

# Prescription Opioid Abuse and Related Outcomes in the Pediatric Population

Joint Meeting of the Drug Safety and Risk Management Advisory Committee  
and the Pediatric Advisory Committee

Christina R. Greene, Ph.D.  
Division of Epidemiology II  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research  
U.S. Food and Drug Administration

# Background and Objectives

- **Background:** For all regulatory questions involving opioids, FDA considers the public health risks associated with misuse and abuse of these drugs
- **Objective:** Review available epidemiologic data to inform considerations of these risks relating to pediatric opioid use

# Outline

1. Defining Misuse and Abuse
2. Descriptive Epidemiology of Pediatric Opioid Misuse/Abuse
3. Literature on Risk of Misuse/Abuse and Substance Use Disorders Following Pediatric Prescription Opioid Therapy
4. Limitations
5. Overall Summary

# Defining Misuse and Abuse

- **Misuse:** Intentional use, for therapeutic purposes, of a drug in a way other than prescribed or by an individual for whom it was not prescribed
- **Abuse:** Intentional, non-therapeutic use of a drug for its desirable psychological or physiological effects

Terminology varies by data source

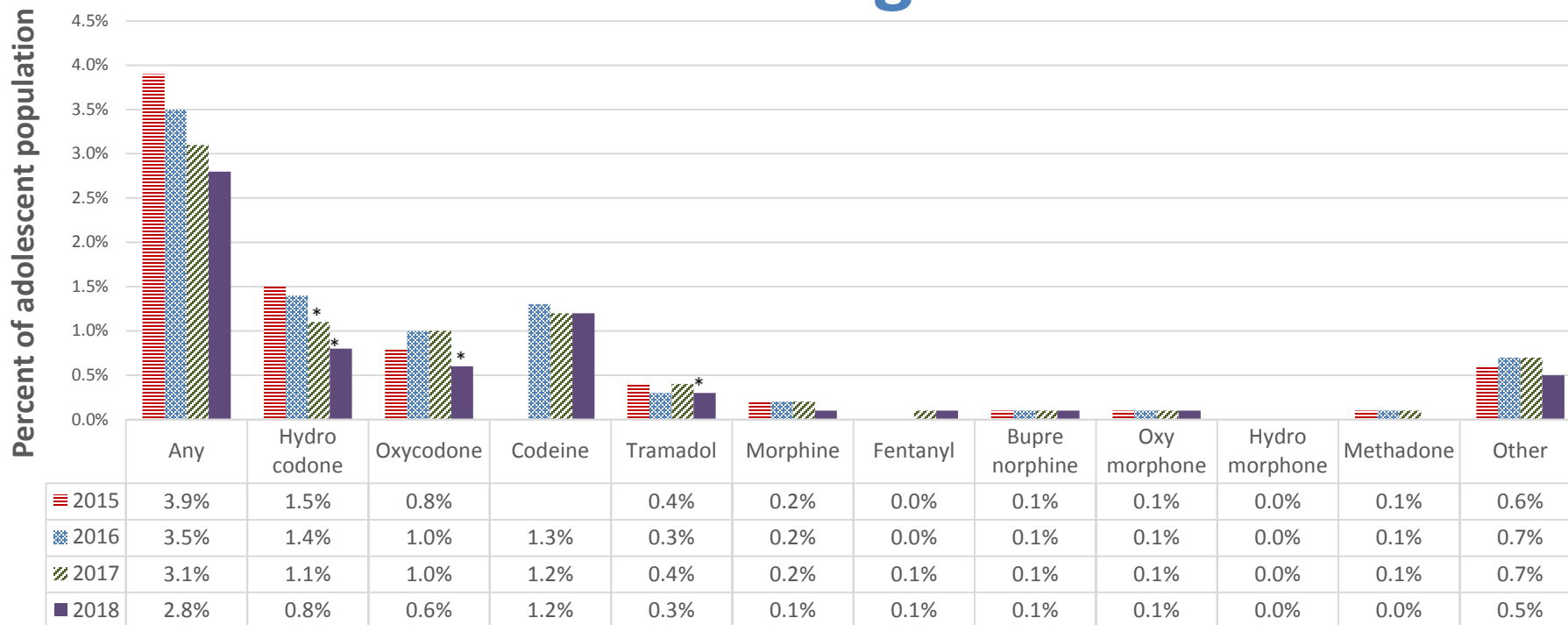
Source: FDA, Drug Abuse and Dependence Section of Labeling for Human Prescription Drug and Biological Products: Guidance for Industry (2019)

# **Descriptive Epidemiology of Pediatric Opioid Misuse/Abuse**

# Data Sources

- **Prevalence of misuse/abuse**
  - National Survey on Drug Use and Health (NSDUH): 2015-2017
  - Monitoring the Future (MTF): 2010-2018
- **Emergency Department visits**
  - National Electronic Injury Surveillance System - Cooperative Adverse Drug Event Surveillance (NEISS-CADES): 2016-2017
- **Calls to U.S. Poison Control Centers**
  - National Poison Data System (NPDS): 2000-2015
- **Drug Overdose Deaths**
  - National Vital Statistics System mortality files: 2016-2017

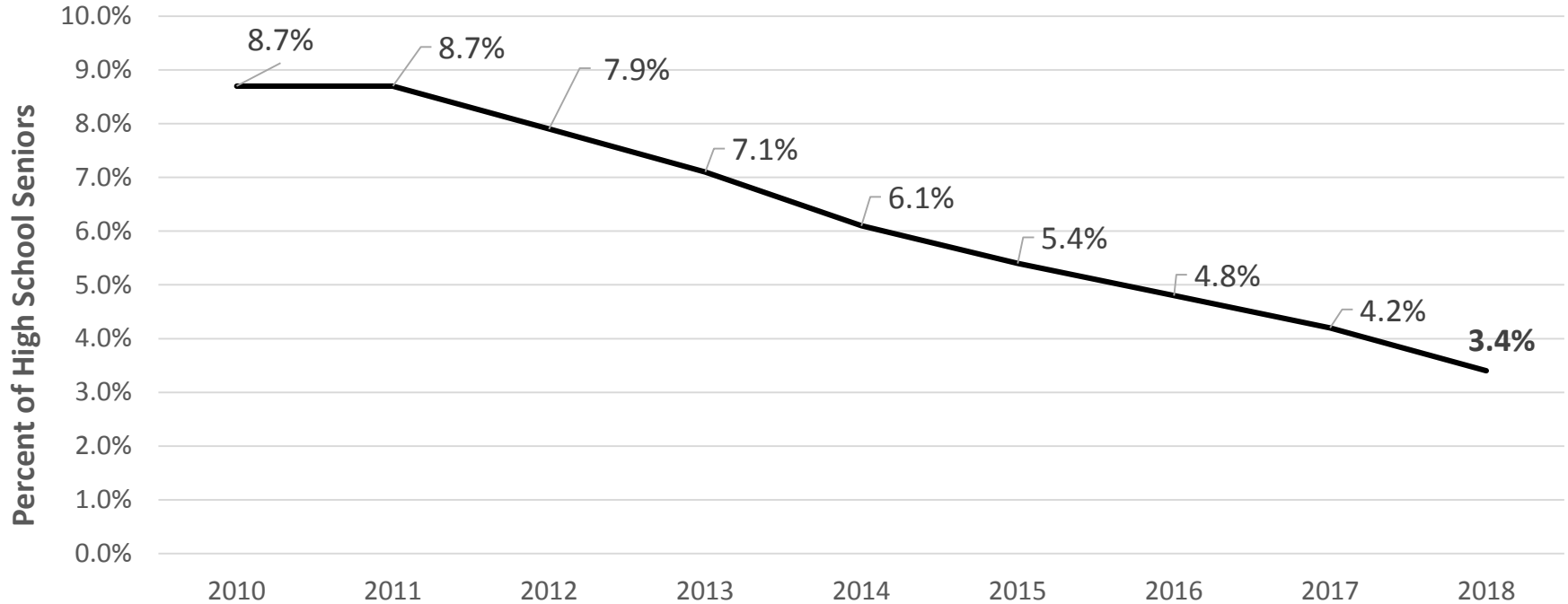
# Past-year Misuse/Abuse: U.S. Adolescents Ages 12 to 17



\*Statistically significant decline from previous year

Source: NSDUH, SAMHSA detailed tables, Tables 1.98 A-B, 1.98D (2016-2017), Tables 1.99A-B, 1.99D (2018).

# Past-year Misuse/Abuse of Prescription Opioids\*: High School Seniors



Source: The Monitoring the Future Study 2018, the University of Michigan, Table 2.

\*Term is "Narcotics other than heroin" in this survey





# Source of Prescription Opioids for Misuse/Abuse in Adolescents Ages 12 to 17

| Source  | Percent of those reporting past-year misuse/abuse |
|---|---|
| Received from friends or relatives (taken/given/bought) | 49.5%   |
| Personal prescription                                   | 34.1%   |
| Other (drug dealer, stranger, stolen)                   | 12.9%   |

Source: NSDUH 2018, SAMHSA detailed tables, Tables 6.5A-B.

# Source of Prescription Opioids for Misuse/Abuse: High School Seniors



| Source                                   | Percent of those reporting past-year misuse/abuse |
|--|---|
| Given for free by friend/relative        | 48.2%   |
| Bought from friend/relative              | 26.1%   |
| Took from friend/relative without asking | 13.7%   |
| Personal prescription                    | 31.9%   |
| Bought from drug dealer/stranger         | 17.4%   |
| Other method                             | 14.5%   |

Source: The Monitoring the Future Study 2018, the University of Michigan, Table 9-10.

NOTE: Categories are not mutually exclusive.

# U.S. ED Visits for Adverse Events from Prescription Opioid Use, 2016-2017



|  | Average annual estimate | Annual rate per 100,000* | 95% CI of rate |
|--|-------------------------|--------------------------|----------------|
| Prescription opioid <b><u>nonmedical use</u></b> <sup>+</sup> (annual estimate = 127,177 visits) |                         |                          |                |
| <b>Ages 12-17</b>  | 2,130                   | 8.5                      | 4.4-12.6       |
| <b>Ages 18 and older</b>   | 124,980                 | 49.9                     | 36.2-63.6      |
| Prescription opioid <b><u>self-harm</u></b> (annual estimate = 36,057 visits)                    |                         |                          |                |
| <b>Ages 12-17</b>  | 2,617                   | 10.5                     | 6.0-14.9       |
| <b>Ages 18 and older</b>   | 33,374                  | 13.3                     | 10.5-16.1      |

<sup>+</sup> Includes Abuse, Therapeutic Misuse, and Overdose of Undetermined Intent

\*Based on average Census population estimates

NOTE: Visits among patients ages 11 and younger not shown due to small number of cases. Age missing for 3 cases of nonmedical use and 1 case of self-harm.

Source: NEISS-CADES Project, CDC Division of Healthcare Quality Promotion

# U.S. ED Visits for Adverse Events from Therapeutic Prescription Opioid Use, 2016-2017



| Age group  | Average annual estimate | Annual rate per 100,000* | 95% CI of rate |
|--|-------------------------|--------------------------|----------------|
| Therapeutic prescription opioid use‡ (Total annual estimate = 103,786 ED visits) |                         |                          |                |
| <b>Ages 0-11</b> ¥   | 4,600                   | 9.5                      | 6.3-12.6       |
| <b>Ages 12-17</b>  | 1,522                   | 6.1                      | 4.0-8.2        |
| <b>Ages 18 and older</b>   | 97,664                  | 39.0                     | 28.0-50.0      |

Source: NEISS-CADES Project, CDC Division of Healthcare Quality Promotion

\*Based on average Census population estimates

‡Includes adverse events from therapeutic use (e.g., adverse effects, allergic reactions, medication errors, and unsupervised ingestions by children)

¥82.5% of these ED visits were due to unsupervised ingestions

# U.S. Poison Control Calls, 2000-2015: Prescription Opioid Exposures, by Reason and Age



|                          | <b>Ages 0-5 years</b><br>N=112,465 (%) | <b>Ages 6-12 years</b><br>N=19,723 (%) | <b>Ages 13-19 years</b><br>N=56,280 (%) |
|--------------------------|--|--|---|
| Unintentional            | 111,258 (98.9)                         | 16,654 (84.4)                          | 12,051 (21.4)                           |
| General                  | 96,134 (85.5)                          | 5,905 (29.9)                           | 3,759 (6.7)                             |
| Therapeutic error        | 15,124 (13.4)                          | 10,749 (54.5)                          | 8,292 (14.7)                            |
| Intentional - overall    | 201 (0.1)                              | 1,988 (10.1)                           | 40,255 (71.5)                           |
| <b>Suspected suicide</b> | 46 (0.0)                               | <b>360 (1.8)</b>                       | <b>19,239 (34.2)</b>                    |
| <b>Abuse</b>             | 40 (0.0)                               | <b>447 (2.3)</b>                       | <b>11,721 (20.8)</b>                    |
| <b>Misuse</b>            | 86 (0.1)                               | <b>670 (3.4)</b>                       | <b>6,297 (11.2)</b>                     |

Source: Table 1, Allen (2017)

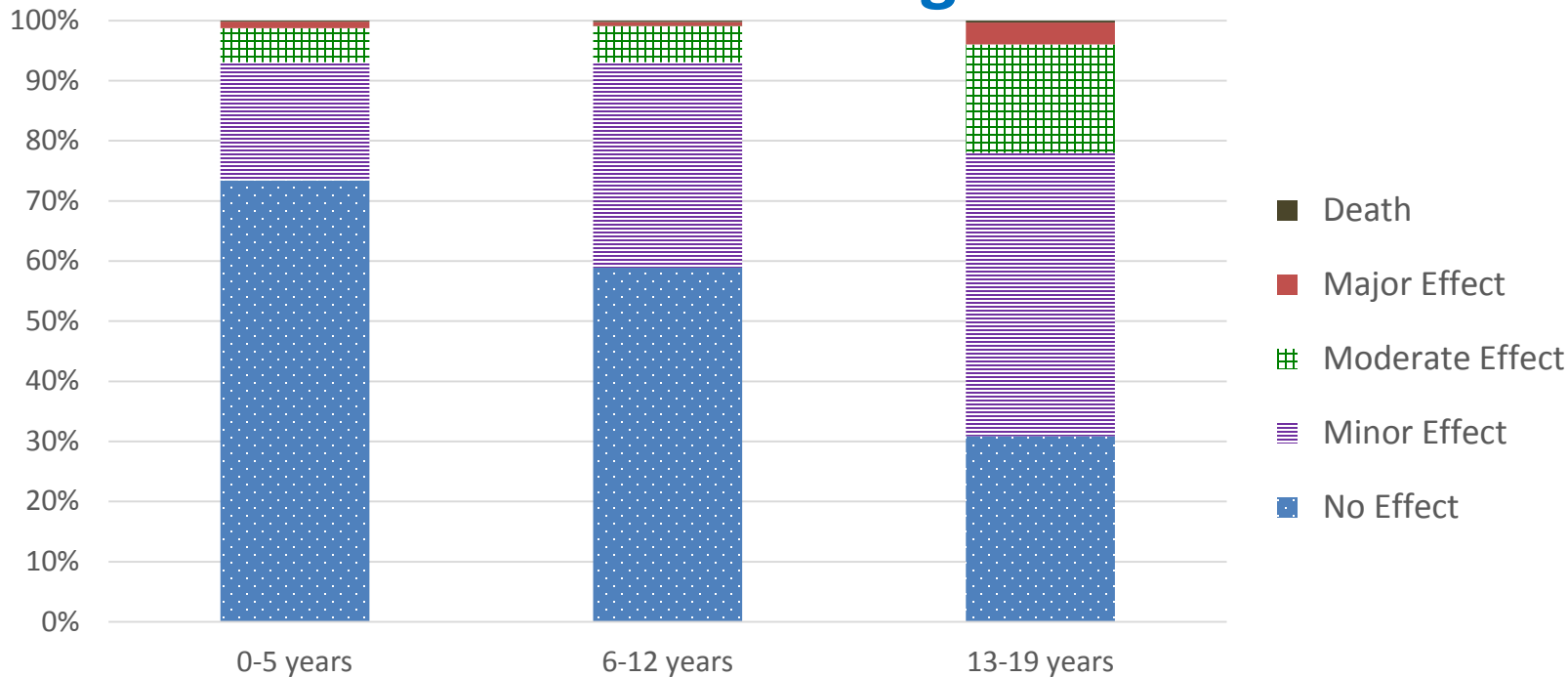
# U.S. Poison Control Calls, 2000-2015: Prescription Opioid Exposure Rates



- The rate\* of these exposures increased from 2000 to 2009, then declined from 2009 to 2015 for both children and adolescents
- This trend was not consistent across all reasons for prescription opioid exposure
  - Rate of **suspected suicide** among teenagers increased by **52.7%** from 2000 to 2015

\*Number of prescription opioid PCC calls per 100,000 population by age group  
Reference: Allen (2017)

# U.S. Poison Control Calls 2000-2015: Prescription Opioid Exposures, by Medical Outcome and Age



Source: Table 2, Allen (2017)

# Rate of Drug Overdose Death Involving Prescription Opioids, by Age, U.S.



| Decedent Age | 2017   |            | 2016-2017        |
|--------------|--------|------------|------------------|
|              | Number | Rate       | % Change in rate |
| 0-14         | 50     | <b>0.1</b> | 0.0              |
| 15-24        | 1,050  | <b>2.4</b> | -7.7             |
| 25-34        | 3,408  | 7.5        | -2.6             |
| 35-44        | 3,714  | 9.1        | -1.1             |
| 45-54        | 4,238  | 10.0       | -1.0             |
| 55-64        | 3,509  | 8.4        | 0.0              |
| ≥65          | 1,055  | 2.1        | +10.5            |

Rates are per 100,000 population

Source: Table 1, Scholl (2019)



# Literature Review

# Literature: Medical Use of Prescription Opioids and Risk of Opioid Analgesic Misuse or Abuse



- Compared to adolescents who did not use any opioids, adolescents who used prescription opioids only as medically directed were more likely to misuse or abuse opioids in the future
  - In early adulthood (Adjusted RR = 1.33, CI: 1.04-1.70)<sup>1</sup>
  - In early mid-life (Adjusted OR = 1.74, CI: 1.10-2.76)<sup>2</sup>
- For high school seniors with a history of both medical use and misuse of opioids, medical use most often preceded initiation of misuse<sup>3</sup>

# Medical Use or Misuse/Abuse of Prescription Opioids and Future Substance Use Disorder Symptoms



| Lifetime use of prescription opioids at age 18 | Any substance use disorder symptoms at age 35 (AOR*) |
|--|--|
| No use   | 1.00 [Reference]                                     |
| Medical use only                               | 1.12 [0.895-1.39]                                    |
| Medical use before misuse/abuse                | 1.18 [0.82-1.72]                                     |
| Medical use after misuse/abuse                 | 2.35 [1.46-3.77]                                     |
| Misuse/abuse only                              | 2.47 [1.74-3.52]                                     |

\*Adjusted for race/ethnicity, sex, parental education, region, metropolitan area, cohort year, past alcohol, marijuana, or other drug use at age 18

Source: McCabe (2019)

# Dentist Prescriptions for Opioids and Risk of Opioid Analgesic Misuse or Abuse



- Examined opioid abuse-related administrative claims\* in 12 months following dental opioid prescription in adolescents and young adults (16-25 years old)
- Patients who received an opioid prescription more likely to have a subsequent abuse-related claim\* compared to non-exposed (5.8% vs. 0.4%)
  - Adjusted\*\* risk difference: 5.3% [CI: 5.0-5.7]

\*Defined as an ICD-9/10 healthcare claim diagnosis code for opioid abuse, opioid use disorder, or opioid overdose

\*\*Adjusted for patient race/ethnicity and history of past other substance use

Source: Schroeder (2019)

# Key Limitations (1)

- Survey-based studies
  - Possible inaccurate reporting/recall
  - Individuals with more advanced SUD may be underrepresented
  - Longitudinal studies: Confounding by indication
- ED visit data
  - Only captures misuse/abuse cases resulting in an ED visit
  - Excludes fatal cases
- Poison center call data
  - Analysis limited to single-substance exposures

## Key Limitations (2)

- Administrative claims studies
  - Do not capture actual opioid use or exposure resulting from someone else's prescription
  - Poor capture of misuse/abuse and substance use disorders
  - Death outcomes incompletely captured
  - Potential unmeasured confounding
    - Undocumented family/personal history of substance abuse

# Summary of Findings (1)

- Approximately 3% of adolescents report having misused or abused prescription opioids in the past year
  - Adolescent prescription opioid misuse and abuse have been declining
  - Most commonly, adolescents obtain prescription opioids for misuse/abuse from a friend or relative, but about a third receive them from their own prescription

# Summary of Findings (2)



- Among adolescents, opioid-related ED visits due to self-harm occur at similar rates as nonmedical use
- Most opioid-related poison center exposure calls involve unintentional exposures in children ages  $\leq 5$  years
  - Calls in adolescents are more likely to be due to misuse/abuse or suicide attempts and to result in more severe medical outcomes
  - Calls involving adolescent suicide attempts involving prescription opioids have been increasing



# Summary of Findings (3)



- Medical use of opioid analgesics may place adolescents at increased risk of future misuse/abuse
- Prescription opioid misuse/abuse in adolescence is associated with substance use disorders (SUDs) in adulthood
  - But, medical opioid use alone (with no misuse/abuse) is not a risk factor for later SUD
- Further research is needed to understand the relationships between medical use and future misuse, abuse, SUD, and related outcomes.



**U.S. FOOD & DRUG**  
ADMINISTRATION