Cocaine Use Disorders & Prescription Medication Misuse

MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Timothy E. Wilens, MD

Director, Center for Addiction Medicine
Chief, Division of Child and Adolescent Psychiatry,
Massachusetts General Hospital
Harvard Medical School

MGH 1811

MassGeneral Hospital for Children

VE RI TAS

Faculty Disclosure

Timothy Wilens, M.D. has served as a consultant, or has received grant support from the following:

- Arbor, Otsuka, NIH (NIDA), Ironshore, Vallon
- Licensing agreement with Ironshore (Before School Functioning Questionnaire)
- Clinical care: MGH, Bay Cove Human Services, Gavin/Phoenix, National Football League (ERM Associates), Major/Minor League Baseball
- (Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford); ADHD Across the Lifespan (Cambridge), MGH Comprehensive Clinical Psychiatry (Elsevier), MGH Psychopharmacology and Neurotherapeutics (Elsevier)

Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (e.g., substance use disorders)

Cocaine: Epidemiology

- 4.2 million US residents use cocaine yearly
- >900,000 US residents with cocaine use disorder
- Cocaine is a tropane ester alkaloid found in leaves of the Erythroxylum coca plant, a bush that grows in the Andes Mountain region of South America
- Cocaine is the illegal drug most often associated with visits to US hospital emergency departments

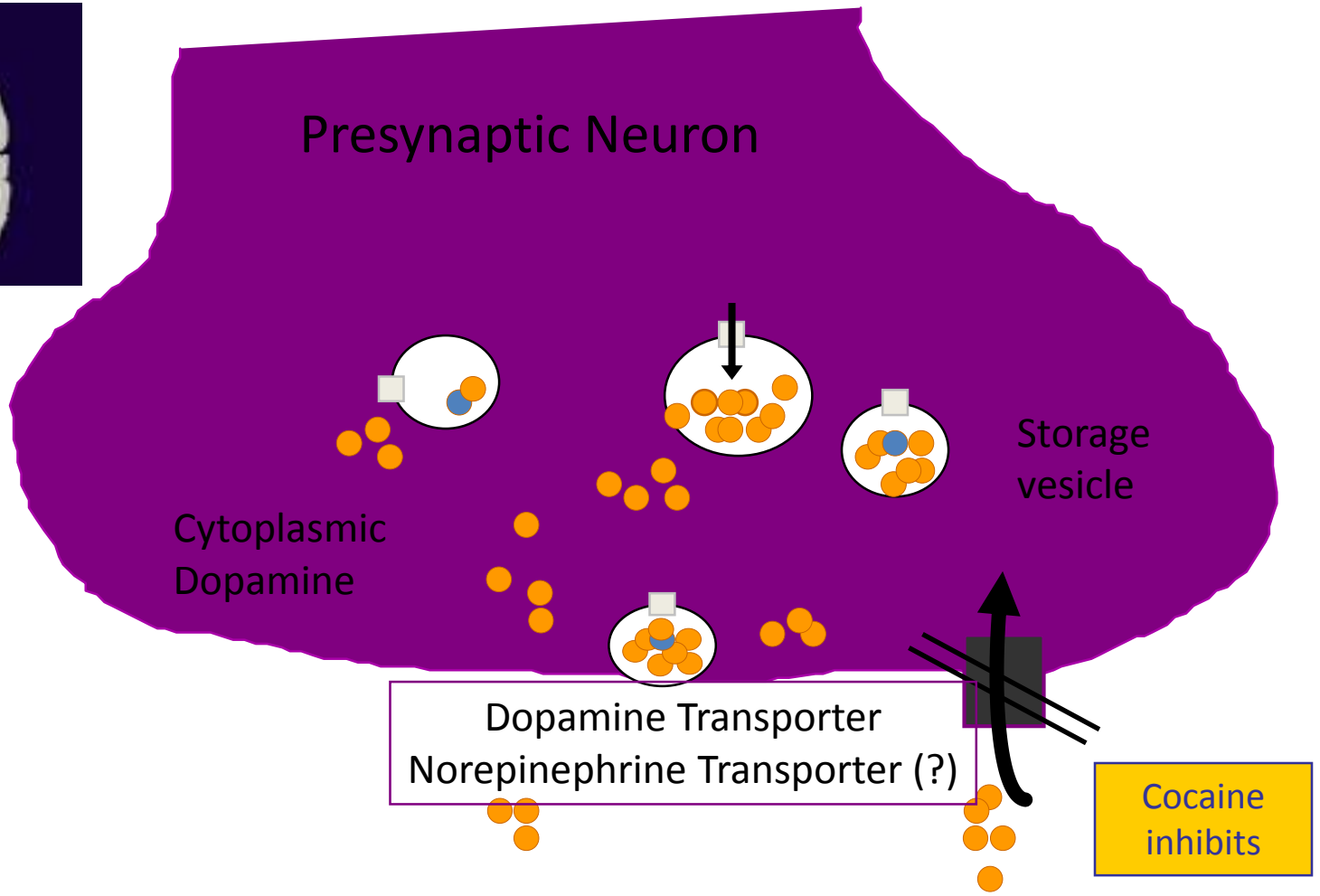
Results from the 2013 National Survey on Drug Use and Health, NSDUH Series H-48, HHS Publication No. (SMA) 14-4863, Rockville, MD 2014

Cocaine: Clinical Effects

- **Typical cocaine doses: 12 to 15 g orally (coca leaf), 20 to 100 mg intranasally, 10 to 50 mg intravenously, and 50 to 200 mg smoked**
- **Potent CNS Stimulation**
  - **Disinhibition, euphoria, elevation, enhanced sense of self, energy**
  - **Tachycardia, increased heart rate**
- **Adverse effects**
  - **Acute: anxiety, talkativeness, agitation, paranoia, psychosis, stereotypies/picking, dyskinesias, cardiovascular/stroke, hyperthermia, circulatory failure**
  - **Chronic: sensitization or tolerance, depression, weight loss, neuropsychological impairment, cardiovascular (myocardial infarction, arrhythmias, hypertension), respiratory symptoms (smoked)**
- **Withdrawal (immediate to 2+ weeks)**
  - **Intense crash/ sleep**
  - **Irritability, agitation, depression, urges/cravings**

Mechanism of Action of Cocaine

(Wilens T. J Clin Psych 2006).

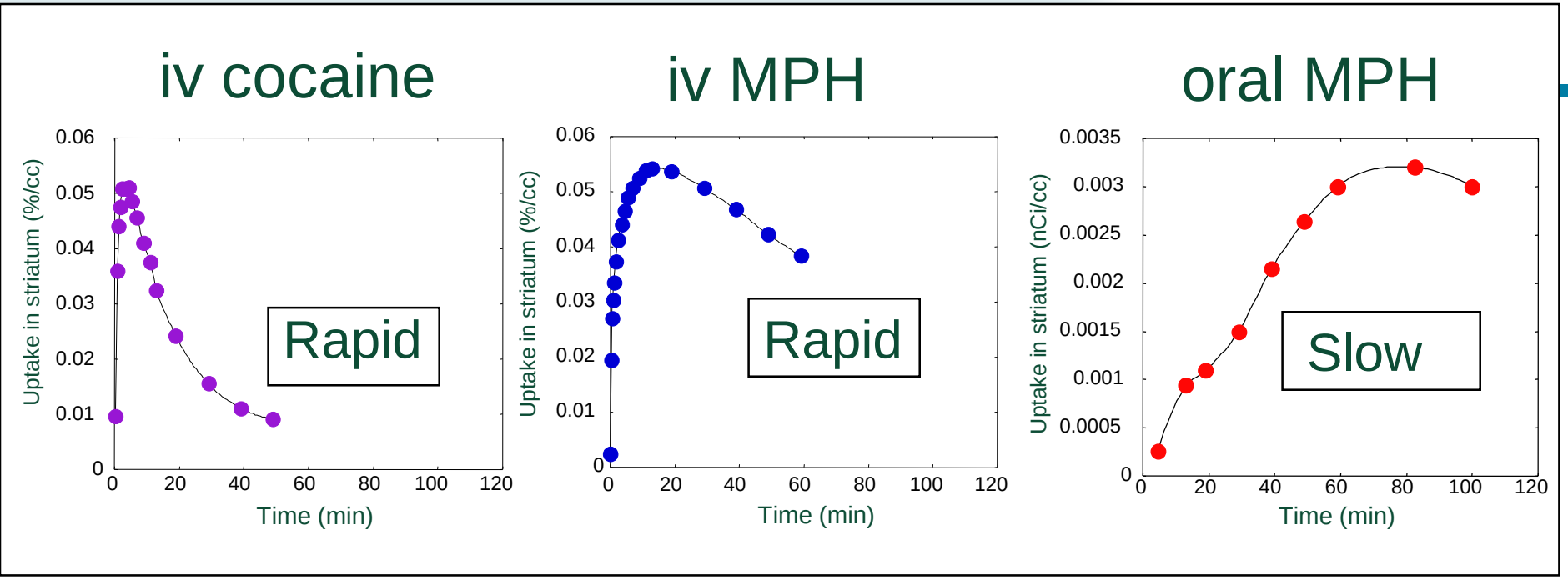


Cocaine: Testing

- Screening tests
- Blood (12 hr cocaine, 48 hr benzoylecgonine)
- Oral Fluid (similar to blood, improving detection)
- Urine (benzoylecgonine only)- two to three days after cocaine use, but *may be positive up to two weeks* after chronic heavy use

Cone EJ, Weddington WW Jr. J Anal Toxicol 1989; 13:65.

Rate of Drug Uptake Into the Brain Linked to Likeability



Cocaine (iv) and methylphenidate [MPH] (iv) produce a “high” but methylphenidate (oral) does not

The slow brain uptake of oral methylphenidate permits effective treatment without a “high”

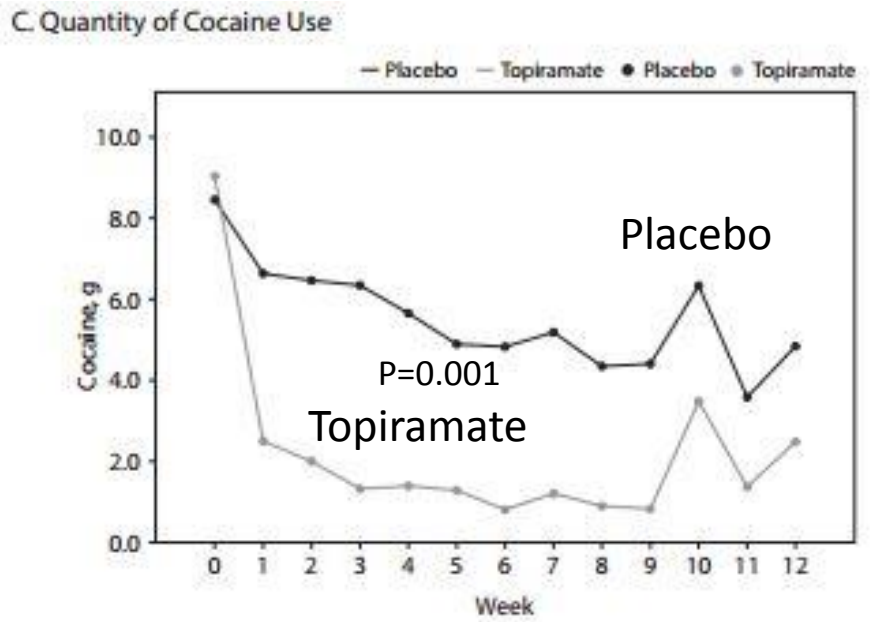
(Volkow et al., Arch Gen Psych 52:1995, J Neurosci 2001)

Cocaine Treatment

- Some similarities to methamphetamine use disorder
- Smoked cocaine among the most difficult SUD to treat
- Twelve Step (Cocaine Anonymous)/ Rational Recovery
- Cognitive Behavioral Therapy +/- MI
- Contingency Management

Lee and Rawson, Drug Alc Rev 2008: 27: 309-17

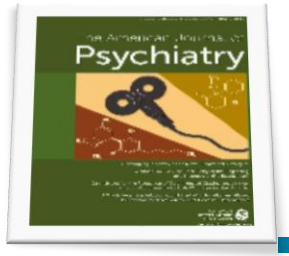
Treatment of Crack Cocaine with Topiramate



Design: RCT; N=29/group; dosing to 200 mg/day
Adjunct Tx: Motivational interviewing, group Tx

J Clin Psychiatry 2016;77(3):398–406
dx.doi.org/10.4088/JCP.14m09377

A Single Ketamine Infusion Combined With Mindfulness-Based Behavioral Modification to Treat Cocaine Dependence: A Randomized Clinical Trial



Elias Dakwar, M.D., Edward V. Nunes, M.D., Carl L. Hart, Ph.D., Richard W. Foltin, Ph.D., Sanjay J. Mathew, M.D., Kenneth M. Carpenter, Ph.D., C.J. "Jean" Choi, M.S., Cale N. Basaraba, M.P.H., Martina Pavlicova, Ph.D., Frances R. Levin, M.D.

Objective: Research has suggested that subanesthetic doses of ketamine may work to improve cocaine-related vulnerabilities and facilitate efforts at behavioral modification. The purpose of th… infusion impro… adults engage…

Methods: Fift… randomly assi… fusion of keta… condition) du… also initiated a… prevention. C… and urine toxi… study abstinence and time to relapse (defined as first use or dropout).

Results: Overall, 48.2% of individuals in the ketamine group maintained abstinence over the last 2 weeks of the trial, compared with 10.7% in the midazolam group (intent-to-treat analysis). The ketamine group was 53% less likely (hazard ratio=0.47; 95% CI=0.24–0.92) to relapse (dropout or use …group, and craving …group throughout …nces were statisti… …ated, and no par… …a result of adverse …mproved a range of …-dependent adults …l modification, in… …g craving, and re… ducing risk of relapse. Further research is needed to replicate these promising results in a larger sample.

Conclusions: A single ketamine infusion improved a range of important treatment outcomes in cocaine-dependent adults engaged in mindfulness-based behavioral modification, including promoting abstinence, diminishing craving, and reducing risk of relapse. Further research is needed to replicate these promising results in a larger sample.

Am J Psychiatry 2019; 176:923–930; doi: 10.1176/appi.ajp.2019.18101123

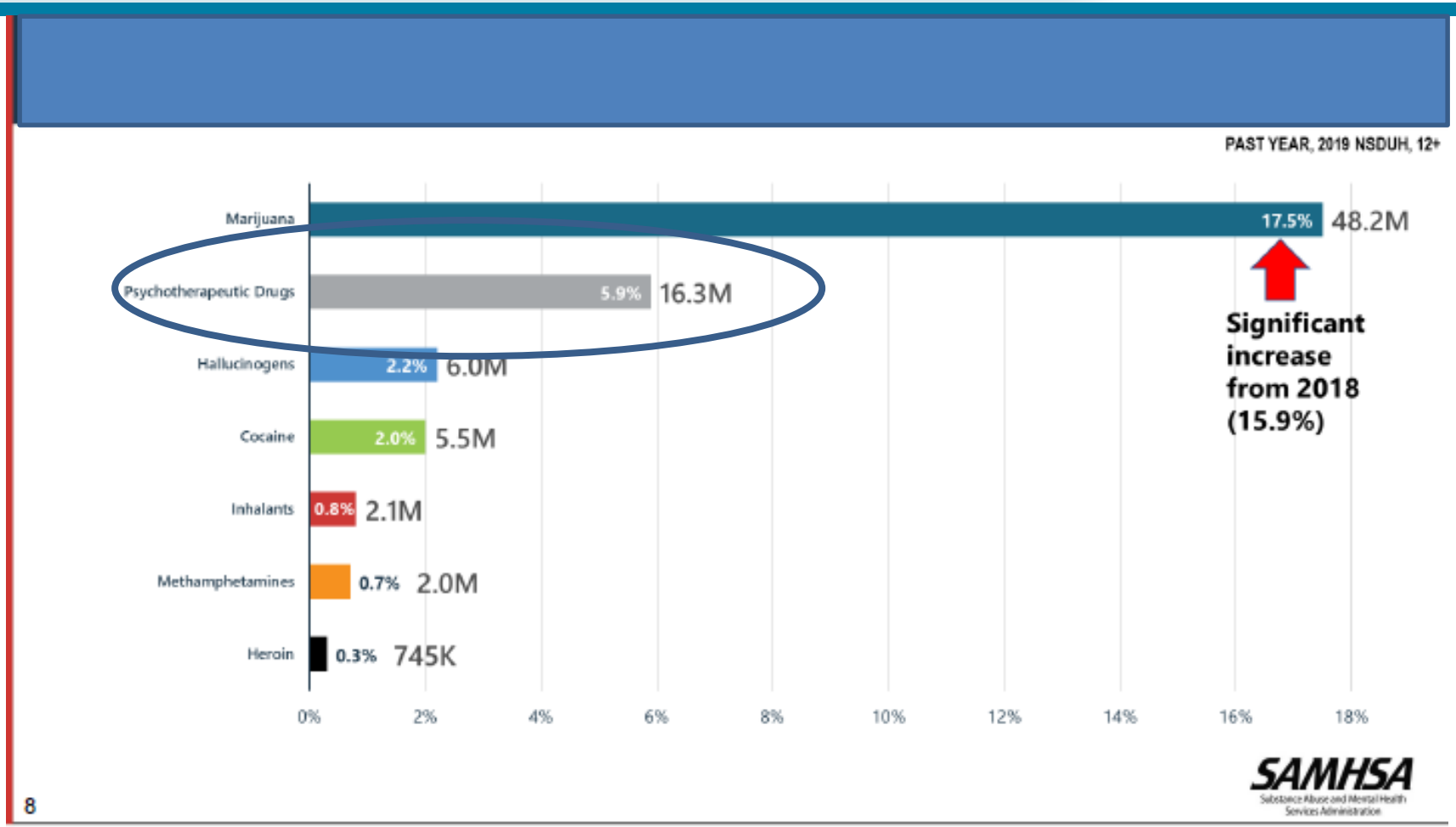
Dakwar, et al. Am J Psychiatry 176:11, November 2019
Viewed online at https://doi-org.treadwell.idm.oclc.org/10.1176/appi.ajp.2019.18101123

Cocaine: Pharmacotherapy

- Topirimate
- N-Acetylcysteine (NAC)
- Disulfiram (linked to DBH genotype?)
- Modafinil
- Galantamine (?)
- Agonist therapies (e.g. stimulants)
- Cocaine vaccine (experimental)

Dackis et al, Neuropsychopharmacology (2005) 30, 205–211
Johnson B et al., JAMA Psychiatry. 2013;70(12):1338-1346
Martell et al, 2009 Arch.Gen.Psychiatry 66,1116–1123; Kosten et al, 2014 Drug and Alcohol Dependence 140,42–47). ,

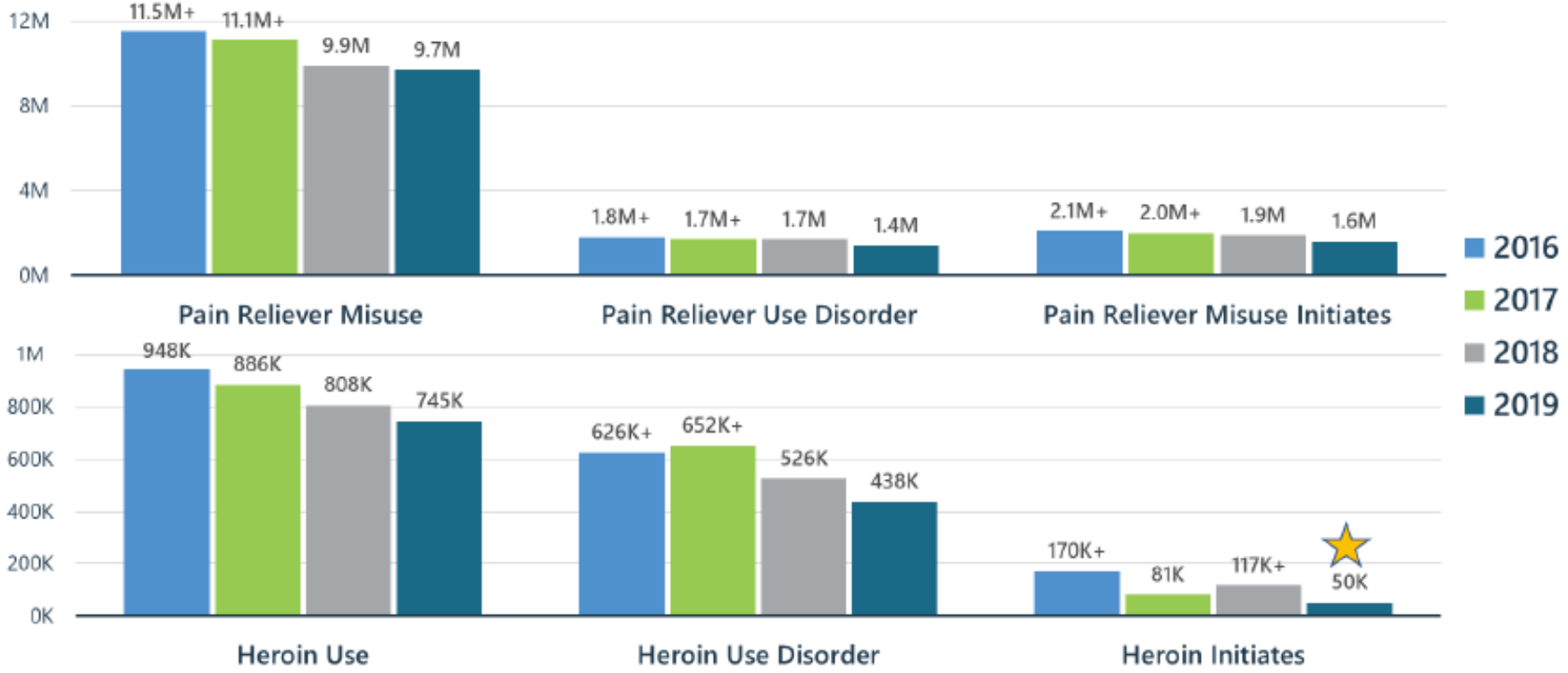
Prescribed Psychotropics Are Frequently Misused



https://www.samhsa.gov/data/sites/default/files/reports/rpt29392/Assistant-Secretary-nsduh2019_presentation/Assistant-Secretary-nsduh2019_presentation.pdf

Prescription Pain Reliever Misuse and Heroin Use

PAST YEAR, 2016-2019 NSDUH, 12+



+ Difference between this estimate and the 2019 estimate is statistically significant at the .05 level.

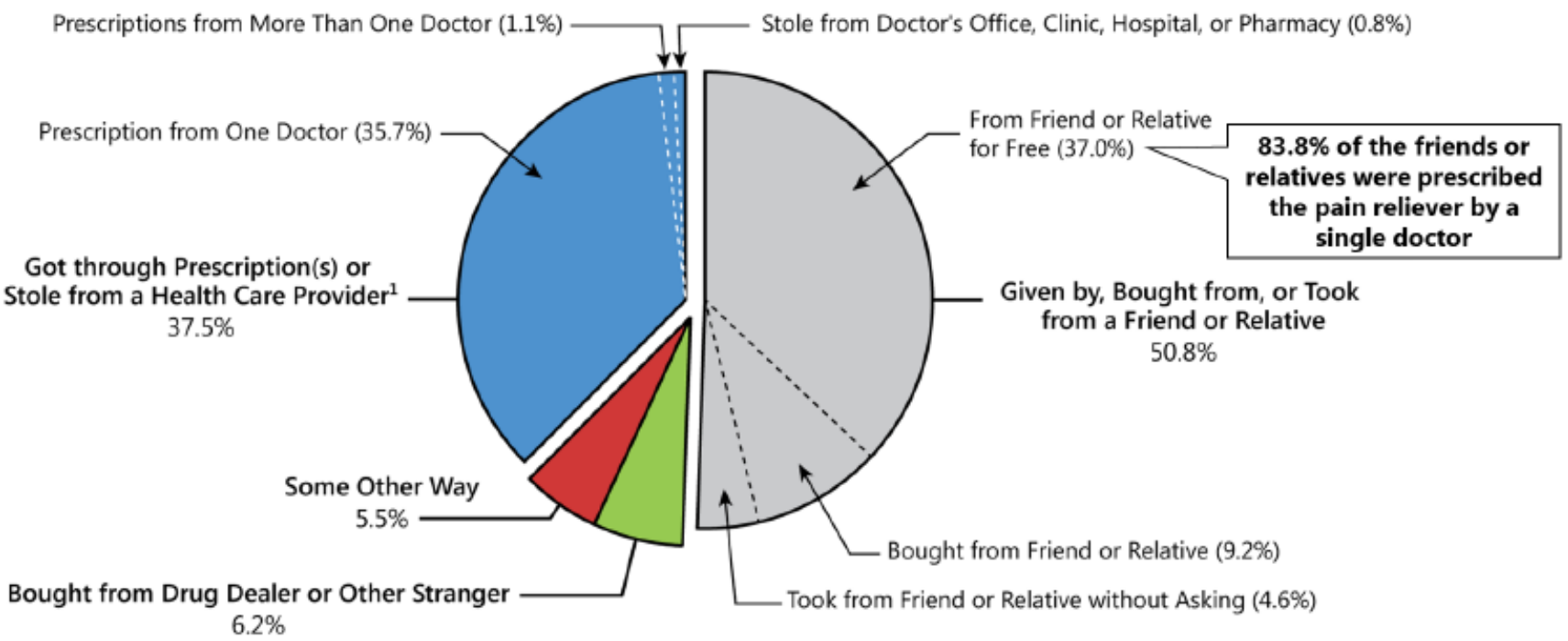
SAMHSA
Substance Abuse and Mental Health Services Administration

11

https://www.samhsa.gov/data/sites/default/files/reports/rpt29392/Assistant-Secretary-nsduh2019_presentation/Assistant-Secretary-nsduh2019_presentation.pdf

Sources Where Pain Relievers Were Obtained for Most Recent Misuse among People Who Misused Prescription Pain Relievers

PAST YEAR, 2019 NSDUH, 12+



9.7 Million People Aged 12 or Older Who Misused Prescription Pain Relievers in the Past Year

SAMHSA
Substance Abuse and Mental Health Services Administration

https://www.samhsa.gov/data/sites/default/files/reports/rpt29392/Assistant-Secretary-nsduh2019_presentation/Assistant-Secretary-nsduh2019_presentation.pdf

Nonmedical Use of Prescription Medications in Young People

- Nonmedical use of prescription opioids in teenage years (12-17) is of great concern due to association with future opioid addiction
  - Nonmedical use of prescription opioids is associated with 19X greater risk of transitioning to heroin use
  - > 80% young adults who inject heroin report they started using prescription opioids before transitioning to heroin
  - Steepest rise in unintentional opioid OD fatalities in young adults (18-25)

Schepis TS, Wilens TE, McCabe SE. Prescription drug misuse: sources of controlled medications in adolescents. J Am Acad Child Adolesc Psychiatry. 2019;58:670-680.

Nonmedical Use of Prescription Drugs

- 11.0% of high school seniors reported past-year NMUPD
- (n = 1,917)

Past-Year NMUPD	Students with Past-Year NMUPD (N=1917) % (n)
Stimulant Use	51.7% (968)
Opioid Use	62.7% (1133)
Tranquilizer Use	38.8% (716)

McCabe et al. *J Addict Dis*. 2018.

Prescription Medication Misuse in Young People

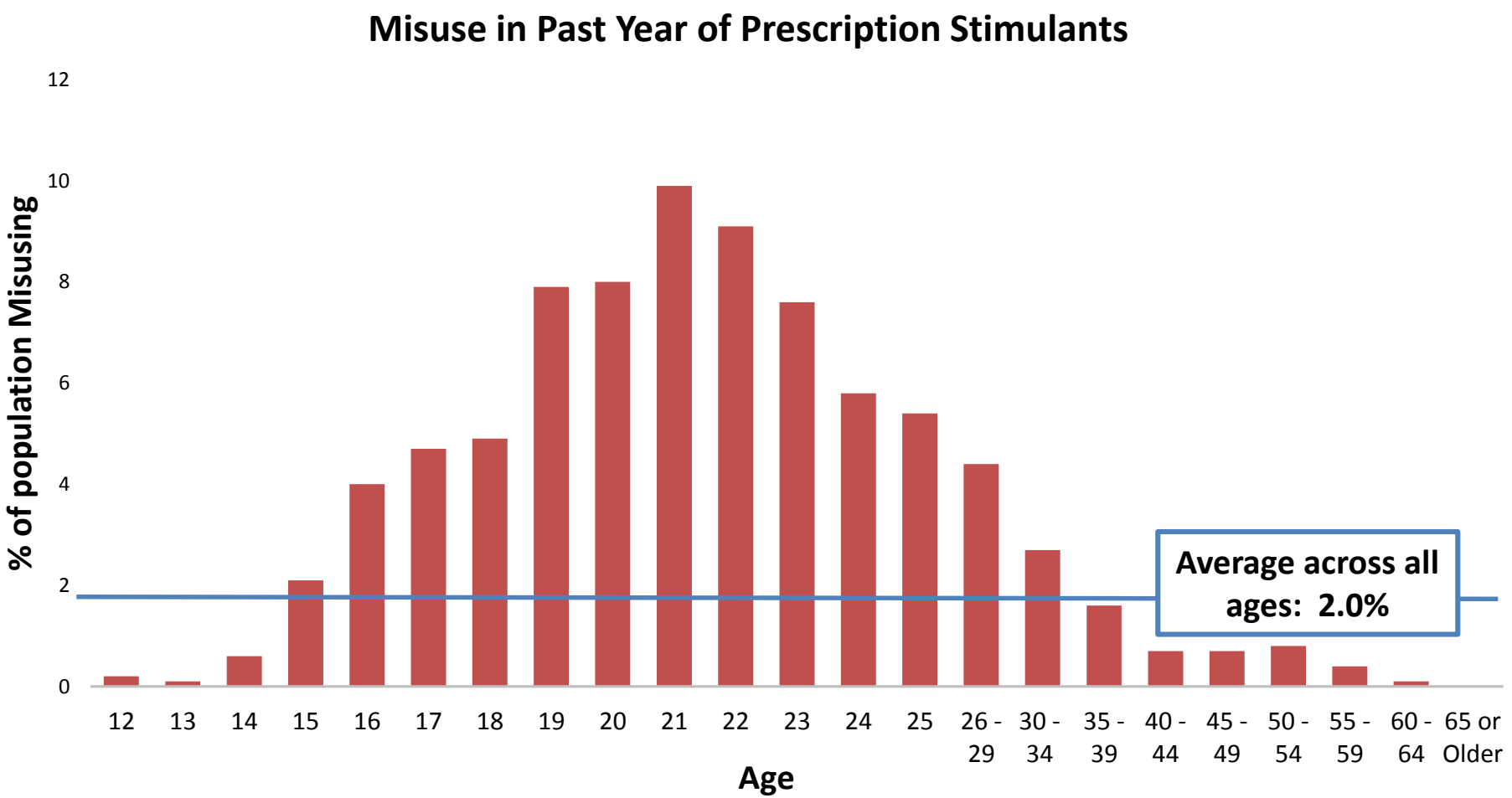
(Schepis et al. JAACAP 201958:670-680**)**

- Data from 2009-2014 National Survey on Drug Use and Health
- 103,920 adolescents aged 12– 17 years

Most common sources	Percentage
Obtaining prescription medications from friends/relatives for free	29.0% - 33.2%
Physician sources for opioids	23.5%
Purchase of stimulants	23.5%
Purchase of sedatives/tranquilizers	22.7%

- Obtaining prescription drugs from multiple sources was associated with SUD risk behaviors

Stimulant Misuse Peaks at Age 21, 10% Report Lifetime Misuse of Stimulants



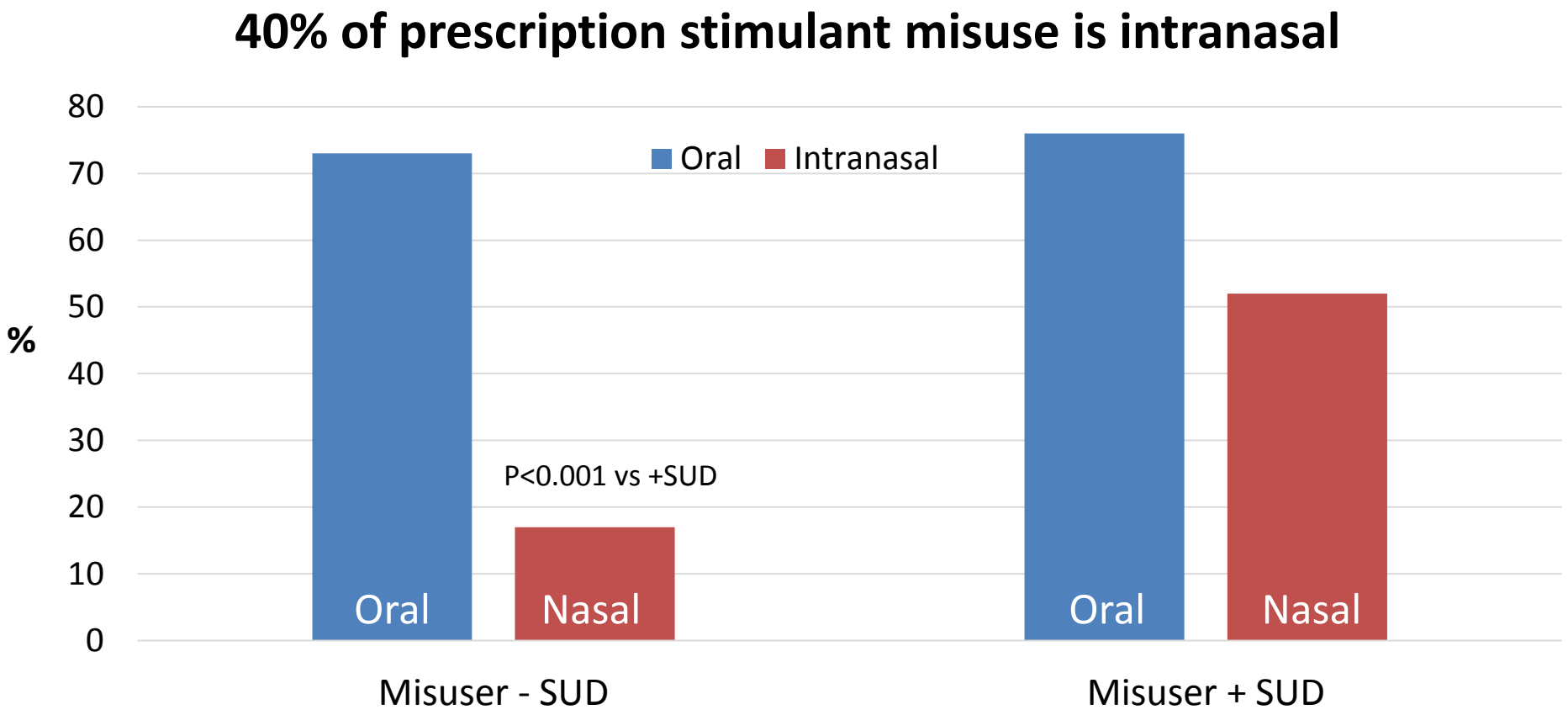
Hughes A, et al. (2016, September). Prescription drug use and misuse in the United States: Results from the 2015 National Survey on Drug Use and Health. NSDUH Data Review. www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm. Accessed June 28, 2019.

Reasons for Misusing Prescription Stimulants (N=100)

To help concentrate or focus better	79%
To stay awake	62%
To reduce distraction	56%
To get more energy	48%
To experiment – to see what it's like	42%
To have a good time with my friends	22%
To feel good or get high	21%
To get through the day	12%

(Wilens et al. Am J Addictions 2020)

Higher Rates of Intranasal Misuse of Stimulants in College Students with SUD (N=100)



(Wilens et al. Am J Addictions 2020)

Prevalence and Consequences of the Nonmedical Use of Amphetamine Among Persons Calling Poison Control Centers

Objective: To describe consequences of the nonmedical use (NMU) of prescription amphetamines (AMPs). **Method:** Data from the U.S. National Poison Data System yielded four groups: intravenous NMU (*IV NMU*) intentionally injected AMP, *Nasal NMU* intentionally inhaled AMP but did not inject, *Oral NMU* intentionally ingested AMP, and *controls* reported unintentional oral exposure to AMP. **Results:** The Nasal NMU group was at greater risk of admission to a health care facility. All NMU groups were at greater risk for adverse clinical effects. IV NMU had the greatest number of adverse effects, followed by Nasal and Oral NMU. Nasal NMU had a greater risk for major medical outcomes versus Oral NMU. The IV NMU group was 21.9 times more likely to die from AMP NMU than controls. Oral NMU conferred a significantly greater risk of suicide attempts. **Conclusion:** Oral and nonoral NMU of AMP are associated with significant risks of morbidity and mortality

Faraone, Hess, Wilens. J Attention Disorder, 2019: 23 (11)

Conclusions Prescription Medication Misuse

1. **Educate and engage** adolescents and adults
    1. Risks and benefits of pain management with and without prescription opioids, use of tranquilizers and stimulants
    2. Proper storage, monitoring/oversight, and disposal.
2. Patients should receive **the minimum quantity at the lowest effective dose of opioid medication**
3. Comprehensive medical and psychiatric evaluation (including substance screening) **for anyone who misuses** prescription medications