Prescription Drug Abuse: It’s **Not** What the Doctor Ordered

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Key Points:

1. Opioid prescription drug abuse is a major problem in USA
2. Heroin addiction in the USA is related to the prescription opioid excesses
3. Behavioral and pharmacokinetic factors differentiate pharmaceutical use from abuse, but addiction issues transcend the differences between pharmaceuticals and related illicit substances
4. Interventions can be effective—both primary prevention and targeting overdose or addiction
High Rates of **Analgesic Misuse**, 2002-2013, USA: Past Month Psychotherapeutic Drug Use, Ages 12+

Difference between this estimate and the 2013 estimate statistically significant at the .05 level.

*Source: SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014*
**Increasing Drug Dependence or Abuse on Analgesics in the Past Year, Ages 12+, 2002-2013, USA**

* Difference from the 2012 estimate is statistically significant at the .05 level.

**Source:** SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014
Analgesics Often First I illicit Drug Initiated:
Past Year Initiator, Ages 12+, 2013, USA

2.8 Million Initiates of Illicit Drugs

Note: The percentages do not add to 100 percent due to rounding or because small number of respondents initiated multiple drugs on the same day. The first specific drug refers to the one that was used on the occasion of first-time use of any illicit drug.

Source: SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014
Near Tripling of Opioid Prescriptions Dispensed by U.S. Retail Pharmacies, Years 1991-2013, USA

IMS Health, National Prescription Audit, Years 2012-2013, Data Extracted 2014
Doubled Treatment for Analgesic Use, 2002 – 2013, USA: Most Recent Treatment in the Past Year for the Use of Pain Relievers among USA Persons Aged 12 or Older

* Difference from the 2013 estimate is statistically significant at the .05 level.

Source: SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014
Marked Increases in Opioid-related Deaths (parallel to opioid sales and Rx opioid treatment admits), USA

2012 OD Deaths:
• 41,502 Any Drug
• 22,114 Rx Drug
• 16,007 Rx opioid
• 5,927 Heroin

Sources: National Vital Statistics System, DEA Automation of Reports and Consolidated Orders System, SAMHSA TEDS
The Dynamic relationship between rates of opioid prescriptions and rates of opioid-related overdose deaths in the USA – 2002, 2006, 2009

Source: IMS Vector One National, CDC Wonder, & the US Census
USA Drug Overdose Deaths By Major Drug Type

Overlap of *Benzodiazepines and Opioids* in USA

Opioid Analgesic ED Visits and OD Deaths Involving Benzodiazepines & Benzodiazepine ED Visits and OD Deaths Involving Opioids


*NOTE*: In Preparation for Publication and **NOT TO BE USED WITHOUT PERMISSION** of the Authors.
Trends in Opioid Analgesic and Benzodiazepine Drug Overdose Deaths, United States, 2004-2011

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Trends in Opioid Analgesic and Benzodiazepine ED Visits, United States, 2004 - 2011


NOTE: In Preparation for Publication and NOT TO BE USED WITHOUT PERMISSION of the Authors.
Increasing Past Year Heroin Use Among Persons Aged 12+, 2002-2013, USA

Difference between this estimate and the 2013 estimate is statistically significant at the .05 level. Note: Estimated numbers for the age groups may not sum to the total due to rounding.

Growing evidence suggests a shift to heroin: Recent increase in heroin use accompanied a downward trend in OxyContin abuse following introduction of abuse-deterrent formulation.
Increasing Heroin Deaths in North Carolina

Source: Dasgupta, et al., Drug and Alcohol Dependence, 2014;145:238-241
Which Drug is the First Opioid Used in Addicts?
Shifting Pattern of Heroin vs. Rx Opioid First

Percentage of Heroin-Addicted Treatment Admissions that Used Heroin or Prescription Opioid as First Opioid

1960s: more than 80% started with heroin.

2000s: 75% started with prescription opioids.

2010-2013: Increasing initiation with heroin

Source: Cicero et al. JAMA Psychiatry. 2014;71(7):821-826
Data in Several States Show That *Hepatitis C Virus* Among Adolescents and Young Adults Has Increased in Recent Years

Of cases with available risk data, *injection drug use (IDU)* was the most common risk factor for HCV transmission. Although only a small number of these cases responded to further investigation…..

- 92% reported opioid analgesic abuse
- 89% reported heroin use
- 95% used opioid analgesics before switching to heroin
- During the preceding 6 months, the most frequently injected drugs were heroin (50%) and opioid analgesics (30%)

*CDC, MMWR, May 6, 2011/60(17); 537-541*;  *CDC, MMWR, October 28, 2011/60(42):1457-1458*
Why Do People Abuse Prescription Drugs?

Opioid prescription drugs, like other drugs of abuse (cocaine, heroin, marijuana) raise brain dopamine levels.

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**Dopamine Neurotransmission**

- Prefrontal cortex
- Nucleus accumbens
- VTA

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**MORPHINE**

- Dose (mg/kg): 0.5, 1.0, 2.5, 10
- Graph showing % of Basal Release over Time After Morphine (5hr)

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**FOOD**

- Graph showing % of Basal Release over Time (min) with Empty Box and Feeding periods

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*Di Chiara et al.*
The fine balance in connections that normally exists between brain areas active in reward, motivation, learning and memory, and inhibitory control becomes severely disrupted in addiction.
What is the Difference Between \textit{Therapeutic Use} and \textit{Abuse}?

- **Dose and Frequency of Dosing**
  \textit{Lower, fixed regimes vs higher, escalating use}

- **Route of Administration**
  \textit{Oral vs injection, smoking, snorting}

- **Expectation of Drug Effects**
  \textit{Expectation of clinical benefits vs euphoria “high”}

- **Context of Administration**
  \textit{School, clinic, home vs bar, party}
Rate of Drug Uptake Into the Brain

**iv cocaine**

**iv methylphenidate**

**oral methylphenidate**

*Slower uptake of oral Ritalin permits effective treatment with less intrinsic reward (perceived “high”)*
Rewarding Effects Depend on How Fast the Drug Gets into the Brain

$[^{11}\text{C}]\text{Cocaine}$

$[^{11}\text{C}]\text{Methylphenidate}$

"High"
Glucose Metabolism Was Greatly Increased By the *Expectation* of the Drug

Increases in Metabolism Were About 50% Larger When MP Was Expected Than Unexpected

People Abusing Analgesics **DIRECTLY & INDIRECTLY Obtain Them by Prescription**: Most Recent Pill Source

Source Where Respondent Age 12+ Obtained Analgesics:

- More than One Doctor (2.6%)
- One Doctor (21.2%)
- Other\(^1\) (4.3%)
- Bought on Internet (0.1%)
- Drug Dealer/Stranger (4.3%)
- Bought/Took from Friend/Relative (14.6%)
- Free from Friend/Relative (53.0%)

Source Where Friend/Relative Obtained

- More than One Doctor (3.3%)
- One Doctor (83.8%)
- Free from Friend/Relative (5.1%)
- Bought/Took from Friend/Relative (4.9%)
- Drug Dealer/Stranger (1.4%)
- Bought on Internet (0.3%)
- Other\(^1\) (1.2%)

\(^1\)Other category includes Wrote Fake Prescription, "Stole from Doctor’s Office/Clinic/Hospital/Pharmacy," and "Some Other Way."

**Source**: SAMHSA, 2012 and 2013 National Survey on Drug Use and Health
Source of Prescription Narcotics among Those who Used in the Past Year, 12th Grade*

*Categories not mutually exclusive

SOURCE: University of Michigan, 2014 Monitoring the Future Study
Prescription Drug Abuse:

What can be done?
Universal Drug Abuse Prevention Reduces Prescription Drug Misuse

In this study, for 100 young adults in general population starting Rx abuse, only 35 young adults from an intervention community started.

**Overall, three studies now suggest the impact of universal prevention on prescription drug abuse.**

Notes: General=Misuse of narcotics or CNS depressants or stimulants.

**p<.01; ***p<.001; Relative Reduction Rates (RRRs)= 65-93%**
**Prevention: Need for New Medications**

- Develop medications with **lower abuse potential** including drugs that don’t cross the **Blood-Brain-Barrier** *(i.e., CbR2 agonist)*

- Develop **slow release formulations** (low dose and long duration)

- Develop novel formulations to **reduce abuse liability** including mixture formulations *(e.g., naloxone and buprenorphine)*
Doctors (and other clinicians) Need to Know…
What Prescriptions Have Been Given to Their Patients By Other Practitioners

This information should be:

1) included in the patients’ electronic health care records

2) accessible through a Prescription Drug Monitoring Program (PDMP) that provides immediate information
Overdose Intervention

• **Naloxone Distribution** for opioid overdose victims. The *potential* for direct intervention to save lives.
  - Note the April 3, 2014 FDA approval of the naloxone auto-injector (called “Evzio”)

• **Naloxone Nasal Spray Development**

  Needle-free, unit-dose, ready-to-use opioid overdose antidote.
  - NIDA STTR Grantee – AntiOp, Inc., Daniel Wermeling, CEO
  - NIDA clinical study with Lightlake Therapeutics, Inc.
Medical Treatment May Reduce Deaths

### Additional Challenge…

**Lack of uptake of medication-assisted treatment**

<table>
<thead>
<tr>
<th>Addiction Specialty Programs Offering Services</th>
<th>As % of all programs surveyed (N=345)</th>
<th>Within adopting programs, % of eligible patients receiving Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid Tx Med:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>7.8</td>
<td>41.3</td>
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<tr>
<td>Buprenorphine</td>
<td>20.9</td>
<td>37.3</td>
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<tr>
<td>Tablet naltrexone</td>
<td>22.0</td>
<td>10.9</td>
</tr>
</tbody>
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**TOO FEW ARE TREATED**
Prescription Drug Abuse: What can be done?

- Primary Prevention
- Less abusable analgesics
- Overdose Intervention
- Better Access to Effective Addiction Treatments (especially medications for opioid addiction)
- Public and Clinician Education
Reduced Numbers of Analgesic Misuse Initiators: Past Year Drug Initiates, Ages 12+, 2002-2013

Difference between this estimate and the 2012 estimate is statistically significant at the .05 level.

Source: SAMHSA, 2013 National Survey on Drug Use and Health, released September 2014
Fewer High School Seniors Reporting Use of Narcotics Other than Heroin, in USA

Denotes significant difference between 2013 and 2014.

SOURCE: University of Michigan, 2012 Monitoring the Future Study
Fewer Students Reporting Nonmedical Use of OxyContin in Past Year, in USA

SOURCE: University of Michigan, 2014 Monitoring the Future Study

Denotes significant difference between 2013 and 2014
Fewer Students Reporting Nonmedical Use of Vicodin in Past Year, in USA

SOURCE: University of Michigan, 2014 Monitoring the Future Study
Few Students Reporting Use of Heroin in Past Year, in USA

SOURCE: University of Michigan, 2014 Monitoring the Future Study
Recent Slight Reductions in Opioid-related Deaths in USA

2012 OD Deaths:

- **41,502 Any Drug**
  - (41,340 in 2011)
- **22,114 Rx Drug**
  - (22,810 in 2011)
- **16,007 Rx opioid**
  - (16,917 in 2011)
- **5,927 Heroin**
  - (4,397 in 2011)

Sources: National Vital Statistics System, CDC
Prescription Drug Abuse: *A Need for New Thinking*

- Opioid prescription drug abuse is a major problem in USA
  - *Direct* and *indirect* pathways from MDs (especially via friends/family) suggest the importance of changes in prescribing patterns
    - ✔ Policy and regulatory approaches
    - ✔ Clinical education
    - ✔ Practice-based research

- Heroin addiction in the USA is related to the opioid abuse issues
  - Need for greater availability of treatment
Behavioral and pharmacokinetic factors differentiate medical use from abuse

- Addiction issues transcend the differences between pharmaceuticals and related illicit substances

Interventions can be effective

- Primarily prevention
- Education (clinician) addressing relaxed attitudes and misperceptions about prescription drugs
- Overdose interventions (naloxone)
- Medication assisted treatment for addiction
- Need for research and practice developments
Summary: **The Urgent Problem of Prescription Drug Abuse**

When used properly, opioids have so many clear benefits. Balancing therapeutic benefits versus risks is necessary and complicated. Coordinated national and local responses are necessary.
Now NIDA resources are with you wherever you go!

We’re connecting communities with a new mobile Web site that gives you drug-related information by topic, audience, and format—when you need it, where you need it.

The new mobile site (m.drugabuse.gov) provides:

- Easy access to NIDA's resources through iPhone, Android, iPad, and other smartphones and tablets.
- A convenient way to find, view, request, and share publications—right in the palm of your hand.
- E-books of all publications to allow offline reading on all major e-readers, including Kindle and NOOK.
- New Spanish-language content on drugs of abuse and related topics.