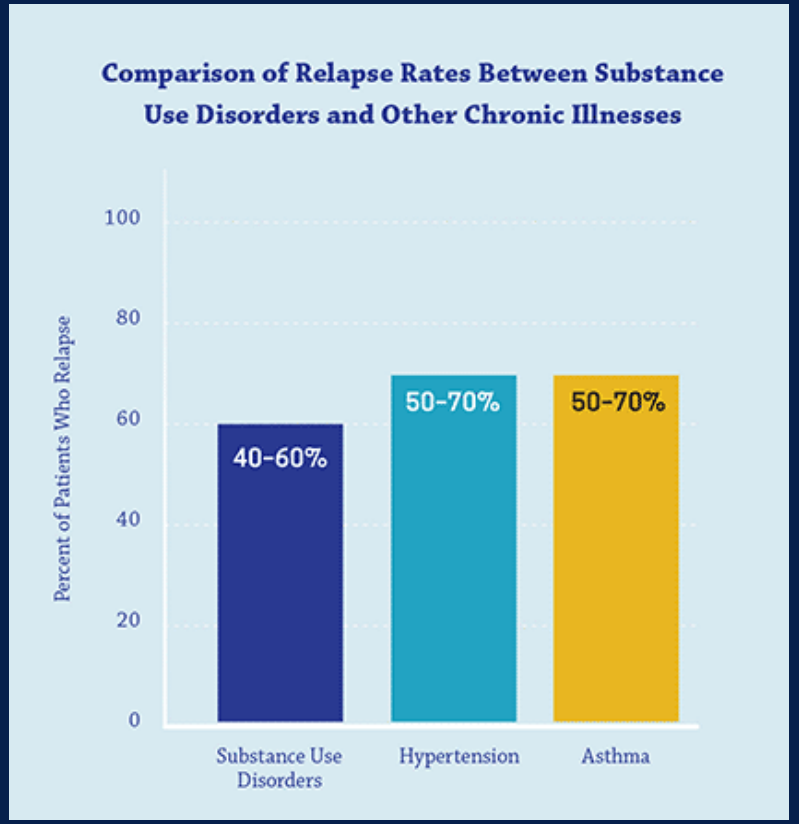
- Current treatment options are confined to primarily behavioral therapies
- Different types of medications that may help:
  - Treating withdrawal
  - Staying in treatment
  - Preventing relapse

National Institute on Drug Abuse.

The Need for Treatment

Although relapse is common, it is comparable across other chronic illnesses

- Indicates necessity for treatment
- Substance use disorders must be treated like other chronic illnesses – requires deep-rooted behavior change
- **Medication is the first line of treatment**

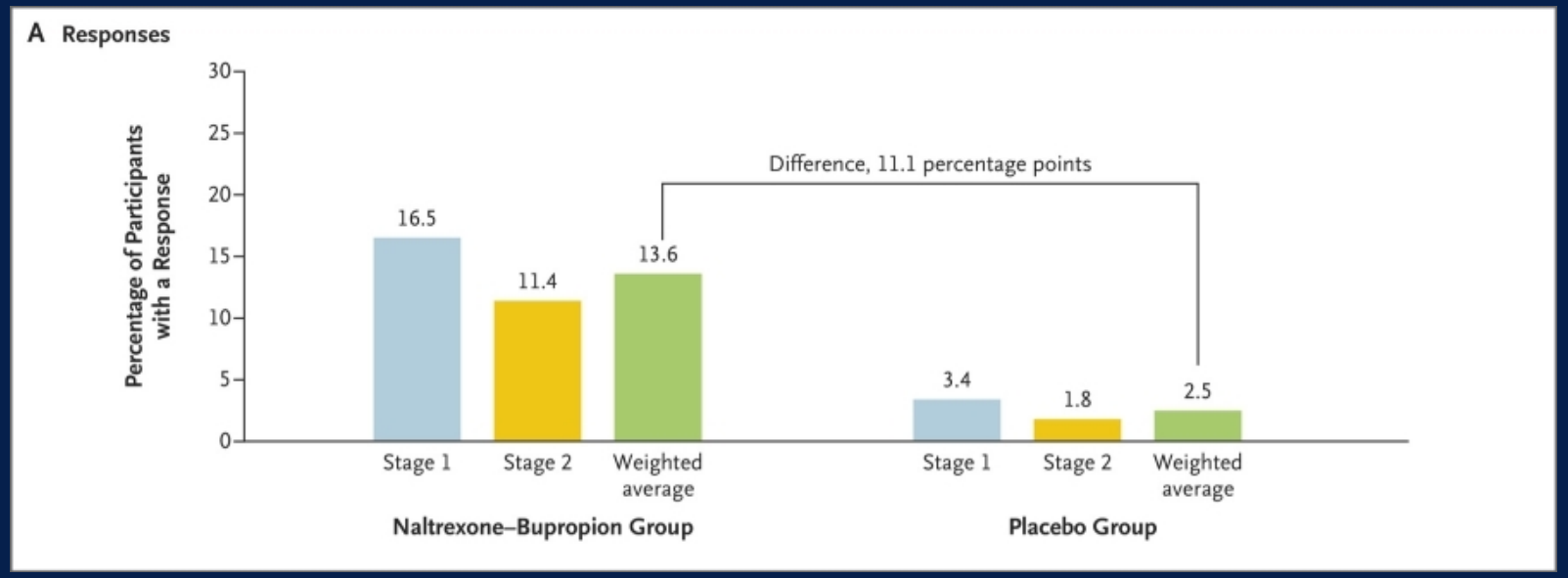


McLellan et al. (2000). *JAMA*.

Methamphetamine Use Disorder

ADAPT-2

- Accelerated Development of Additive Pharmacotherapy Treatment for Methamphetamine Use Disorder
  - Tested naltrexone plus bupropion as a possible treatment for methamphetamine use disorder



Trivedi et al. (2021). *N Engl J Med.*

ADAPT-2

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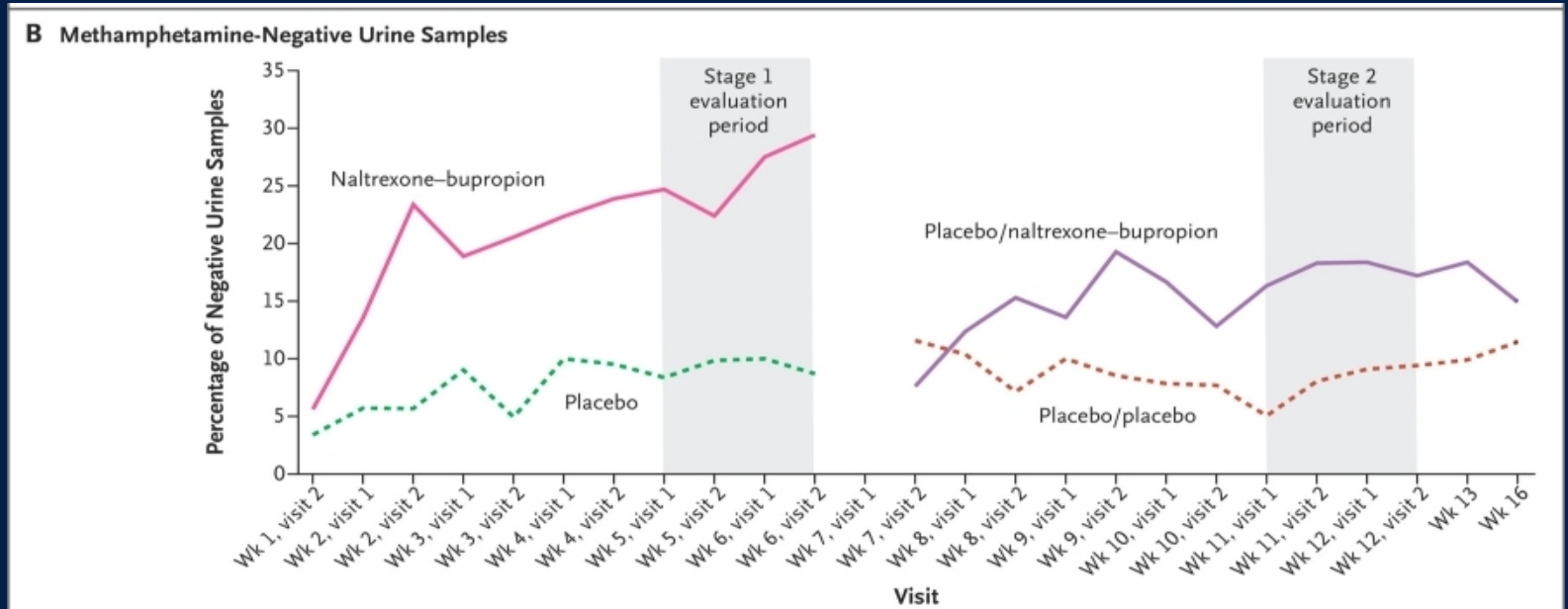

No. of Urine Samples Obtained at Each Visit	Stage 1											Stage 2												
Naltrexone–bupropion	89	96	77	90	73	85	67	81	67	80	68													
Placebo	265	280	229	266	223	260	210	239	203	240	207													
Placebo/naltrexone–bupropion												92	97	85	103	83	96	78	98	82	98	93	98	87
Placebo/placebo												95	106	84	100	82	102	91	99	87	99	85	101	96

Trivedi et al. (2021). *N Engl J Med.*

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Emerging Therapies

- Newest study (KMD; CTN-0132) will investigate the feasibility of 6 weeks of intravenous ketamine versus midazolam in individuals with methamphetamine use disorder

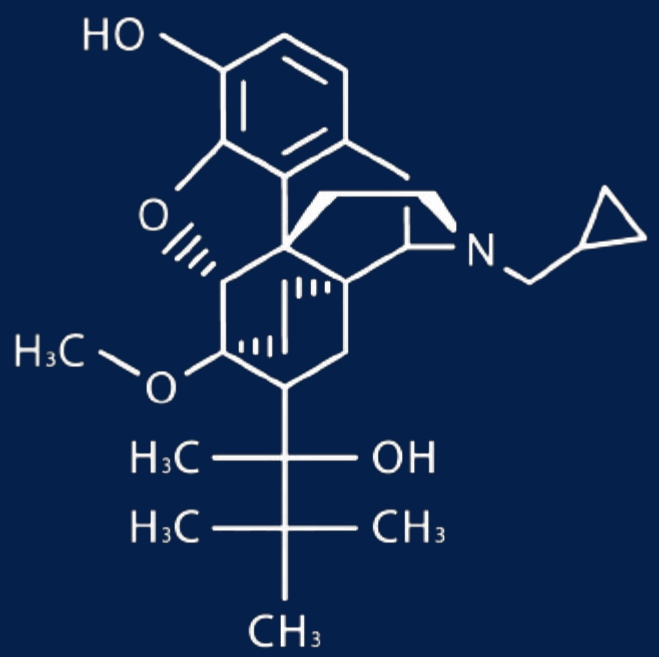
- Evaluate the efficacy and safety of ketamine compared to midazolam during 6 weeks of follow-up

Cocaine Use Disorder

Cocaine Use Reduction with Buprenorphine: Rationale and Limitations

CURB: Reducing stimulant addiction with medication(s)

- Buprenorphine is a mu agonist *and* a kappa antagonist
- Naloxone blocks the mu agonist effects of buprenorphine
- Adherence problems that resulted in inconsistent buprenorphine levels in the blood across participants, leading to insignificant results
- Secondary analysis of compliant participants found that those with detectable buprenorphine blood levels fared significantly better than those receiving placebo



Buprenorphine
$C_{29}H_{41}NO_4$

Ling et al. (2016). *Addiction*.

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CURB-2: Overcoming Limitations

Newest study will investigate extended-release versions of medication to ensure compliance and prevent similar adherence concerns from the original study

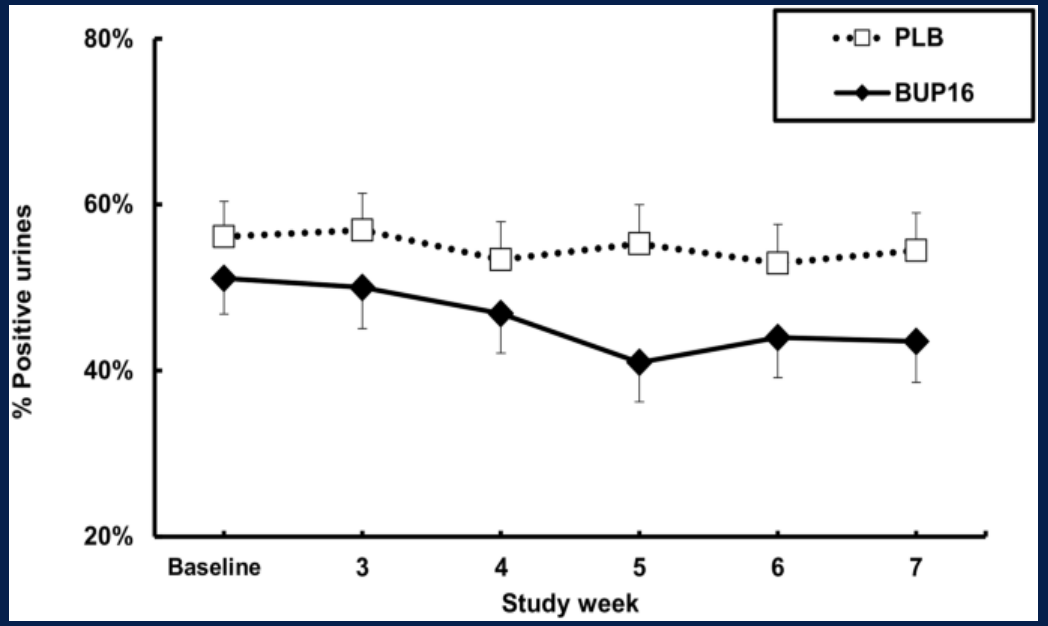
- Creating a kappa antagonist by administering naltrexone first
  - Blocks mu opioid receptors: euphoric effects eliminated
- Buprenorphine administered after
  - Triggers kappa antagonist receptors

Positive findings may produce far-reaching impact for effective pharmacotherapy treatment options

Considerations for Treating Cocaine Use Disorder

A recent study demonstrated a potential involvement of *prodynorphin* genetic variation in how participants responded to buprenorphine plus naltrexone during cocaine use disorder treatment

- Need for biomarker research to further elucidate mechanisms in the body that could improve substance abuse treatment



Percentage of cocaine-positive urine toxicology screens in the cross-ancestry group for each week across the trial for the PLB and BUP16 treatment groups

Nielsen et al. (2022). *Eur J Clin Pharmacol.*

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Implications

- Historically, research on pharmacological therapies for stimulant use disorders has been minimal
- Recent advancements in medications for the treatment of methamphetamine use disorder and cocaine use disorder hold immense promise for the future of addiction medicine
- Substance use disorders require tailored care that may benefit from biomarker research

References

1. Centers for Disease Control and Prevention, National Center for Health Statistics. (2023).

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Thank You