

Stimulant Safety in ADHD Virtual Seminar

Diversion Control Division ★ Drug Enforcement Administration

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Prescription Stimulant Medical Use, Nonmedical Use, and Substance Use Disorders

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Disclosure

I have no conflicts of interest to disclose.

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Thank You...

...for the extensive work by the U.S. Drug Enforcement Administration (DEA), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the National Institute on Drug Abuse (NIDA), the American Society of Addiction Medicine (ASAM), the American Academy of Addiction Psychiatry (AAAP), The College on Problems of Drug Dependence (CPDD) and Substance Use Researchers with Lived and Living Experience (SURLE).

Topics

- Patterns and trends of medical and nonmedical use of prescription stimulants;
- Trajectories of nonmedical use of prescription stimulants and associated substance-related risks;
- Identify sub-groups at risk for substance use disorder;
- Telehealth prescribing of stimulants and substance use disorder.

Monitoring the Future (MTF) Main and Panel Studies

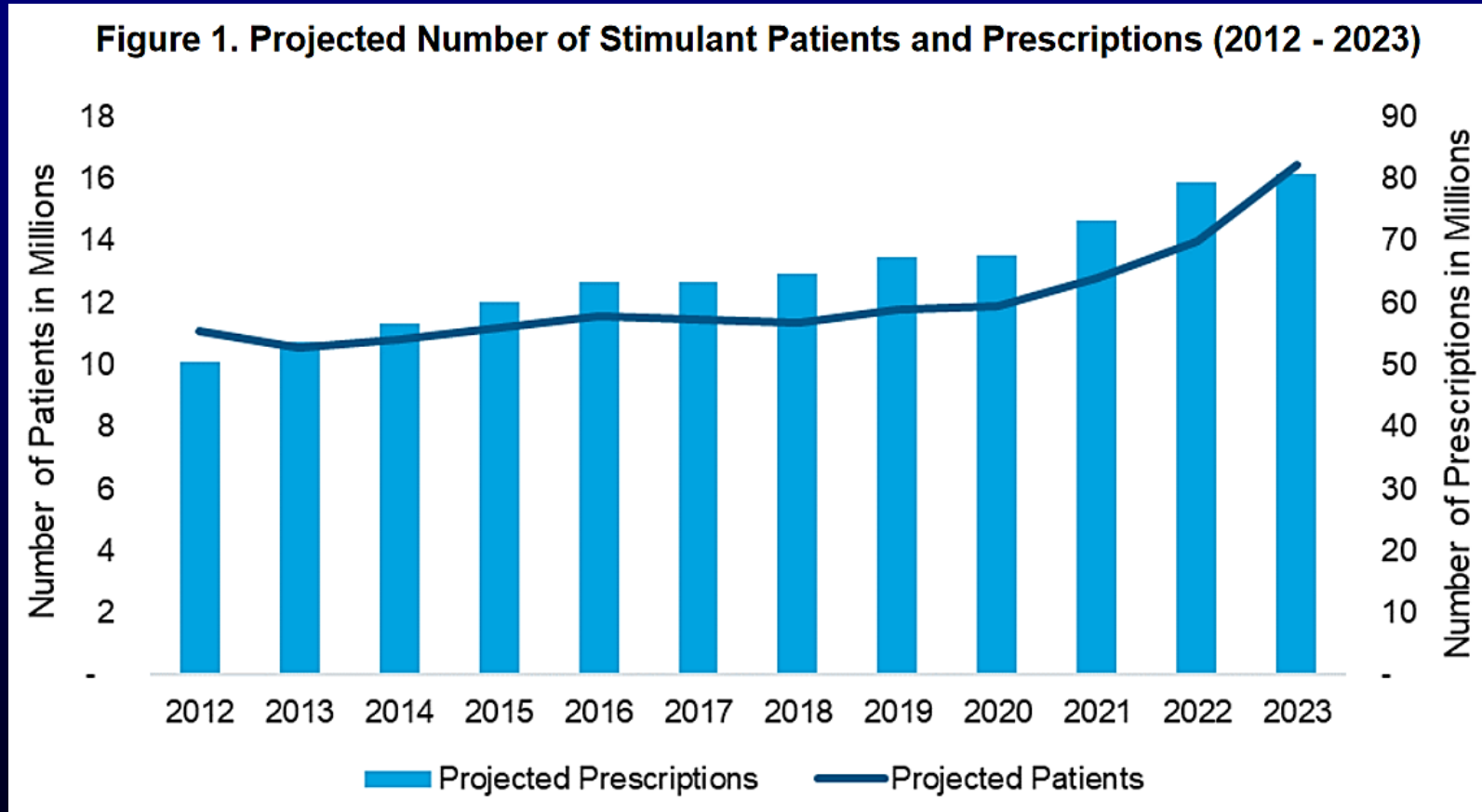
- A long-term national epidemiological study surveying trends in licit and illicit drug use among U.S. adolescents and adults in secondary schools.
- Survey conducted by researchers at the University of Michigan's Institute for Social Research and funded by research grants from NIH's National Institute on Drug Abuse.
- **Main:** Approx 25,000 8th, 10th, and 12th grade students surveyed annually as part of the MTF Main study (12th graders since 1975, and 8th and 10th graders since 1991).
- **Panel:** Approx 20,000 adults ages 17–65 surveyed as part of the MTF Panel study. A subsample of each graduating high school class completes a follow up every two years from ages 19–30 and every five years from age 35 onward.

Monitoring the Future Panel Study – Ages 18 to 65

	Adolescence	Young adulthood						Adulthood						
Age	17-18	19 – 20	21 – 22	23 – 24	25 – 26	27 – 28	29 – 30	35	40	45	50	55	60	65
Cohort years	1976 – present	1977 – present	1979 – present	1981 – present	1983 – present	1985 – present	1987 – present	1993 – present	1998 – present	2003 – present	2008 – present	2013 – present	2018 – present	2023 – present

Background

Rx stimulants ↑ (especially U.S. adults) in past decade.



Rx stimulants
2012



0-20 21+

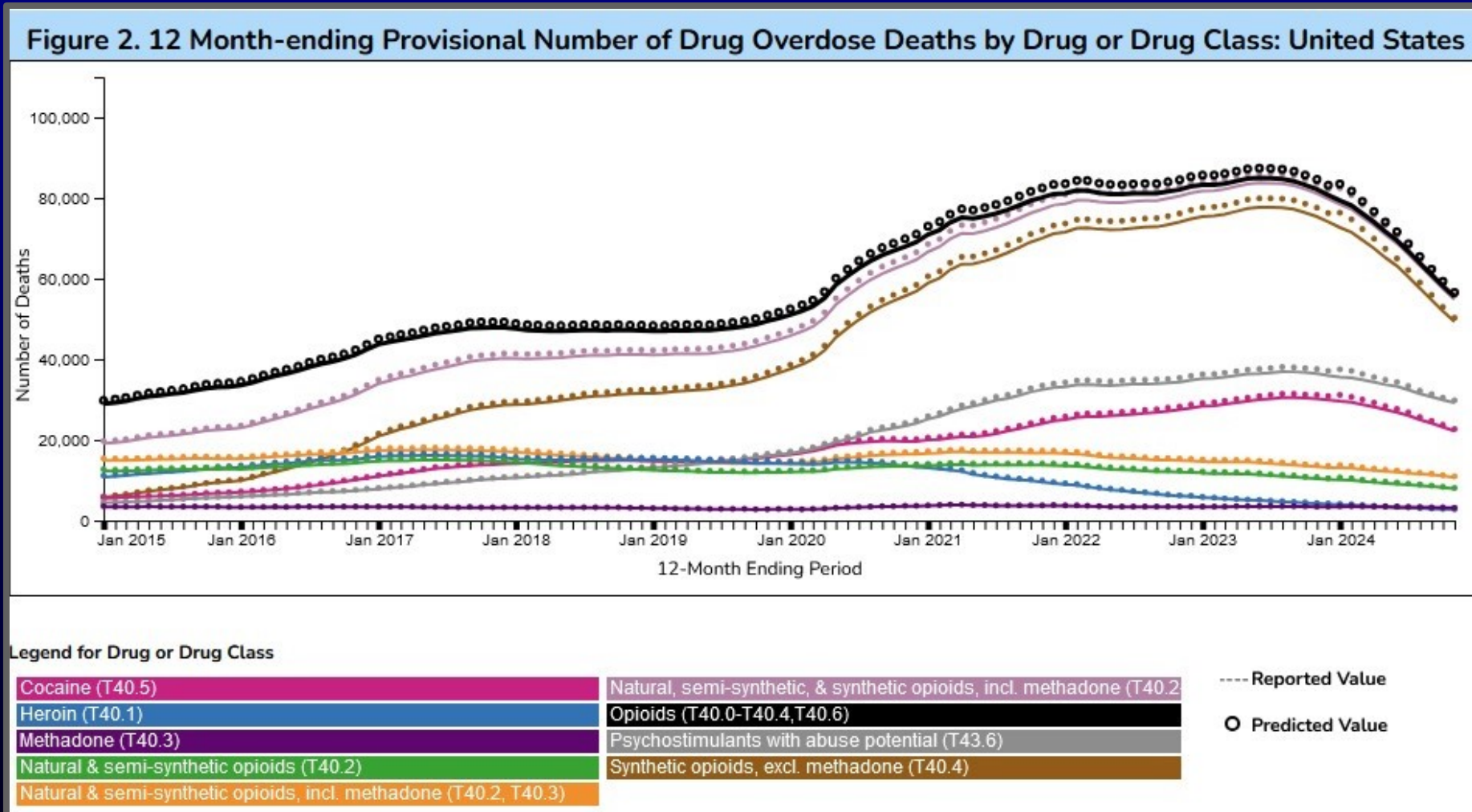
Rx stimulants
2023



0-20 21+

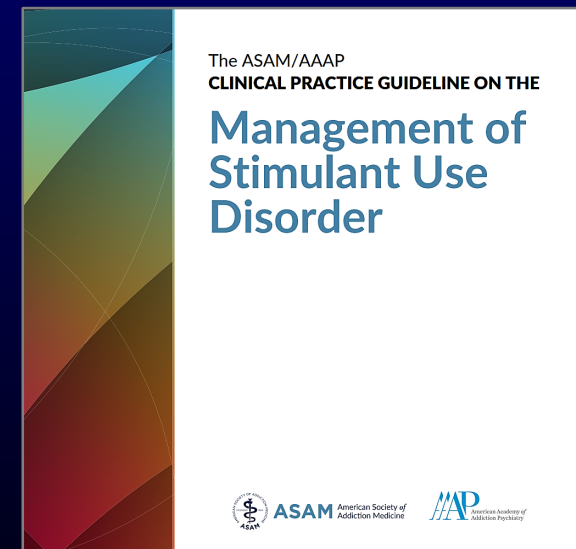
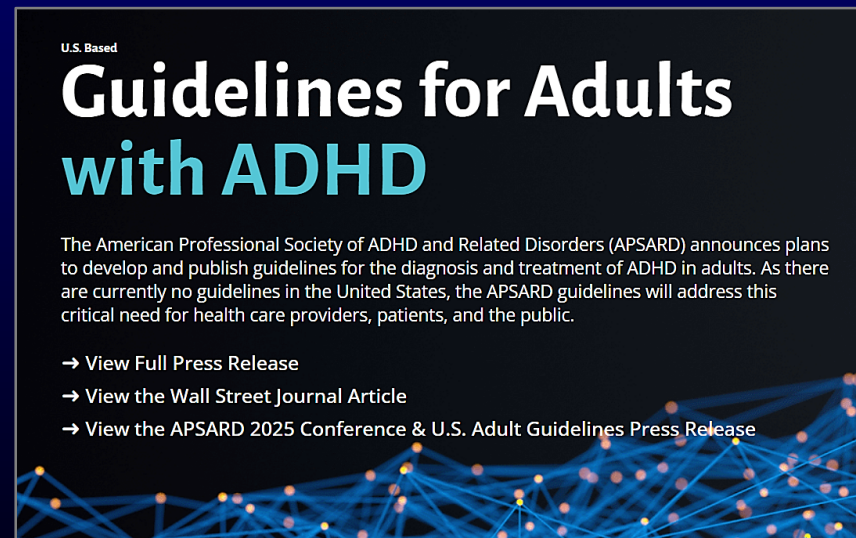
Background

Illicit stimulant overdose deaths have ↑ in the past decade.

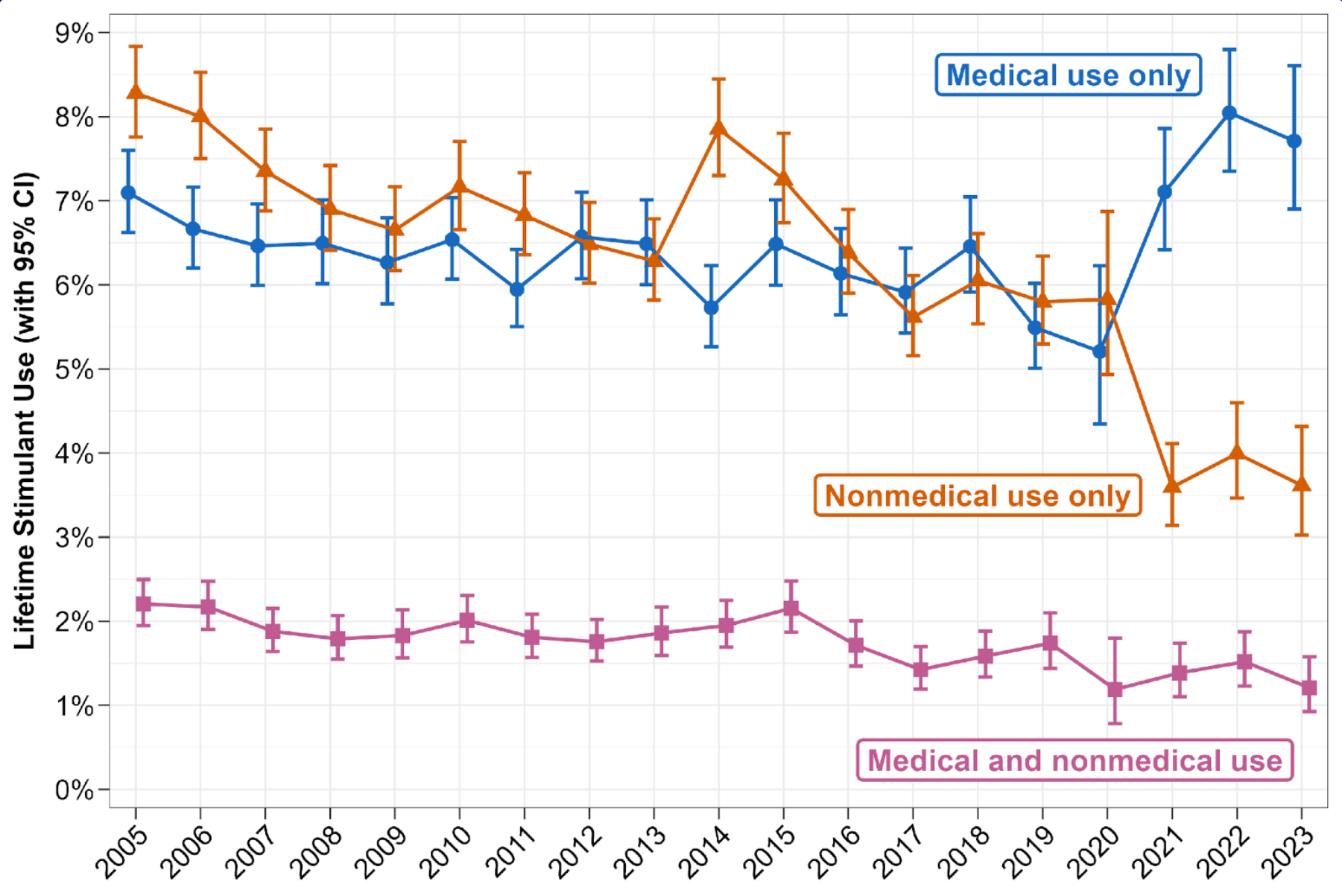


Background

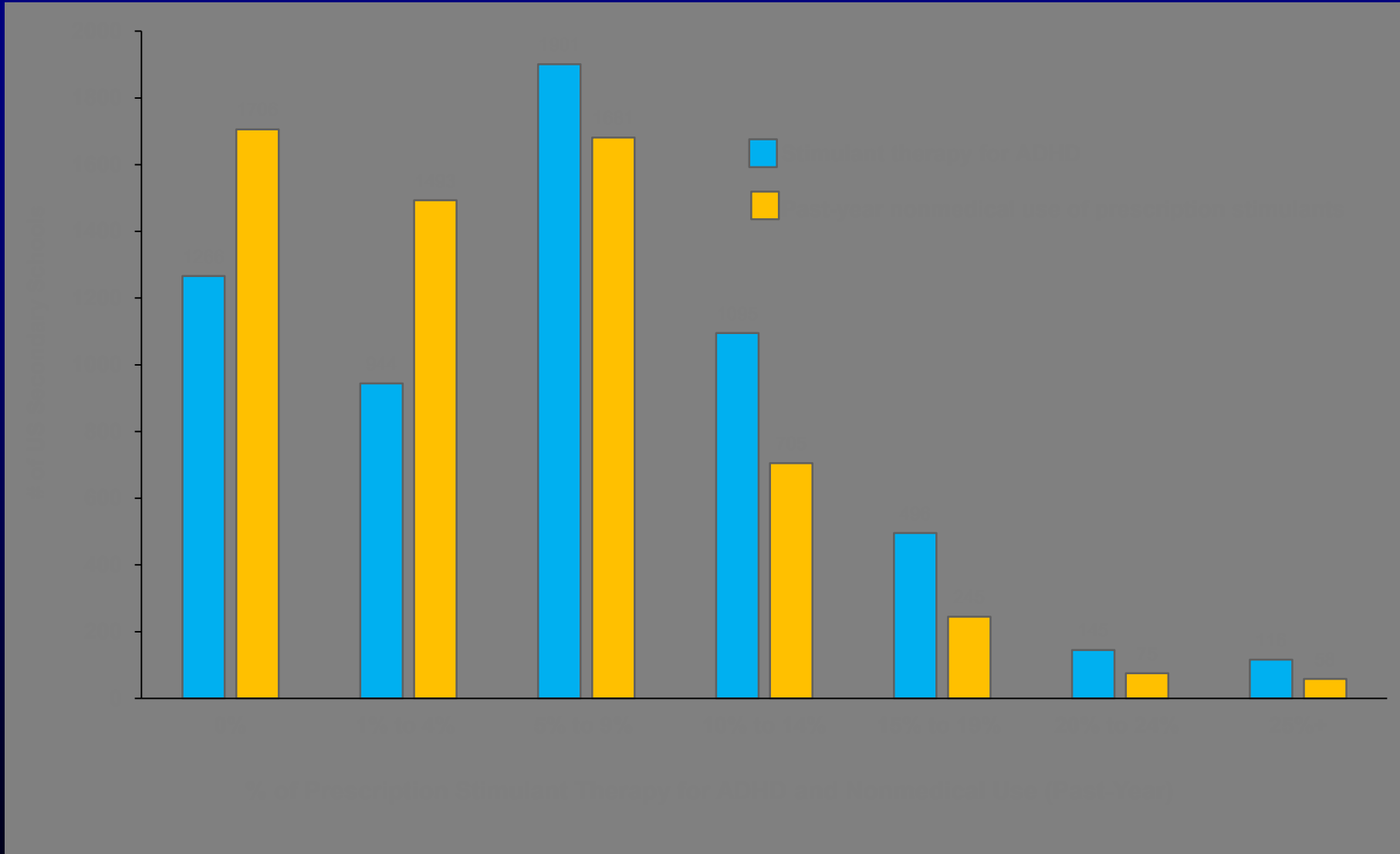
- Multiple clinical and epidemiological data sources to examine longitudinal relationships among medical and nonmedical use of prescription stimulants, illicit stimulant use, illicit opioid use, stimulant and other substance use disorders, polysubstance use, overdose, and other adverse health outcomes.
- This project is among the first to use national prospective data to identify patterns of stimulant therapy for ADHD, nonmedical use of prescription stimulants and other substances.
- The findings provide context for practice guidelines and regulatory decisions.



Medical and nonmedical use of prescription stimulants in US adolescents, 2005-2024



Stimulant therapy use for ADHD and nonmedical use of prescription stimulants in US secondary schools



School-level and individual-level correlates of past-year nonmedical use of prescription stimulants

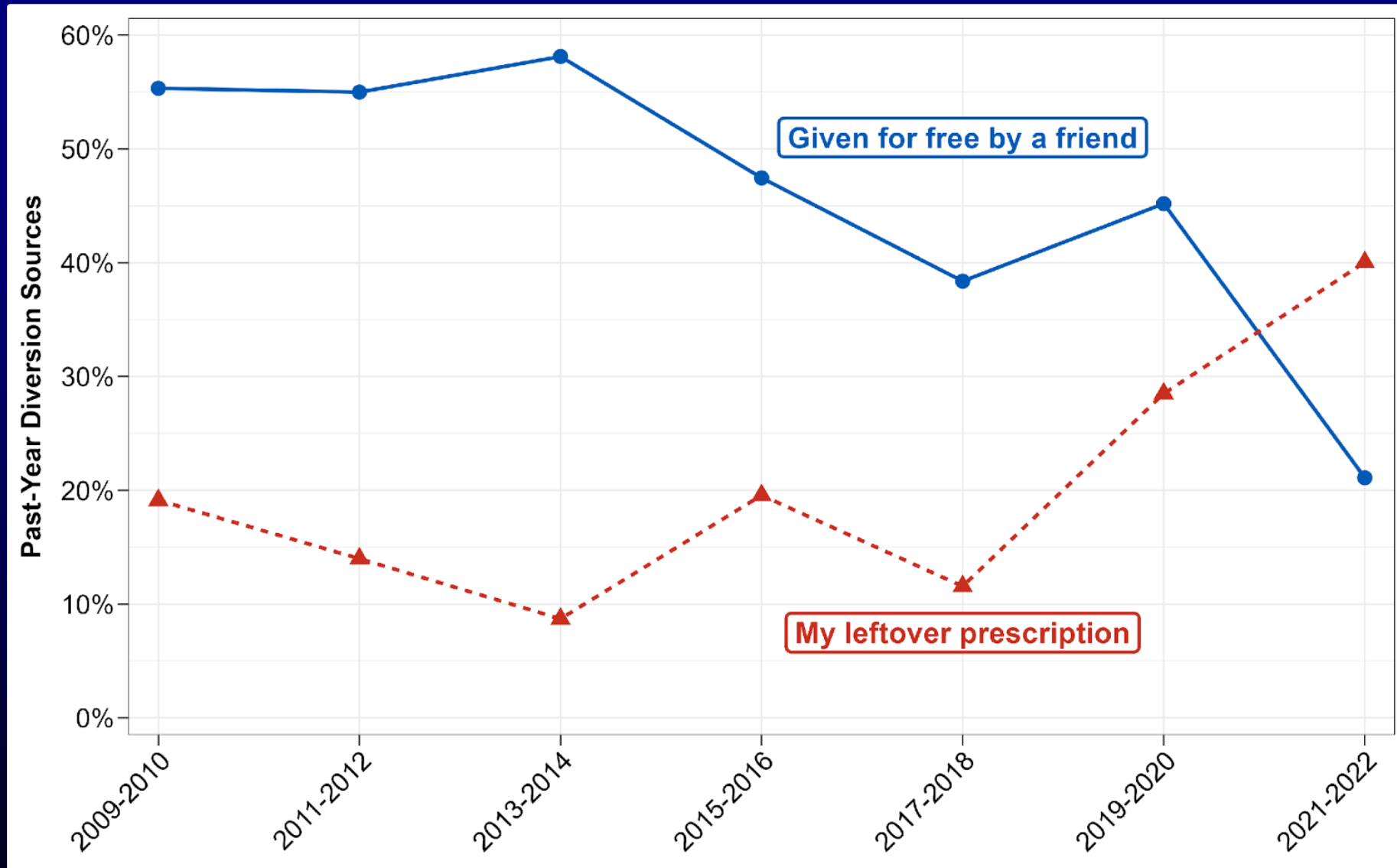
	AOR (95% CI)
<i>Individual-level</i>	
History of stimulant therapy for ADHD	
Never	REF
Previous use	2.44 (2.22, 2.67)
Current use	2.34 (2.09, 2.61)
<i>School-level</i>	
Prevalence of stimulant therapy for ADHD	
None	REF
Low	1.23 (1.08, 1.39)
Medium	1.27 (1.12, 1.45)
High	1.36 (1.20, 1.55)

Key Takeaways

- First study to provide detailed national-level estimates of:
 - Medical use of stimulant therapy for ADHD and nonmedical use of prescription stimulants at the individual and school levels in US secondary school students.
- Current medical use of prescription stimulants for ADHD **increased** between 2005 and 2023, while nonmedical use of prescription stimulants **decreased**.
- Past-year nonmedical use of prescription stimulants ranged from **0% (min) to over 25% (max)** across US secondary schools. The wide variation indicates schools need to assess their own student bodies rather than relying solely on regional/state/national data.
- In controlled analyses, students attending schools with the highest rates of medical use of prescription stimulants had **36% increased odds** of nonmedical use of prescription stimulants compared to schools with no medical use (**AOR = 1.36, 95% CI = 1.20–1.55**).
- **Findings reinforce importance of school surveys** by identifying key individual-level and school-level targets for prevention, screening, monitoring, and risk reduction strategies.



Trends in sources of nonmedical use of prescription stimulants

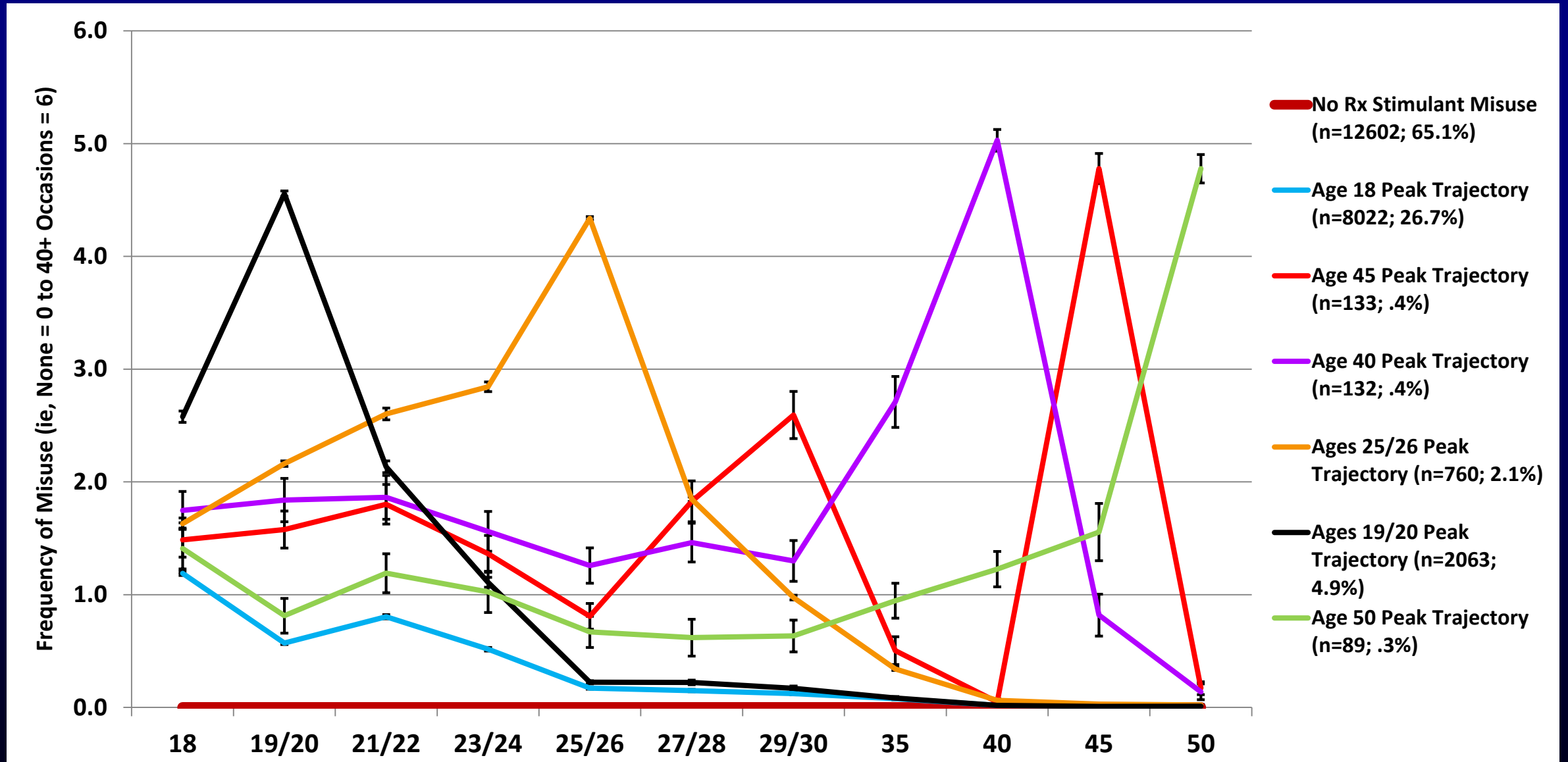


Key Takeaways

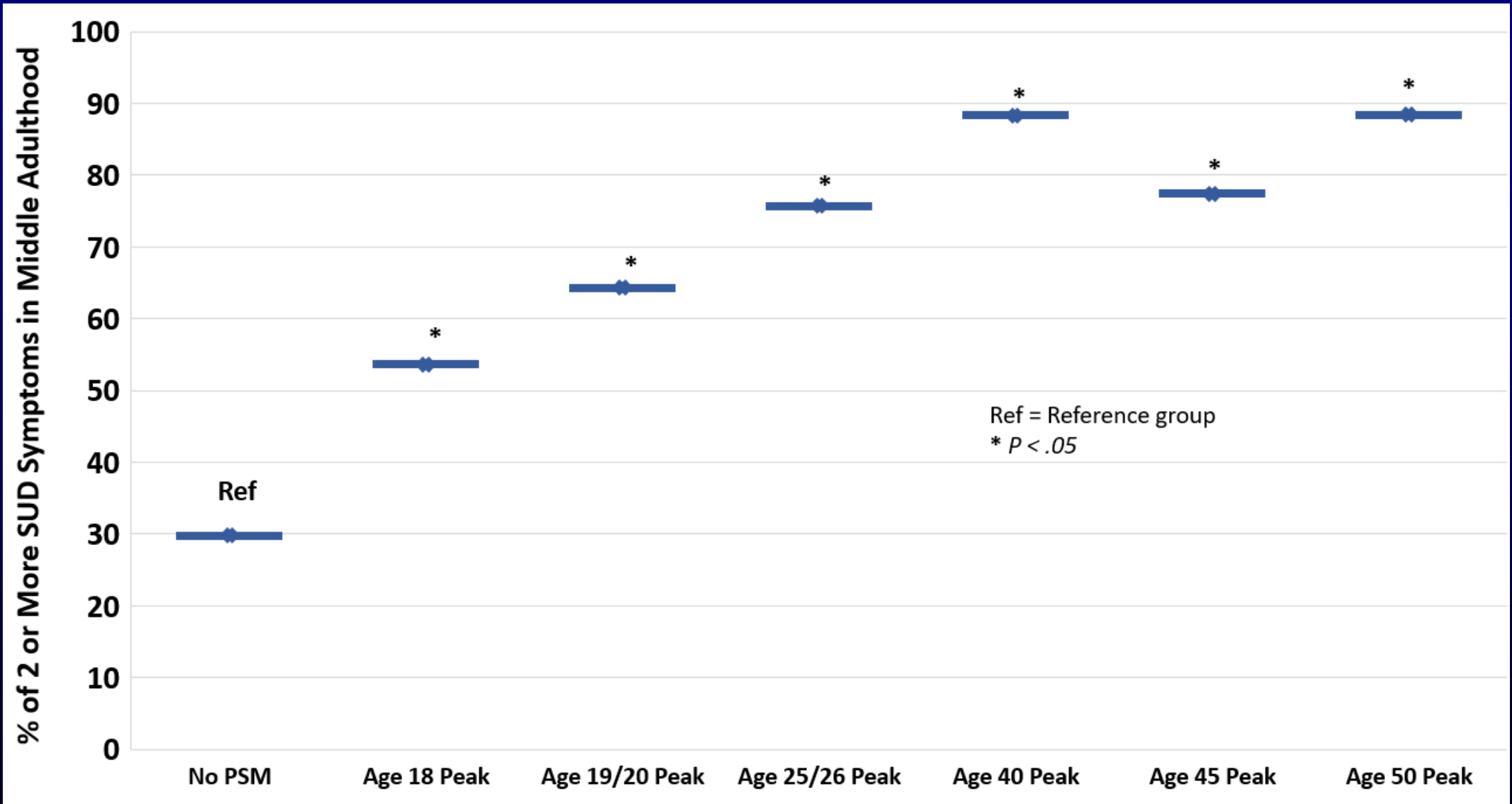
- First study to provide detailed national-level estimates of:
 - Trends in sources in US adolescents who reported nonmedical prescription stimulant use pre- and post-COVID school closures.
- The modal diversion source for nonmedical prescription stimulant use changed between 2009 and 2022:
 - An estimated 55%–58% nonmedical Rx stimulant users were given them for free by a friend between 2009 and 2014, this dropped to 21.1% in 2021–2022.
 - In 2021–2022, one's own leftover prescription medication was the most prevalent diversion source of prescription stimulants (40.0%).
- Clinicians should advise patients and caregivers about the need to monitor and supervise medication storage and administration; and assist with how to safely dispose unused controlled medications prescribed to adolescents.



Trajectories of nonmedical prescription stimulant use from age 18 to 50



Trajectories of nonmedical prescription stimulant use and SUD symptoms

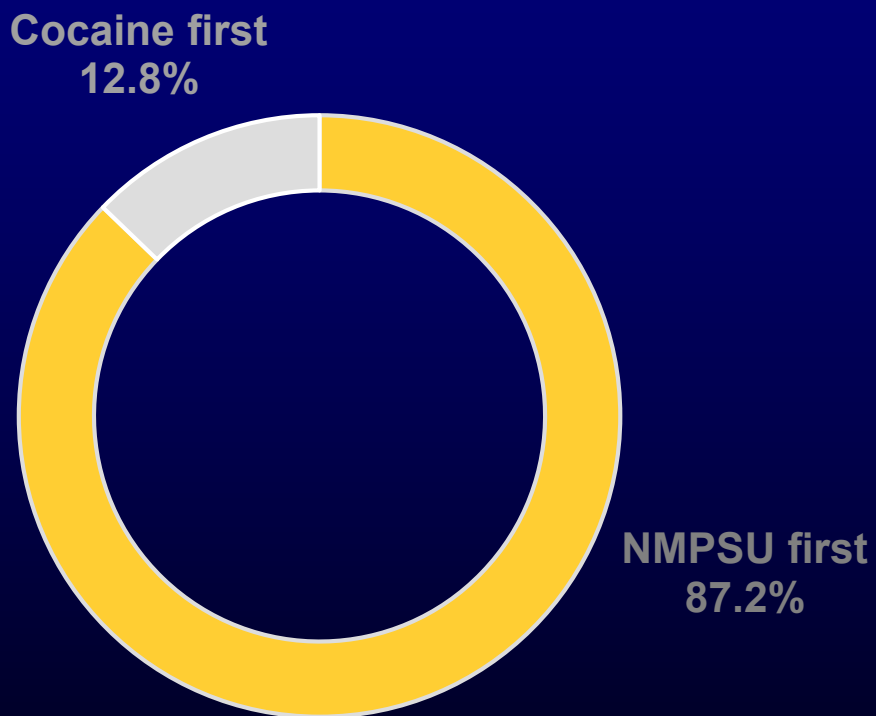


Key Takeaways

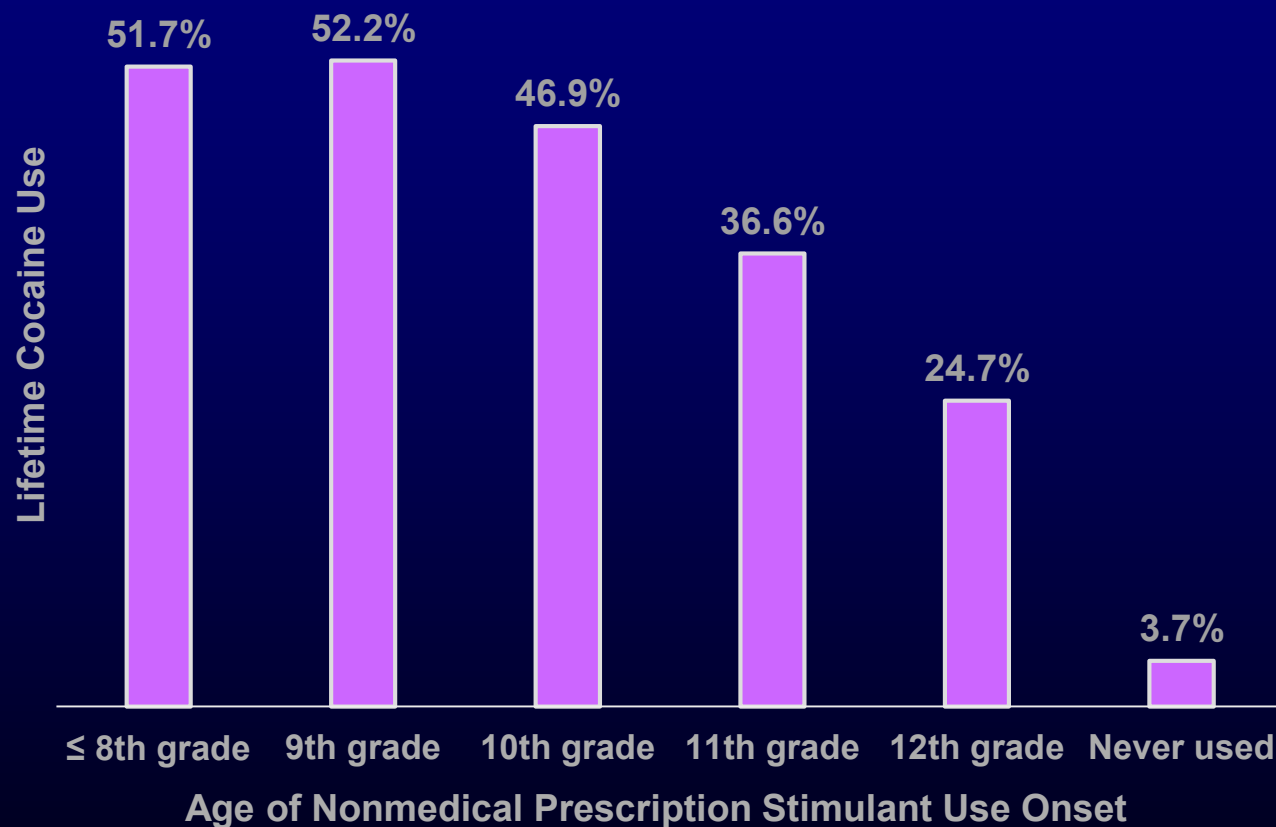
- First prospective study with national-level estimates from age 18 to age 50.
- We identified **6 distinct trajectories** of nonmedical prescription stimulant use.
- All nonmedical prescription stimulant use trajectories had **↑ adjusted odds of multiple (2+) substance use disorder (SUD) symptoms** in middle adulthood, especially the later peak trajectories (**≈90%**).
- The findings reinforce **↑ risk** associated with nonmedical prescription stimulant use and need to screen for SUD.

Temporal relationship between nonmedical use of prescription stimulants and cocaine use

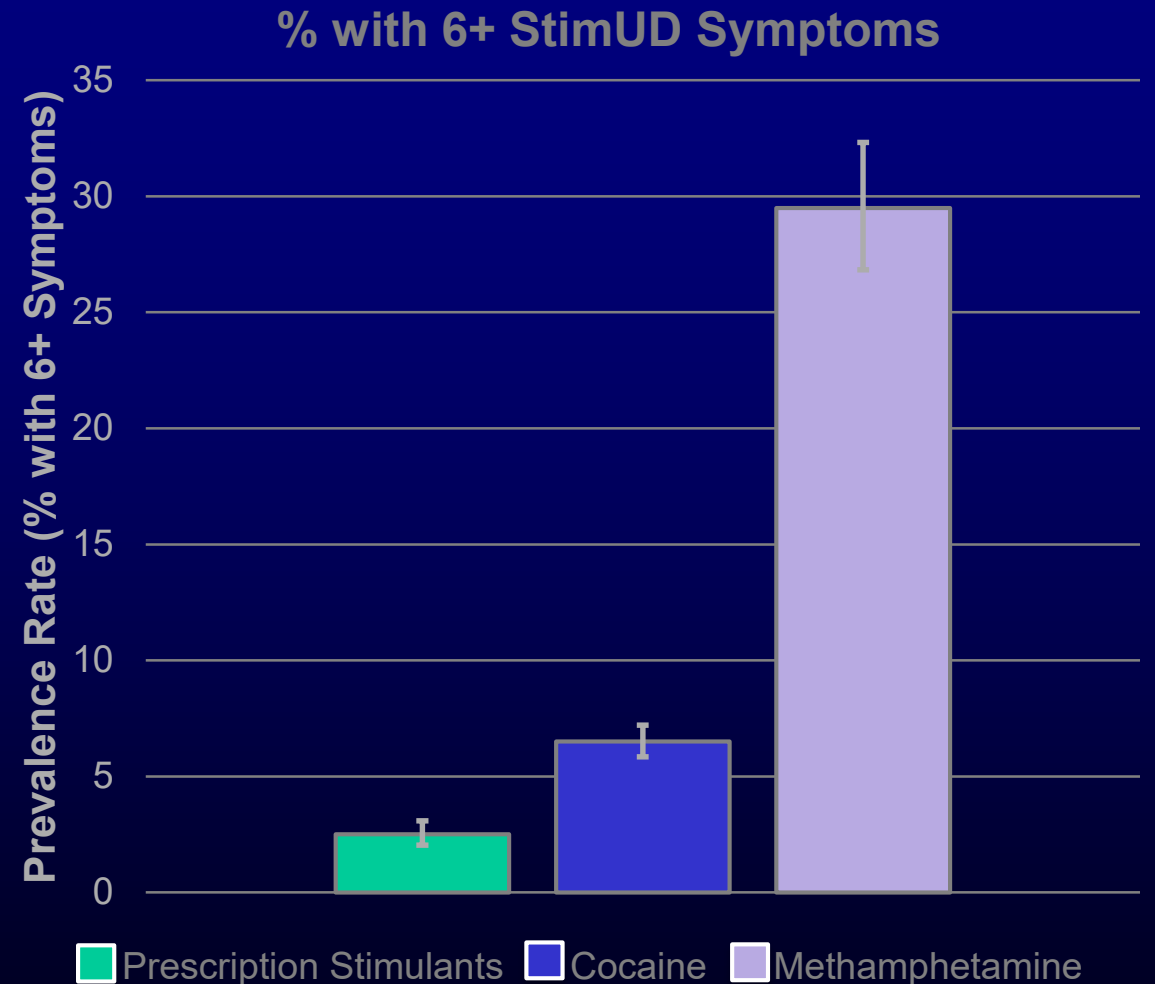
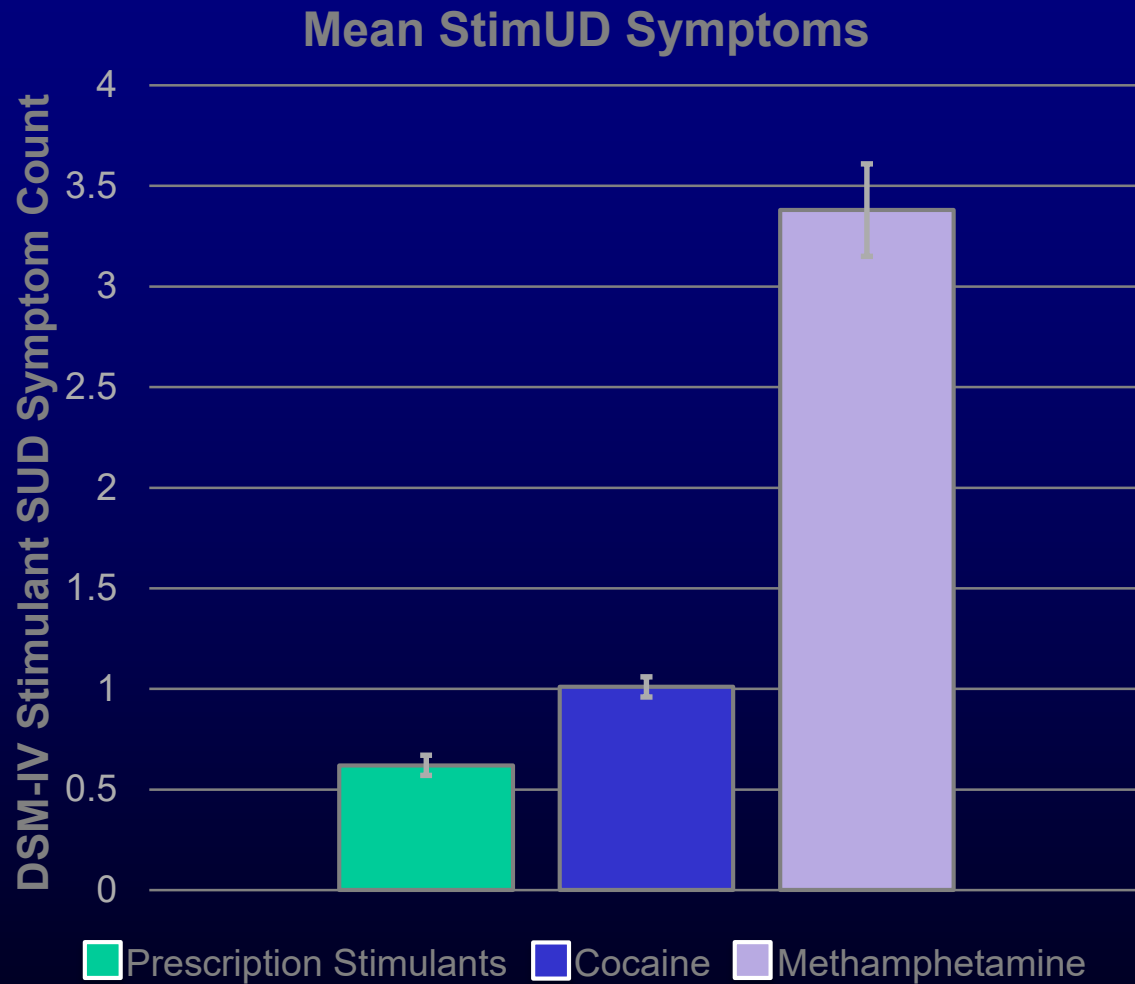
Most youth initiated nonmedical prescription stimulant use before cocaine



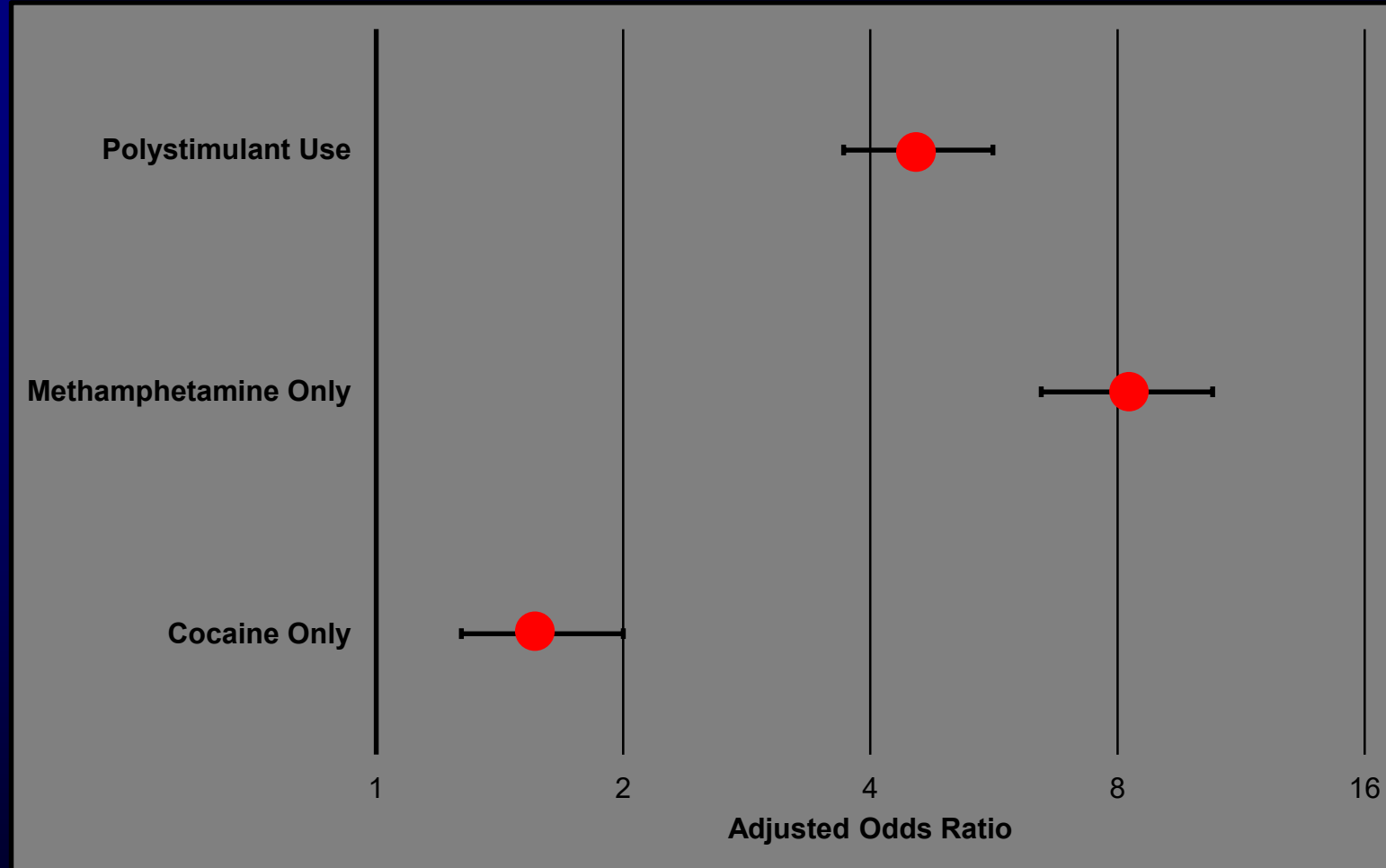
Cocaine use as a function of age of nonmedical prescription stimulant use onset



Stimulant use disorder symptom severity by stimulant type



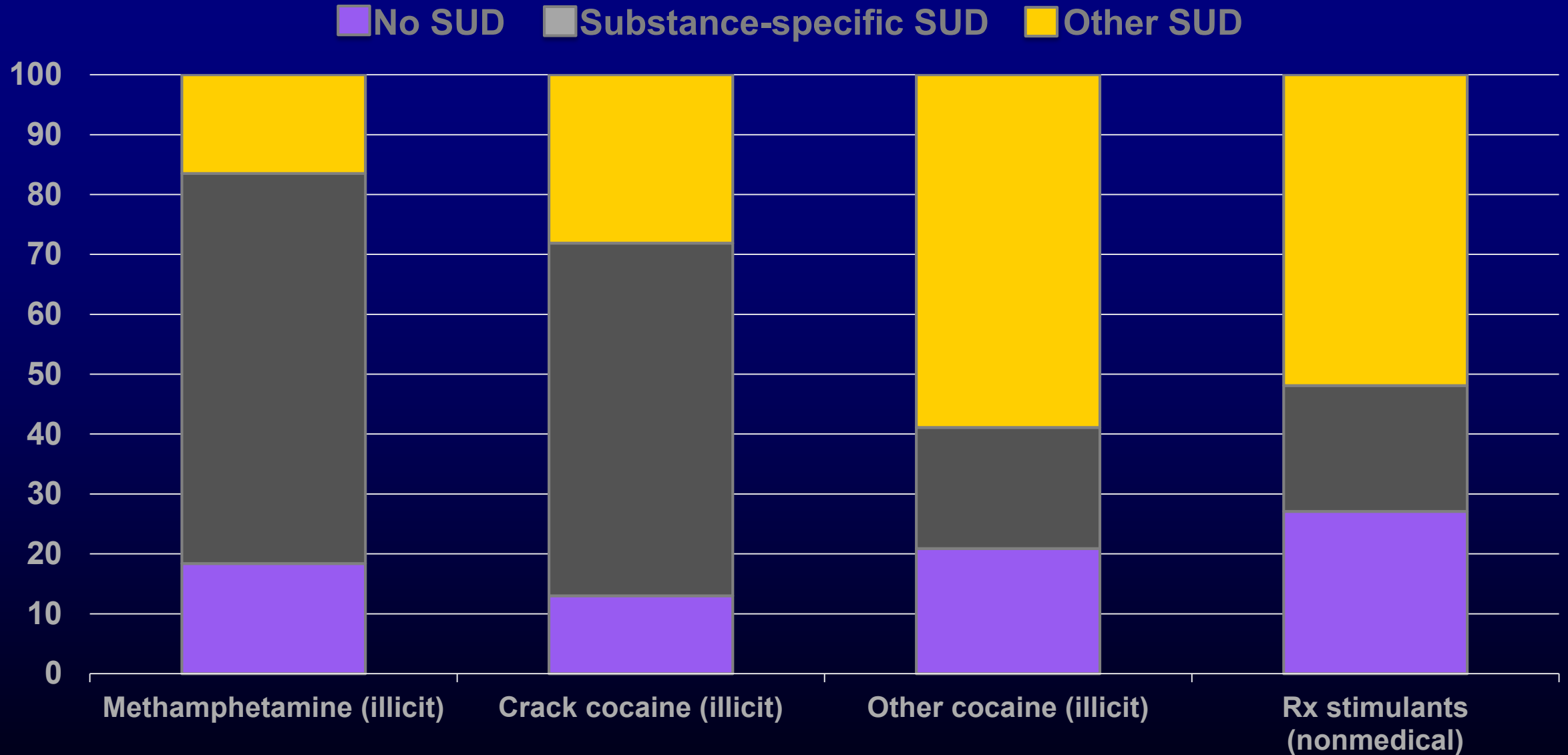
Stimulant use disorder by type of stimulant used



Reference group is Nonmedical Prescription Stimulant Use Only.

Outcomes are captured as adjusted odds ratios controlling for covariates sex, age, race/ethnicity, marital status, household income, insurance status, and population density in area of residence.

% DSM-5 substance-specific SUD vs any SUD in past-year substance use



Key Takeaways

- Of those who report both nonmedical use of prescription stimulants and cocaine use, **87% started nonmedical use of prescription stimulants before cocaine.**
- Using SUD symptom severity indicators, illicit meth use was most concerning:
 - **30% of users had 6+ stimUD symptoms** & overall mean was 3.38 symptoms.
- Most people who use cocaine, illicit methamphetamine or nonmedical prescription stimulants have a DSM-5 SUD (**73%–87%**), **but have very different SUD profiles.**
 - Most crack cocaine and methamphetamine use = substance-specific SUDs
 - Most non-crack cocaine use and nonmedical Rx stimulants = other SUDs
- Findings indicate key differences in stimUD severity between stimulant types that should be considered when treating stimulant use disorder.

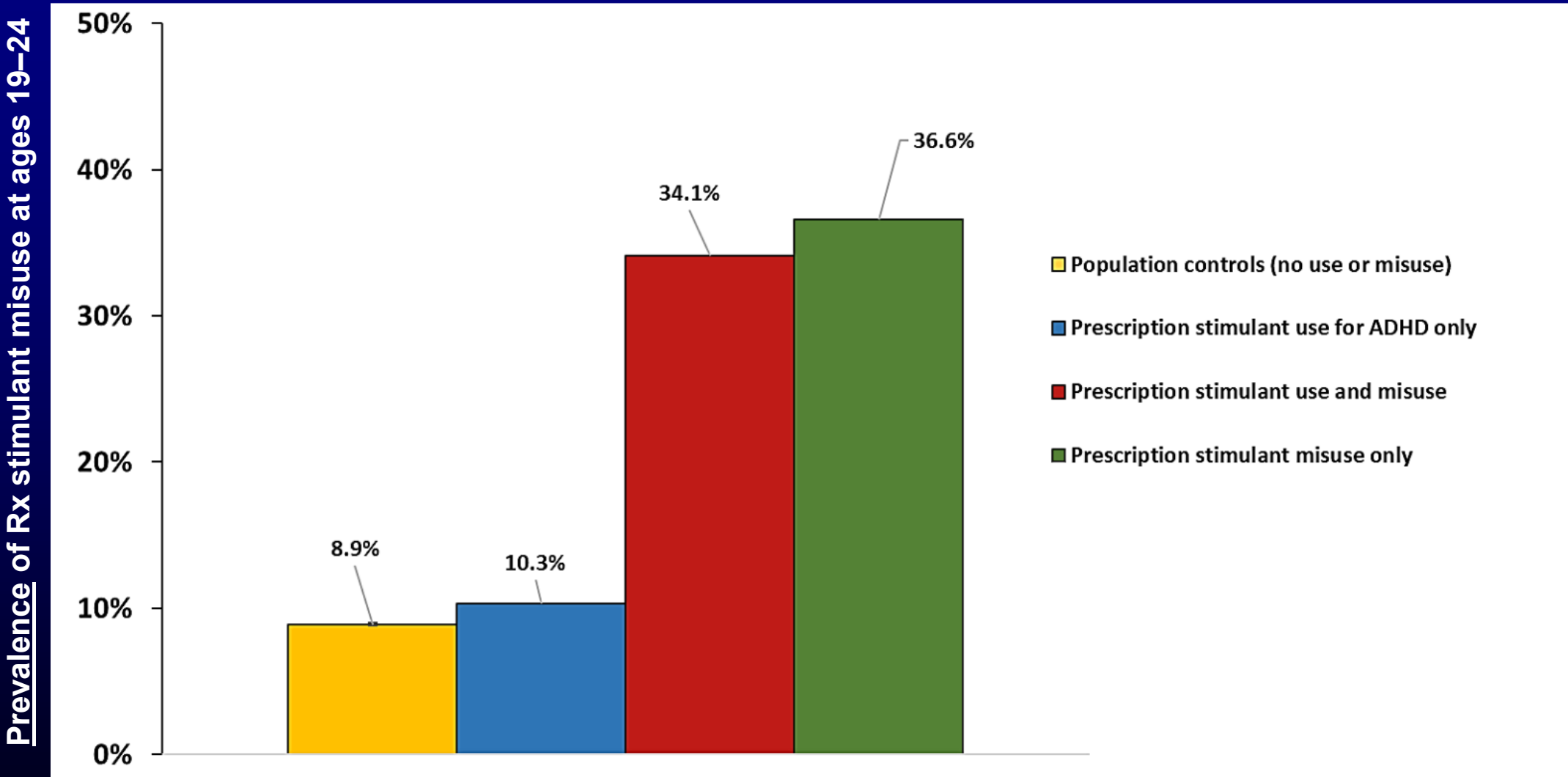
JAMA Psychiatry | **Original Investigation**

Prescription Stimulant Use, Misuse, and Use Disorder Among US Adults Aged 18 to 64 Years

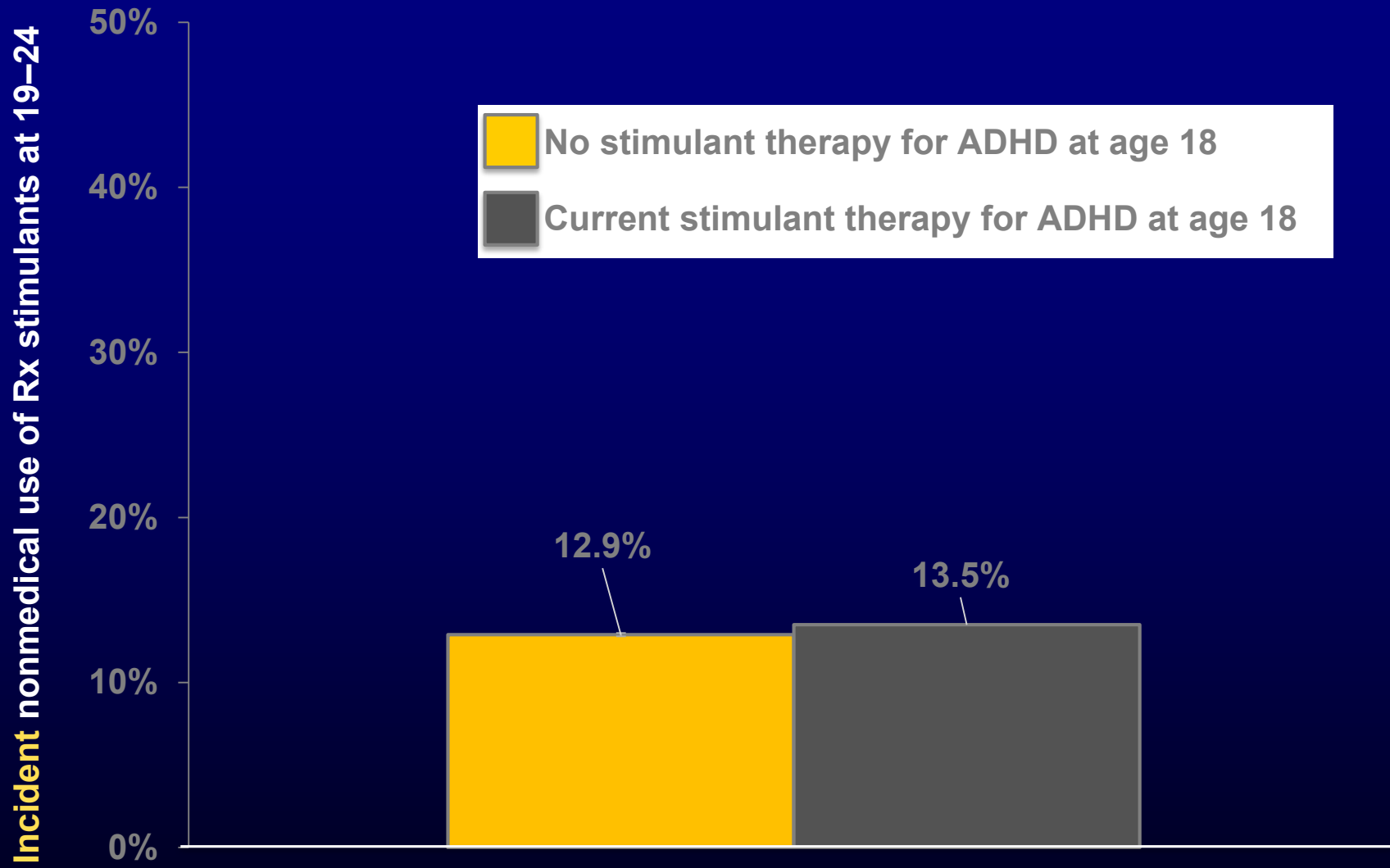
Beth Han, MD, PhD, MPH; Christopher M. Jones, PharmD, DrPH, MPH; Nora D. Volkow, MD; S. Michaela Rikard, PhD; Deborah Dowell, MD, MPH; Emily B. Einstein, PhD; Gery P. Guy, PhD, MPH; Naomi Tomoyasu, PhD; Jean Ko, PhD; Grant Baldwin, PhD; Yngvild Olsen, MD, MPH; Wilson M. Compton, MD, MPE

“Among adults [age 18–64] using prescription stimulants... 25.3% (95% CI, 23.8%–26.8%) reported prescription stimulant misuse, and 9.0% (95%CI, 8.0%–10.0%) had prescription stimulant use disorder.”

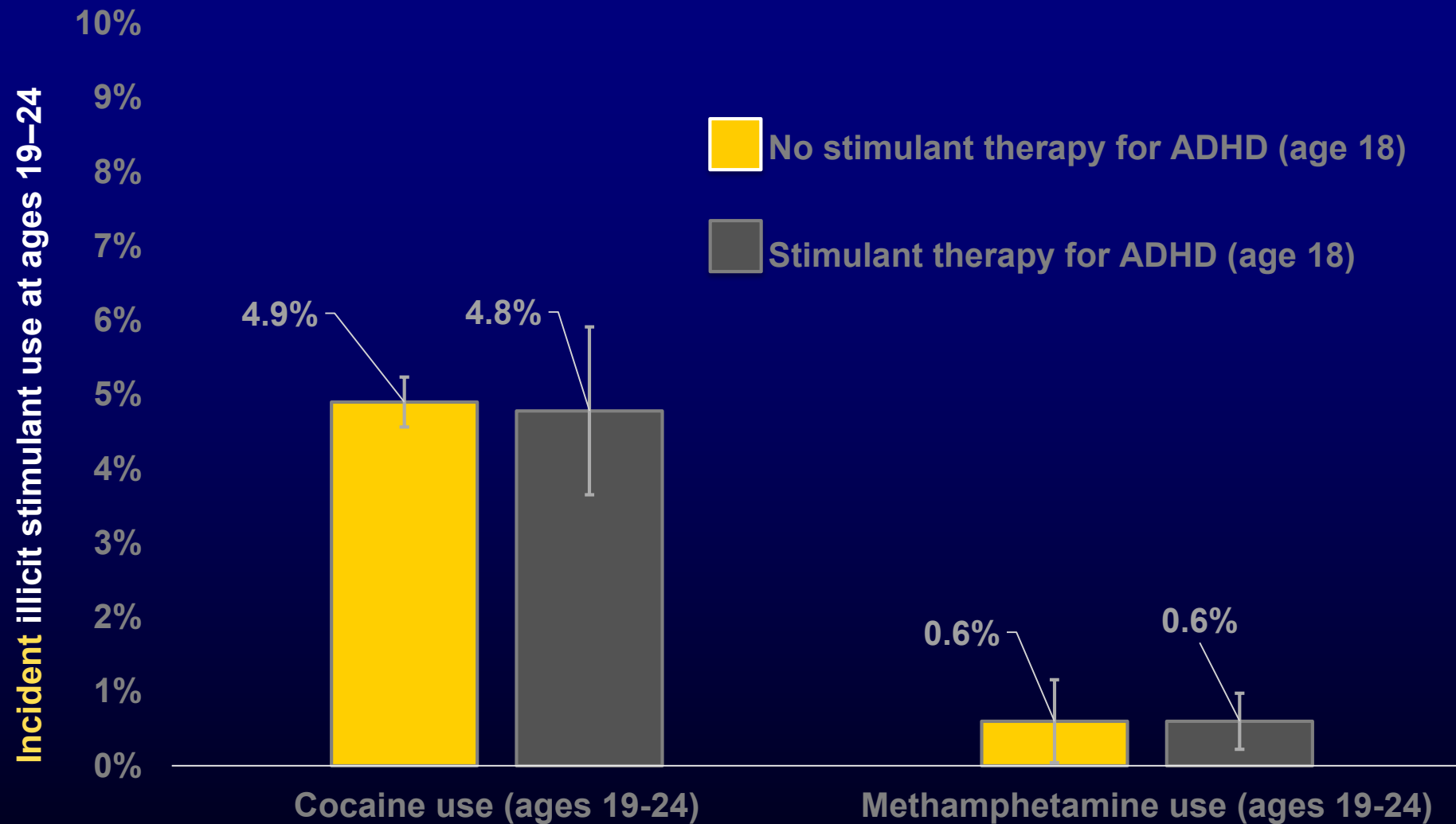
Age 18 stimulant therapy for ADHD and ages 19–24 prescription stimulant misuse



Age 18 stimulant therapy and later incident nonmedical Rx stimulant use at ages 19–24



Age 18 stimulant therapy for ADHD and later incident cocaine and methamphetamine use at ages 19–24



Key Takeaways

- The **prevalence** of nonmedical prescription stimulant use is higher among US adolescents and adults prescribed stimulants (**25%–29%**) compared to the general population.
- **Incident** nonmedical prescription stimulant use or illicit stimulant use does not appear to be higher among US adolescents prescribed stimulants, especially those who use their stimulant medication appropriately.
- Nonmedical prescription stimulant use (with or w/o medical use) is associated with continued nonmedical stimulant use (**34% or 37%**), stimUD (**21%**), and other SUD (**52%**).
- Findings reinforce the value of substance use screening in diagnosing and treating ADHD; more prospective research is warranted in US adults.

NIH Helping to End Addiction Long-term® (NIH HEAL) Initiative

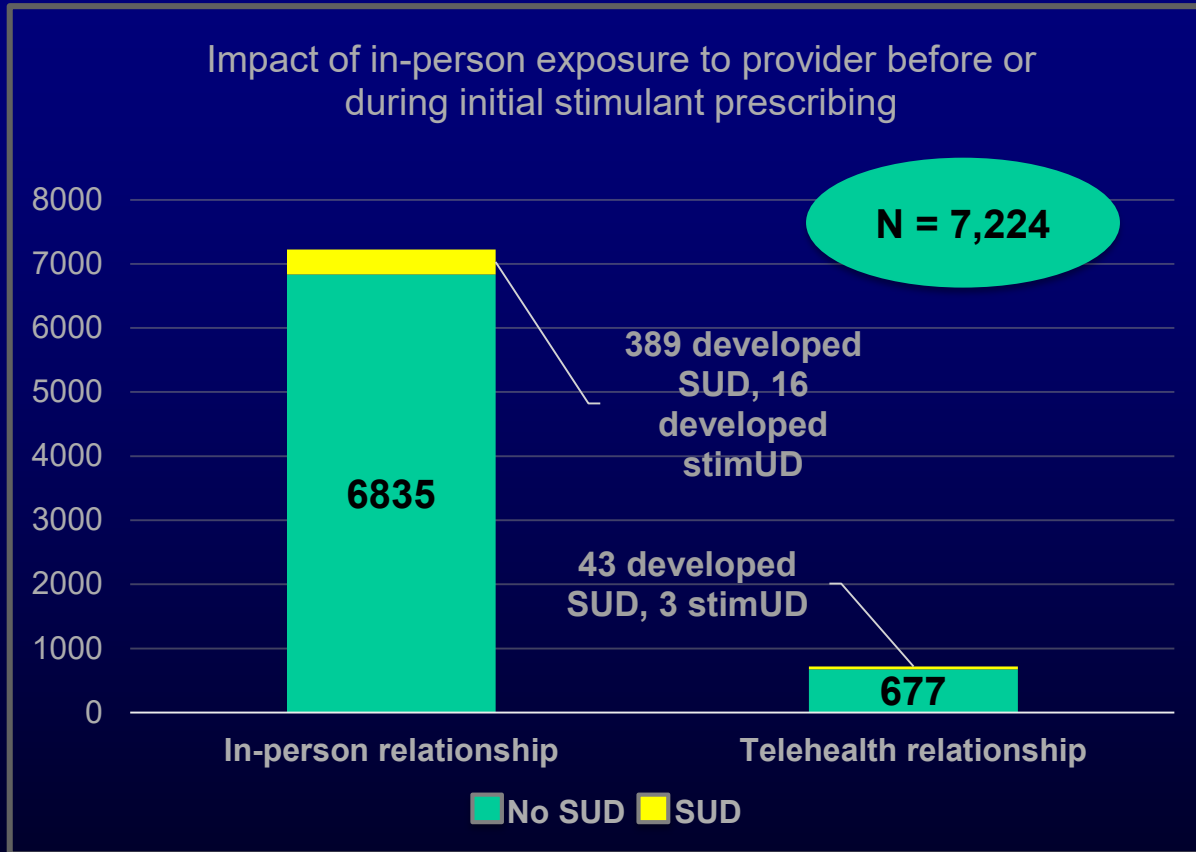
- Regional clinical sample drawn from patients receiving care within the Mass General Brigham (MGB) healthcare system.
- MGB is a large integrated healthcare network in the Northeast providing care for over 2.5 million patients annually at hospital and community health centers across New England.
- Patient characteristics and prescription records were extracted from Epic electronic health records, spanning primary care (adult and pediatric), behavioral health, and other community- and hospital-based practices.
- Sample design included:
 - **Telehealth study:** Patients ≥ 12 years old initially prescribed stimulant pharmacotherapy for ADHD at MGB facilities between 3/1/2020 and 8/25/2023.

Impact of Telehealth on Incident Stimulant and other SUDs

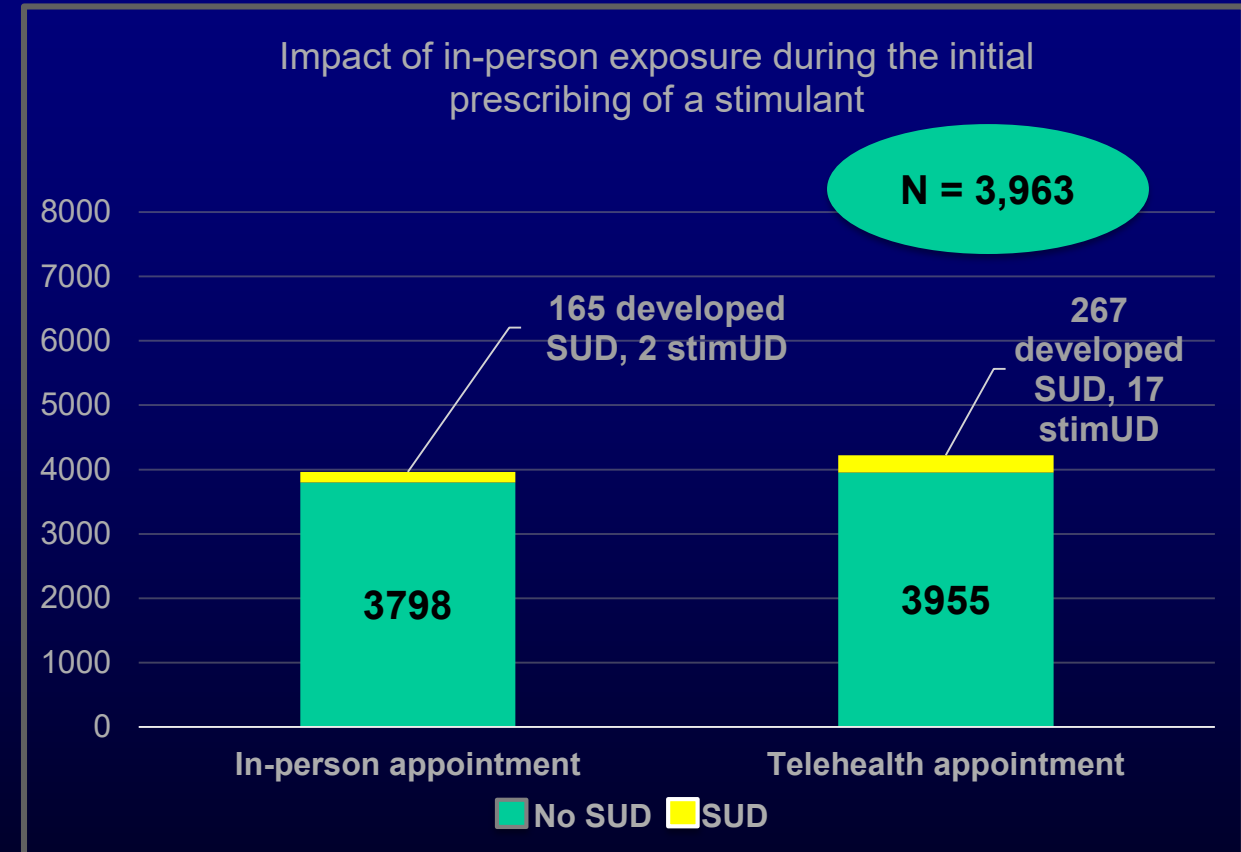
Telehealth prescribing of stimulants for ADHD and associated risk for later stimulant and substance use disorders

Aim 1: Does receiving a stimulant prescription from a provider whom the patient has never seen in person increase risk for SUD?

Aim 2: Does starting a stimulant prescription during a telemedicine visit increase risk for SUD?



SUD (aOR = 1.18 [95% CI: 0.83, 1.66], p = 0.34)
 stimUD (aOR = 0.83 [0.22, 3.08], p = 0.78)

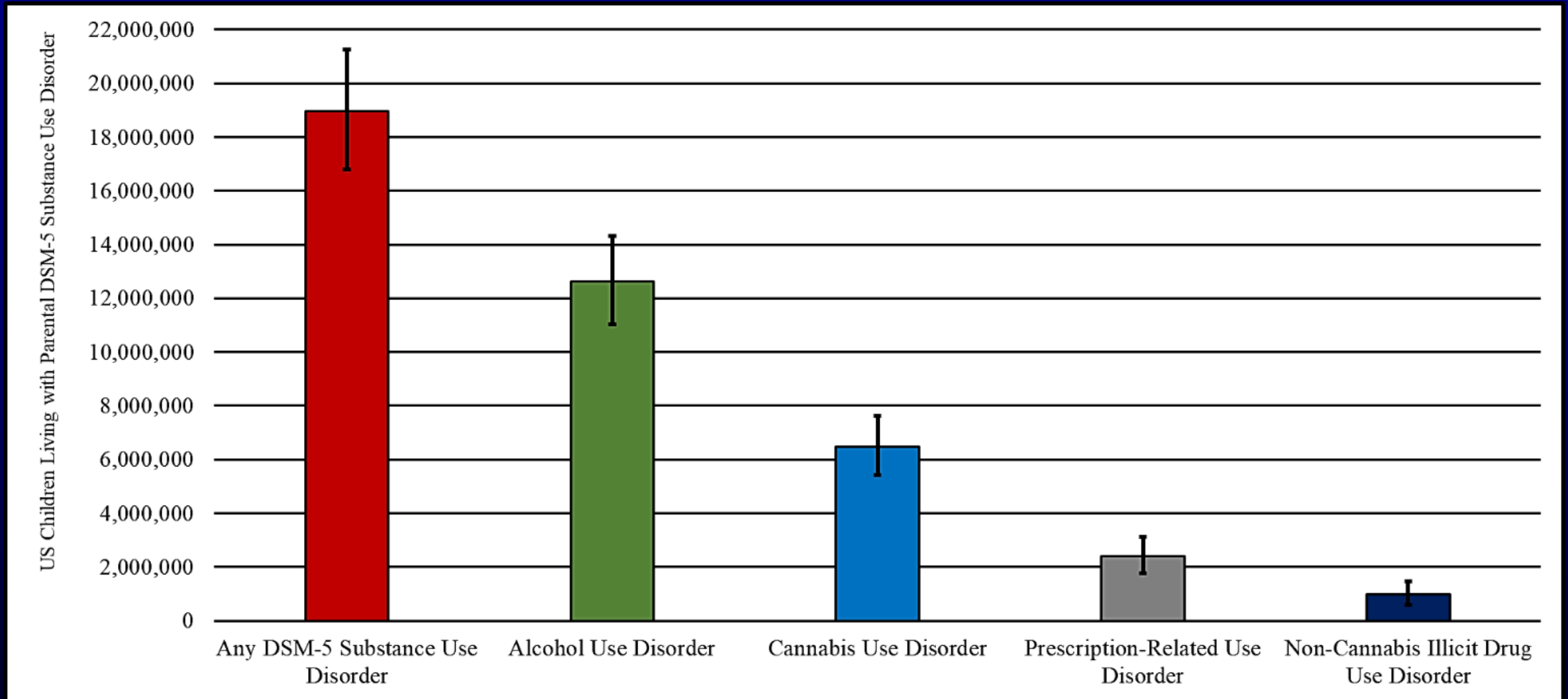


SUD (aOR = 0.87 [0.71, 1.07], p = 0.19)
 stimUD (aOR = 0.30 [0.096, 0.95], p = 0.041)

Key Takeaways

- Telehealth stimulant prescribing **does not increase overall incident SUD risk** compared to in-person care, which are encouraging findings since telemedicine may lower barriers to care and the threshold for ADHD treatment.
- **No added benefit** of an in-person prescriber relationship on SUD or stimUD risk.
- **Higher incident stimUD risk** observed for initial prescriptions via telehealth, which requires further investigation.
- **StimUD was rare in both groups**, but findings should be replicated in larger samples.
- Limited diversity in the sample highlights **ongoing racial/ethnic disparities in ADHD treatment**.
- Findings may not generalize to for-profit telehealth platforms—further examination of outcomes in a wider variety of healthcare settings is important.

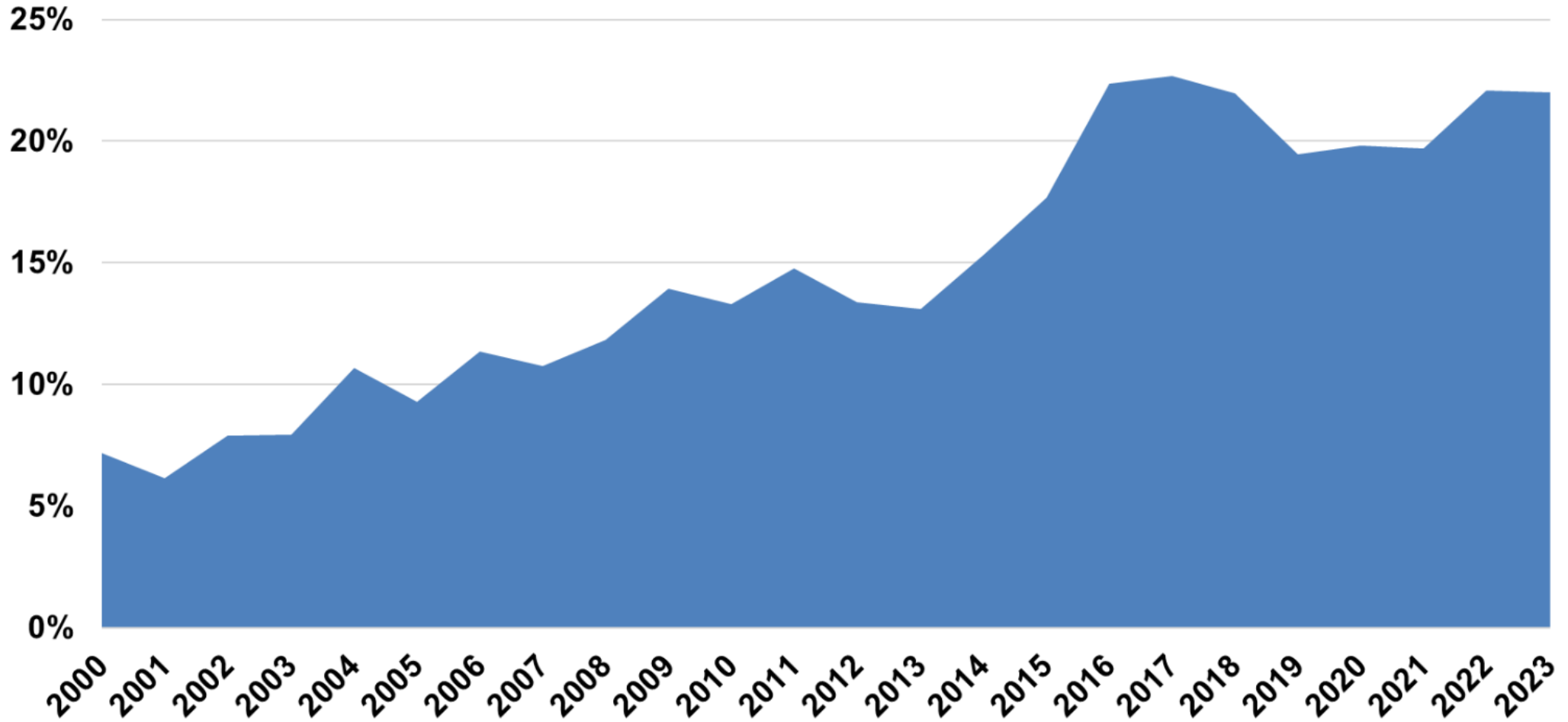
US Children Living with Parents with a DSM-5 Substance Use Disorder, 2023



Notes: Error bars denote the 95% confidence intervals of the subpopulation size. Prescription-related use disorder included prescription opioids, prescription benzodiazepines, or prescription stimulants. Non-cannabis illicit drug use disorder included cocaine, hallucinogens, heroin, inhalants, or methamphetamine.

Let's Not Forget...

Percent of Parentally-Bereaved Children Resulting from Parental Drug Overdose in Michigan, 2000-2023



Key Takeaways

- Over 19 million US children (1 in 4) live with a parent with a DSM-5 substance use disorder.
- The number of US children who have experienced a parental death from a drug overdose has **increased** in the past decade.
- The bereaved children I work with **do not know** the specific drugs that their parents used or that caused their death, but they want us to stop it so other kids never have to experience what they feel every day.

This is why we do this work...

Future Directions

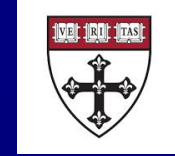
- Use prospective data with **causal inference methods** to determine temporal relationships and potential risks associated with adult onset of stimulant therapy for ADHD.
- Link medical and nonmedical prescription stimulant use patterns with **fatal overdose** data which will allow for the first national prospective study to examine the differences in patterns that are associated with **fatal overdose**.
- Examine **mortality** associated with different patterns of medical and nonmedical use of prescription stimulants to help inform prevention, clinical, and regulatory decisions.

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Abbreviations

- AAAP: American Academy of Addiction Psychiatry
- ADHD: Attention-Deficit/Hyperactivity Disorder
- AOR: Adjusted Odds Ratio
- ASAM: American Society of Addiction Medicine
- CDC: Centers for Disease Control and Prevention
- CI: Confidence Interval
- CPDD: The College on Problems of Drug Dependence
- DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*
- DSM-5: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*
- FDA: US Food and Drug Administration
- MTF: Monitoring the Future Panel Study
- NIDA: National Institute on Drug Abuse
- NIH: National Institutes of Health
- NIH HEAL Initiative[®]: NIH Helping to End Addiction Long-Term[®] Initiative
- NSDUH: National Survey on Drug Use and Health
- Rx: Prescription
- StimUD: Stimulant Use Disorder
- SUD: Substance Use Disorder



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Questions?