

# CESAR *FAX* →

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

---

## *CESAR FAX: Buprenorphine*

**Updated 1/25/12**

CESAR  
Center for Substance Abuse Research  
University of Maryland  
4321 Hartwick Road, Suite 501  
College Park, MD 20740  
301-405-9770 (phone)  
301-403-8342 (fax)  
cesar@umd.edu  
www.cesar.umd.edu

CESAR is pleased to provide this compilation of *CESAR FAX* issues focusing on buprenorphine. While research indicates that buprenorphine is an effective drug for treating opioid dependence, we feel that the potential for its nonmedical use and related unintended consequences may be going unnoticed. The most recent publications on buprenorphine were designed to highlight several indicators of the increased availability, diversion, and misuse of buprenorphine. CESAR will continue to monitor the diversion and abuse of buprenorphine and report on developments as they arise.

**CESAR FAX Issues on Buprenorphine**  
(updated 1/25/12)

**Table of Contents by Year and Issue Number**

**VOLUME 12 (2003)**

<u>TITLE</u>	<u>ISSUE NUMBER</u>
Buprenorphine Now Available for Treating Heroin Dependence in U.S. ....	13
Despite Some Obstacles, Physicians Still Optimistic About Prescribing Buprenorphine to Opiate-Addicted Patients .....	46

**VOLUME 20 (2011)**

<u>TITLE</u>	<u>ISSUE NUMBER</u>
Buprenorphine Treatment for Opioid Dependence.....	22
U.S. Retail Distribution of Buprenorphine Approaches 1.5 Million Grams.....	23
Number of Law Enforcement-Seized Buprenorphine Items Analyzed by U.S. Labs Increases Dramatically .....	24
Number of U.S. Emergency Department Visits Related to the Nonmedical Use of Buprenorphine More Than Triples Since 2006.....	25
61% of Buprenorphine-Related Emergency Department Visits for Nonmedical Use.....	26
Nearly All Emergency Department Visits for the Accidental Ingestion of Buprenorphine Occur in Children Under the Age of Six .....	27
Fentanyl and Buprenorphine Have Higher Rates of Nonmedical Use ED Visits per Dosage Units Distributed to Dispensing or Retail Institutions Than Other Opioids.....	28
Continuing Medical Education Improves Buprenorphine-Waivered Physicians' Knowledge and Practice Behaviors .....	29
Small Rhode Island Study Finds IDUs More Likely to Use Diverted Buprenorphine/ Naloxone to Self-Medicare; Non-IDUs More Likely to Use to Get High.....	30
Multisite Demonstration Project Finds Buprenorphine/Naloxone Effective in Treating Opioid Dependence in HIV-Infected Patients .....	31

Buprenorphine/Naloxone Treatment for Opioid Dependence in HIV-Infected Persons  
Improves Quality of HIV Care Received .....32

2011 Media Reports of Buprenorphine Diversion and Misuse.....33

Buprenorphine Availability, Diversion, and Misuse: A Summary of the *CESAR FAX* Series...34

Clinical Trial Finds That While Buprenorphine-Naloxone Maintenance Reduced Other  
Opioid Use Among Those Dependent on Prescription Opioids, 91% Were Not  
Opioid-Free at Follow-Up .....46

**VOLUME 21 (2012)**

Drug Users, Treatment Providers, and Law Enforcement Officers Describe Increasing  
Suboxone Misuse in Ohio .....2

## A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

### *Buprenorphine Now Available for Treating Heroin Dependence in U.S.*

**What is buprenorphine?** Buprenorphine is an opiate used for the treatment of opiate dependence. It is the active ingredient in the prescription medications Subutex® and Suboxone®. Subutex®, which contains only buprenorphine, is intended for use at the beginning of treatment. Suboxone® contains both buprenorphine and naloxone (to decrease the potential for abuse by injection) and is used in the maintenance treatment of opiate addiction.

**How is buprenorphine used?** Both Subutex® and Suboxone® are tablets that are placed under the tongue and dissolved. Buprenorphine abusers either inject the drug intravenously or chew or swallow the tablets.

**What are the effects of buprenorphine use?** The most common reported side effects of the drug include cold or flu-like symptoms, headaches, sweating, sleeping difficulties, nausea, and mood swings. Buprenorphine has been associated with breathing difficulty, especially when combined with depressants. Misuse of the drug by using it with other drugs (e.g., benzodiazepines, depressants), by injecting it, or by taking large oral doses can be lethal.

**How effective is buprenorphine in treating opiate dependence?** Studies have shown that buprenorphine is more effective than a placebo and is equally as effective as moderate doses of methadone and LAAM in opioid maintenance therapy. A Swedish study published earlier this year reports that 75% of opiate-dependent patients receiving buprenorphine treatment were still in treatment after one year, compared to 0% of those receiving a placebo.

**What is the abuse potential of buprenorphine?** Buprenorphine can be abused, both by individuals who are and who are not dependent on opioids. A recent study in France (where buprenorphine has been prescribed since 1996) found that 47% of patients on buprenorphine maintenance treatment reported ever injecting the drug. The addition of naloxone decreases the likelihood of abuse because naloxone blocks the desired “high” abusers seek when injecting buprenorphine and can cause severe withdrawal symptoms.

**How is buprenorphine obtained?** Subutex® and Suboxone® are the first narcotic drugs used for the treatment of opiate dependence that can be prescribed in an office setting. A list of physicians currently qualified to prescribe these drugs under the Drug Addiction Treatment Act of 2000 (DATA 2000) is available online ([http://buprenorphine.samhsa.gov/bwns\\_locator/index.html](http://buprenorphine.samhsa.gov/bwns_locator/index.html)).

**What is the legal status of buprenorphine?** In 2002 the Drug Enforcement Agency (DEA) reclassified buprenorphine from a Schedule V to a Schedule III narcotic based on a re-evaluation of evidence regarding the potential for abuse, diversion, dependence, and side effects.

SOURCE: A complete list of sources is available on the CESAR website (<http://www.cesar.umd.edu/cesar/cesarfax.asp>). For more information on buprenorphine, visit <http://www.buprenorphine.samhsa.gov> and [http://www.fda.gov/cder/drug/infopage/subutex\\_suboxone/default.htm](http://www.fda.gov/cder/drug/infopage/subutex_suboxone/default.htm).

•• 301-403-8329 (voice) •• 301-403-8342 (fax) •• CESAR@cesar.umd.edu •• www.cesar.umd.edu ••

CESAR FAX is supported by VOIT 1996-1002, awarded by the U.S. Department of Justice through the Governor's Office of Crime Control and Prevention. CESAR FAX may be copied without permission. Please cite CESAR as the source.

**Sources**  
**CESAR FAX Volume 12, Issue 13**

Center for Drug Evaluation and Research, U.S. Food and Drug Administration, *Subutex and Suboxone Questions and Answers*, 2002. Accessed 3/17/2003 ([http://www.fda.gov/cder/drug/infopage/subutex\\_suboxone/subutex-qa.htm](http://www.fda.gov/cder/drug/infopage/subutex_suboxone/subutex-qa.htm)).

Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, *About Buprenorphine Therapy*, undated. Accessed 3/17/2003 (<http://buprenorphine.samhsa.gov/about.html>).

*Drug Addiction Treatment Act of 2000: Title XXXV – Waiver Authority for Physicians Who Dispense or Prescribe Certain Narcotic Drugs for Maintenance Treatment or Detoxification Treatment*. Accessed 3/17/03 (<http://www.buprenorphine.samhsa.gov/fulllaw.html>).

Kakko J., Svanborg K. D., Kreek M. J., Heilig M. “1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomized, placebo-controlled trial,” *The Lancet* 361(9358):662-668, 2003.

Kintz P. “A new series of 13 buprenorphine-related deaths,” *Clinical Biochemistry* 35 (7):513-516, 2002.

National Institute on Drug Abuse, “Ready, Set, Go: Bringing Buprenorphine to the U.S. Treatment Market.” In *Problems of Drug Dependence 2001: Proceedings of the 63<sup>rd</sup> Annual Scientific Meeting*, Research Monograph Series 182, April 2002.

Strain E.C., Walsh S. L., Bigelow G. E. “Blockade of hydromorphone effects by buprenorphine/nalaxone and buprenorphine,” *Psychopharmacology* 159:161-166, 2002.

U.S. Food and Drug Administration, *Subutex and Suboxone Approved to Treat Opiate Dependence*, October 2002. Accessed 3/17/2003 (<http://www.fda.gov/bbs/topics/ANSWERS/2002/ANS01165.html>).

Vidal-Trecan G., Varescon I., Nabet N., Boissonnas A. “Intravenous use of prescribed sublingual buprenorphine tablets by drug users receiving maintenance therapy in France,” *Drug and Alcohol Dependence* 69(2):175-181, 2003.

## A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

### *Despite Some Obstacles, Physicians Still Optimistic About Prescribing Buprenorphine to Opiate-Addicted Patients*

In October 2002, buprenorphine was approved by the FDA as a medication to treat opiate-addicted patients in an outpatient setting. Qualified physicians were able to start prescribing Subutex® and Suboxone®, two types of buprenorphine, effective May 22, 2003. Join Together, a project of the Boston University School of Public Health, recently conducted a telephone poll of physicians qualified to prescribe these drugs. Two-thirds of the physicians polled have treated patients with either Subutex® (9%), Suboxone® (34%), or both drugs (23%). The remaining 34% of the physicians polled had not yet prescribed buprenorphine. Following are some of the barriers to prescribing the drugs:

- The most common complaint by physicians was that they had a difficult time finding pharmacies that carried either drug. One physician remarked, “I wish there was a way of educating pharmacies because so few are aware of the drug, which makes it hard to get” (p. 4).
- Problems with federal, state, and local regulations were the second most common barrier. For example, federal law limits physicians to prescribing buprenorphine to no more than thirty patients. One doctor reports “having to turn away dozens of patients” because he had reached his limit (p. 3).
- Costs and a lack of insurance coverage were other limitations that physicians cited as barriers to prescribing Subutex® or Suboxone®. One physician stated, “Some [patients] find it so difficult or so expensive that they give up and resume opiate use” (p. 3).

The authors conclude, “Although many obstacles still prevent widespread buprenorphine use for addiction treatment, it appears as though availability and use are headed in an encouraging direction. Most physicians seem optimistic about buprenorphine, and many of the physicians who are not yet prescribing indicated that they planned to start treating patients with the medication soon” (p. 7). More information about buprenorphine is available online at <http://buprenorphine.samhsa.gov>.

NOTES: The physicians polled were those listed in an on-line directory maintained by the Substance Abuse and Mental Health Services Administration (SAMHSA) [http://buprenorphine.samhsa.gov/bwns\\_locator/index.html](http://buprenorphine.samhsa.gov/bwns_locator/index.html). The physicians were contacted via phone, email, and fax over the months of June and July 2003. Of the 863 physicians listed on the SAMHSA web site, 419 agreed to participate in the poll (a 53% response rate).

SOURCE: Adapted by CESAR from “National Poll of Physicians on Barriers to Widespread Buprenorphine Use,” *Join Together*, October 2003. Available online at <http://www.jointogether.org/sa/files/pdf/bupereport.pdf>.

•• 301-405-9770 (voice) •• 301-403-8342 (fax) •• CESAR@cesar.umd.edu •• www.cesar.umd.edu ••

CESAR FAX is supported by VOIT 1996-1002, awarded by the U.S. Department of Justice through the Governor’s Office of Crime Control and Prevention. CESAR FAX may be copied without permission. Please cite CESAR as the source.

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Buprenorphine Treatment for Opioid Dependence*

*Buprenorphine is a synthetic opioid that is used for pain management and was approved in 2002 to treat opioid dependence. This issue of the CESAR FAX answers frequently asked questions about buprenorphine. Future issues will provide more detailed information on buprenorphine retail distribution, potential diversion, and adverse effects of misuse.*

**What are the forms of buprenorphine?** Although there are several forms of buprenorphine (including Buprenex®, an injectable liquid used for pain treatment), only Subutex® and Suboxone® have been approved for opioid addiction treatment. Subutex, which is also available in a generic form, contains buprenorphine alone and is usually given during the first few days of treatment. Suboxone contains both buprenorphine and naloxone, and is typically used during the maintenance phase of treatment. Naloxone is included to discourage abuse; when this drug is injected or snorted it blocks the effects of opioids and precipitates withdrawal symptoms.

**What does buprenorphine look like?** Subutex is an oval white tablet and the generic version is a round white tablet. Suboxone is available as an hexagonal orange tablet and as a film. Both products are dissolved under the tongue.

**How does buprenorphine compare to methadone?** Both methadone and buprenorphine are approved to treat opioid addiction. However, buprenorphine has weaker opioid effects, is less likely to result in overdose, and produces a lower level of physical dependence. Methadone must be dispensed by a federally regulated Opioid Treatment Program (OTP), while buprenorphine is currently the only opioid medication that can be prescribed for opioid treatment outside the OTP setting (e.g., in a certified physician's office). A patient can receive a 30-day take home dose of buprenorphine shortly after beginning treatment. In contrast, methadone patients must visit an OTP for daily dosing and must comply with treatment for two years to be eligible to receive a 30-day take home dose.

**Who can prescribe buprenorphine?** Physicians who have received buprenorphine training and obtained a federally approved waiver can prescribe Subutex and Suboxone or approved generic equivalents. The number of patients receiving a prescription for Subutex or Suboxone from U.S. outpatient retail pharmacies increased from slightly less than 20,000 in 2003 to more than 600,000 in 2009. In 2009, 97% of these prescriptions were for Suboxone, up from 77% in 2003.

**Is buprenorphine being diverted?** Numerous data sources indicate that buprenorphine, known on the street as Bupe, Subs, Subbies, and Orange Guys, is being diverted for use by those who do not have a prescription. Law enforcement authorities in Maine, Massachusetts, New York, and West Virginia are reporting an increase in seizures of buprenorphine together with other controlled prescription drugs. The estimated number of buprenorphine drug items analyzed by state and local forensic law enforcement labs in the U.S. has increased from 21 in 2003 to 8,172 in 2009. Buprenorphine has been smuggled into state prisons, including those in Maine, Massachusetts, New Jersey, New Mexico, Pennsylvania, and Vermont. The number of emergency department visits related to the nonmedical use of buprenorphine has increased from 4,440 in 2006 to 14,266 in 2009.

**How is buprenorphine abused?** Buprenorphine is abused by injecting or snorting the crushed tablets. While the naloxone in Suboxone provides some protection from abuse, the DEA reports that Suboxone is being abused by snorting.

**What are the adverse effects of buprenorphine abuse?** According to the manufacturer's safety information for Suboxone, buprenorphine "can cause serious life-threatening respiratory depression and death, particularly when taken by the intravenous (IV) route in combination with benzodiazepines or other central nervous system (CNS) depressants (i.e., sedatives, tranquilizers, or alcohol)." They also note that "intravenous misuse or taking [Suboxone] . . . before the effects of full-agonist opioids (e.g., heroin, hydrocodone, methadone, morphine, oxycodone) have subsided is highly likely to cause opioid withdrawal symptoms." In addition, "chronic use of buprenorphine can cause physical dependence."

SOURCE: A complete list of sources is available by accessing the PDF version of this issue online at [www.cesar.umd.edu](http://www.cesar.umd.edu). For more information, contact Erin Artigiani at [erin@cesar.umd.edu](mailto:erin@cesar.umd.edu) or 301-405-9794.

**CESAR FAX Volume 20, Issue 22 (June 13, 2011)**  
**“Buprenorphine Treatment for Opioid Dependence”**

**Source List**

- American Academy of Addiction Psychiatry (AAAP), the American Osteopathic Academy of Addiction Medicine (AOAAM) and the American Psychiatric Association (APA), *Physicians’ Clinical Support System – Buprenorphine (PCCSS-B) Training Website*, [www.pcassb.org](http://www.pcassb.org), accessed June 13, 2011.
- Drug Enforcement Administration, Office of Diversion Control, Drug and Chemical Evaluation Section, *Buprenorphine (Trade Names: Buprenex®, Suboxone®, Subutex®)*, February 2011. Available online at [www.deadiversion.usdoj.gov/drugs\\_concern/buprenorphine.pdf](http://www.deadiversion.usdoj.gov/drugs_concern/buprenorphine.pdf).
- Drug Enforcement Administration, Office of Diversion Control, National Forensic Laboratory Information System (NFLIS), *Special Report: Methadone and Buprenorphine, 2003-2008*, 2009. Available online at [www.deadiversion.usdoj.gov/nflis/methadone\\_buprenorphine\\_srpt.pdf](http://www.deadiversion.usdoj.gov/nflis/methadone_buprenorphine_srpt.pdf).
- Drug Enforcement Administration, Office of Diversion Control, National Forensic Laboratory Information System (NFLIS), *Year 2009 Annual Report*, 2010. Available online at [www.deadiversion.usdoj.gov/nflis/2009annual\\_rpt.pdf](http://www.deadiversion.usdoj.gov/nflis/2009annual_rpt.pdf).
- Goodnough, A. and Zezima, K., “When Children’s Scribble Hide a Prison Drug,” *New York Times*, A1, May 26, 2011.
- Reckitt Benckiser Pharmaceuticals Inc., “Suboxone Important Safety Information,” undated. Available online at [www.suboxone.com/patients/safety/Default.aspx](http://www.suboxone.com/patients/safety/Default.aspx) (accessed 6/13/11).
- Substance Abuse and Mental Health Services Administration, “Opioid Drugs in Maintenance and Detoxification Treatment of Opiate Addiction,” Final Rule, *Federal Register* 66(11):4076-4102, January 1, 2011.
- Substance Abuse and Mental Health Services Administration, *SAMHSA Update*, Presentation given by Nicholas Reuter at the January 19, 2011 CEWG Conference, Scottsdale, AZ.
- Substance Abuse and Mental Health Services Administration, *Buprenorphine Website*, [buprenorphine.samhsa.gov](http://buprenorphine.samhsa.gov) (accessed 6/9/11).
- Substance Abuse and Mental Health Services Administration, Drug Abuse Warning Network (DAWN), National Estimates of Drug-Related Emergency Department Visits, 2004 – 2009, undated. Available online at [dawninfo.samhsa.gov](http://dawninfo.samhsa.gov) (accessed 6/9/11).
- U.S. Department of Justice, National Drug Intelligence Center (NDIC), “Buprenorphine: Potential for Abuse,” NDIC Intelligence Bulletin, September 2004. Available online at [www.justice.gov/ndic/pubs10/10123/index.htm](http://www.justice.gov/ndic/pubs10/10123/index.htm).
- U.S. Department of Justice, National Drug Intelligence Center (NDIC), “Misuse of Buprenorphine-Related Products, SENTRY Drug Alert Watch, February 22, 2011. Available online at [www.justice.gov/ndic/pubs44/44054/sw0009p.pdf](http://www.justice.gov/ndic/pubs44/44054/sw0009p.pdf).
- U.S. Food and Drug Administration, Subutex and Suboxone Questions and Answers, undated. Available online at [www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm191523.htm](http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm191523.htm) (accessed 6/13/11).

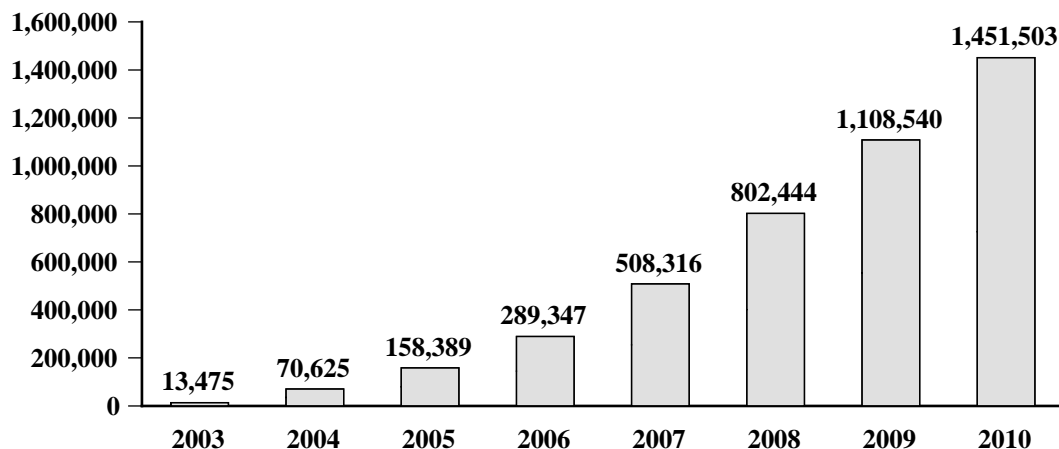
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *U.S. Retail Distribution of Buprenorphine Approaches 1.5 Million Grams*

After buprenorphine was approved to treat opioid dependence in 2002 (see *CESAR FAX*, Volume 20, Issue 22), the DEA's Automation of Reports and Consolidated Orders System (ARCOS) began tracking the retail distribution of this synthetic opioid. ARCOS monitors "controlled substance activity from the point of manufacture and/or distribution to the point of sale to the retail level registrant (e.g., pharmacies, hospitals, practitioners, teaching institutions, researchers, analytical labs, importers/exporters, and narcotic treatment programs)" (Leonhart, p. 3). The number of grams of buprenorphine distributed to these retail outlets has increased from 13,475 in 2003 to 1,451,503 in 2010. Previous research has found that increases in sales of other opioid analgesics are correlated with increases in unintentional overdose deaths involving these drugs (see *CESAR FAX*, Volume 20, Issue 21).

**Number of Grams of Buprenorphine Distributed to Retail Outlets, 2003-2010**



NOTES: ARCOS does not capture transaction information from these retail outlets to end users. ARCOS tracks all Schedule I and II materials (manufacturers and distributors); Schedule III narcotic and gamma-hydroxybutyric acid (GHB) materials (manufacturers and distributors); and selected Schedule III and IV psychotropic drugs (manufacturers only).

SOURCES: Adapted by CESAR from U.S. Drug Enforcement Agency (DEA), Office of Diversion Control, *Special Report: Methadone and Buprenorphine, 2003-2008, 2009* (2003-2006 ARCOS data); DEA, ARCOS data requests 2/17/2009 (2007 data), 1/25/2010 (2008 data), 4/14/2010 (2009 data), 5/2/2011 (2010 data); DEA, Office of Diversion Control, Automation of Reports and Consolidated Orders System (ARCOS) website (<http://www.deadiversion.usdoj.gov/arcos/index.html>), accessed 6/17/11; and Leonhart, M., "Warning: The Growing Danger of Prescription Drug Diversion," *Statement before the Subcommittee on Commerce, Manufacturing and Trade Committee on Energy and Commerce, U.S. House of Representatives*, 4/14/11.

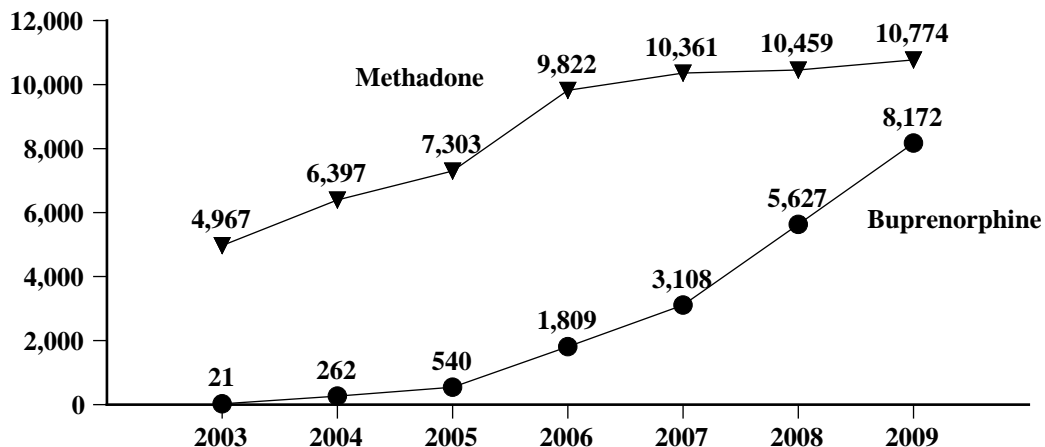
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Number of Law Enforcement-Seized Buprenorphine Items Analyzed by U.S. Labs Increases Dramatically*

The estimated number of buprenorphine drug items secured in law enforcement operations and analyzed by state and local forensic laboratories has increased dramatically since 2003, according to data from National Forensic Laboratory Information System (NFLIS). NFLIS, a Drug Enforcement Administration (DEA) program, provides a means to monitor the diversion of legitimately marketed drugs into illicit channels. Since 2003, the number of buprenorphine drug items analyzed has increased from 21 to 8,172. In comparison, the number of methadone drug items seized and analyzed nearly doubled from 2003 to 2006, then only increased 9% from 2006 to 2009. According to the DEA, “While methadone is still more prevalent in terms of reporting in NFLIS, buprenorphine has increased at a sharper rate, indicating a need for continued monitoring. This is especially true considering the level at which buprenorphine is being distributed and prescribed for legal medical purposes” (p. 10) (see *CESAR FAX*, Volume 20, Issue 23 for more information on retail sales of buprenorphine).

**Estimated Number of Total Methadone and Buprenorphine Drug Items Analyzed by State and Local Forensic Laboratories in the U.S., 2003-2009**



NOTES: NFLIS includes drug chemistry results from completed analyses only. Drug evidence secured by law enforcement but not analyzed by laboratories is not included in the database. State and local policies related to the enforcement and prosecution of specific drugs may affect drug evidence submissions to laboratories for analysis. Laboratory policies and procedures for handling drug evidence may also vary. For example, some analyze all evidence submitted, while others analyze only selected items.

SOURCES: Adapted by CESAR from U.S. Drug Enforcement Agency (DEA), Office of Diversion Control, *Special Report: Methadone and Buprenorphine, 2003-2008, 2009* (online at [http://www.dea diversion.usdoj.gov/nflis/methadone\\_buprenorphine\\_srpt.pdf](http://www.dea diversion.usdoj.gov/nflis/methadone_buprenorphine_srpt.pdf)); and DEA, Office of Diversion Control, *National Forensic Laboratory Information System (NFLIS) Year 2009 Annual Report, 2010* (online at [http://www.dea diversion.usdoj.gov/nflis/2009annual\\_rpt.pdf](http://www.dea diversion.usdoj.gov/nflis/2009annual_rpt.pdf)).

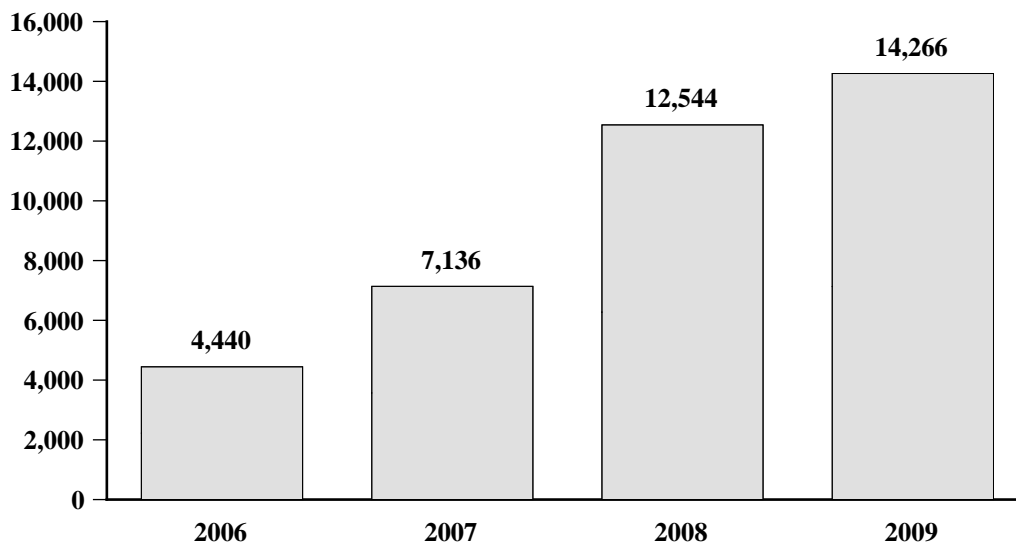
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Number of U.S. Emergency Department Visits Related to the Nonmedical Use of Buprenorphine More Than Triples Since 2006*

The estimated number of emergency department visits related to the nonmedical use of buprenorphine more than tripled from 2006 to 2009, according to data from Drug Abuse Warning Network (DAWN). In 2006, the nonmedical use of buprenorphine was involved as either a direct cause or a contributing factor in an estimated 4,440 emergency department visits, compared to 14,266 in 2009. These increases parallel increases in the number of law-enforcement-seized buprenorphine items analyzed by state and local forensic laboratories (see *CESAR FAX*, Volume 20, Issue 24).

### **Estimated Number of U.S. Emergency Department Visits Related to the Nonmedical Use of Buprenorphine, 2006-2009**



NOTES: Buprenorphine-related emergency department visits are those in which buprenorphine was involved as either a direct cause or a contributing factor to the visit. Nonmedical use of buprenorphine includes taking more than the prescribed dose; taking buprenorphine prescribed for another individual; deliberate poisoning with buprenorphine by another person; and documented misuse or abuse of buprenorphine.

SOURCE: Adapted by CESAR from data from Substance Abuse and Mental Health Services Administration (SAMHSA), Drug Abuse Warning Network (DAWN), *National Estimates of Drug-Related Emergency Department Visits, 2004-2009*, online at [https://dawninfo.samhsa.gov/data/ed/Nation/Nation\\_2009\\_NMUP.xls](https://dawninfo.samhsa.gov/data/ed/Nation/Nation_2009_NMUP.xls) (accessed 6/23/11).

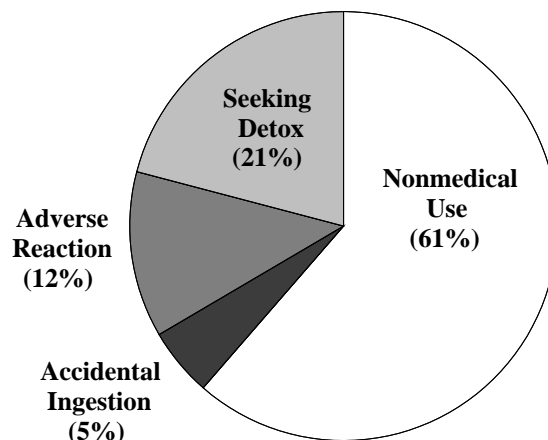
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *61% of Buprenorphine-Related Emergency Department Visits for Nonmedical Use*

More than half of buprenorphine-related emergency department visits in the U.S. are for nonmedical use of the drug, according to data from the Drug Abuse Warning Network (DAWN). Of the estimated 23,450 emergency department visits in 2009 in which buprenorphine was involved as either a direct cause or a contributing factor to the visit, 61% were for nonmedical use of the drug. Approximately one-fifth of the visits were related to seeking detoxification, 12% for adverse reactions, and 5% for accidental ingestion. The estimated number of emergency department visits related to the nonmedical use of buprenorphine has more than tripled since 2006 (see *CESAR FAX*, Volume 20, Issue 25).

### Types of U.S. Buprenorphine-Related Emergency Department Visits, 2009 (N=23,450)



NOTES: *Nonmedical use* of buprenorphine includes taking more than the prescribed dose; taking buprenorphine prescribed for another individual; deliberate poisoning with buprenorphine by another person; and documented misuse or abuse of buprenorphine. *Accidental ingestion* includes childhood drug poisonings, individuals who take the wrong medication by mistake, and a caregiver administering the wrong medicine by mistake. It does not include a patient taking more medicine than directed because the patient forgot to take it earlier. *Adverse reaction* includes visits related to adverse reactions, side effects, drug-drug interactions, and drug-alcohol interactions resulting from using buprenorphine for therapeutic purposes. *Seeking detox* includes patients seeking substance abuse treatment, drug rehabilitation, or medical clearance for admission to a drug treatment or detoxification unit. Suicide attempts are not included because the number of buprenorphine-related ED visits categorized as suicide attempts did not meet DAWN's standards of precision (i.e., the estimate had a standard of error greater than 50% or the unweighted count or estimate was less than 30). Percentages do not sum to 100 due to rounding and the exclusion of data not categorized as these four types of visits.

SOURCE: Adapted by CESAR from data from the Substance Abuse and Mental Health Services Administration (SAMHSA), *Drug Abuse Warning Network, 2009: Selected Tables of National Estimates of Drug-Related Emergency Department Visits*, online at <https://dawninfo.samhsa.gov/data/default.asp?met=All> (accessed 6/23/11).

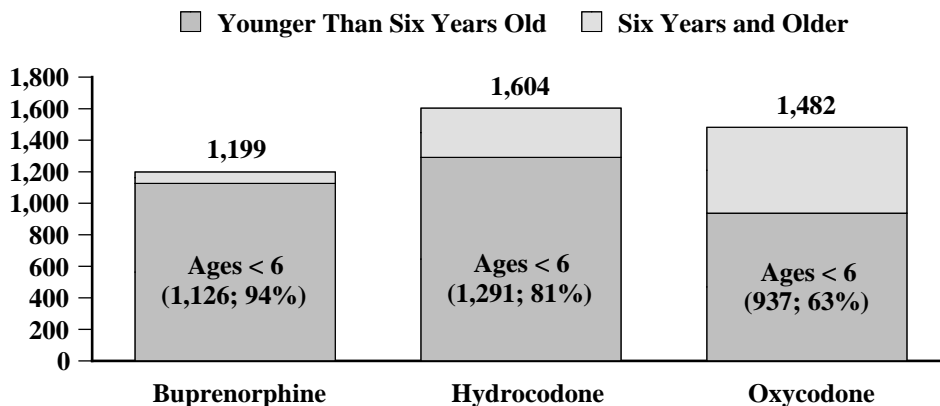
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Nearly All Emergency Department Visits for the Accidental Ingestion of Buprenorphine Occur in Children Under the Age of Six*

There were an estimated 1,199 emergency department (ED) visits related to the accidental ingestion of buprenorphine in 2009—more than double the number of visits in 2008 and representing 5% of all buprenorphine-related ED visits in 2009 (see *CESAR FAX*, Volume 20, Issue 26). According to data from the Drug Abuse Warning System (DAWN), 94% of these accidental ingestion visits involved children under the age of six, compared to 81% for hydrocodone and 63% for oxycodone<sup>1</sup> (see figure below). In addition to the increasing availability of buprenorphine (see *CESAR FAX*, Volume 20, Issue 23), the tablet formulation's resemblance to candy may also be a factor in the high rate of accidental ingestion by children. A recent study of buprenorphine exposure in toddlers admitted to a pediatric intensive care unit in the northeast United States<sup>2</sup> concluded that “the sublingual buprenorphine resemblance to candy in appearance and taste may pose a special risk to toddlers and lead to more severe intoxication from chewing, rather than swallowing, the tablet” (p. e103). It is possible that the sublingual film version of Suboxone approved in 2010 may have a lower risk of accidental ingestion than the tablet because it is packaged in a single-dose, child-resistant pouch.

### **Estimated Number of U.S. Emergency Department Visits Related to the Accidental Ingestion of Buprenorphine, Hydrocodone, and Oxycodone, 2009**



<sup>1</sup>Estimates for accidental exposure visits for other narcotic analgesics, including methadone, were unavailable because the estimate either had a relative standard error greater than 50% or an unweighted count or estimate less than 30.

<sup>2</sup>Pedapati, E. and Bateman, S.T., “Toddlers Requiring Pediatric Intensive Care Unit Admission Following At-Home Exposure to Buprenorphine/Naloxone,” *Pediatric Critical Care Medicine*, 12(2):e102-e107, 2011.

NOTES: Accidental ingestion includes childhood drug poisonings, individuals who take the wrong medication by mistake, and a caregiver administering the wrong medicine by mistake. It does not include a patient taking more medicine than directed because the patient forgot to take it earlier.

SOURCE: Adapted by CESAR from data from Substance Abuse and Mental Health Services Administration (SAMHSA), Drug Abuse Warning Network (DAWN), *National Estimates of Drug-Related Emergency Department Visits, 2004-2009: Accidental Ingestion Visits*, online at [https://dawninfo.samhsa.gov/data/ed/Nation/Nation\\_2009\\_Accidental.xls](https://dawninfo.samhsa.gov/data/ed/Nation/Nation_2009_Accidental.xls) (accessed 7/11/11).

• 301-405-9770 (voice) • 301-403-8342 (fax) • CESAR@cesar.umd.edu • www.cesar.umd.edu •  
CESAR FAX may be copied without permission. Please cite CESAR as the source.

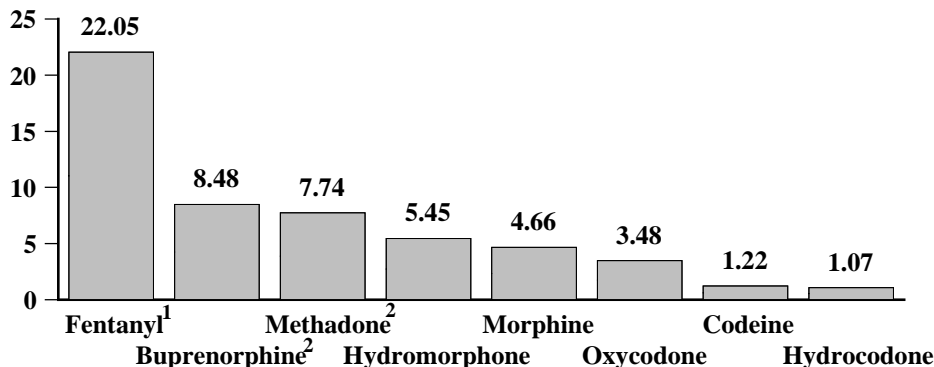
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Fentanyl and Buprenorphine Have Higher Rates of Nonmedical Use ED Visits per Dosage Units Distributed to Dispensing or Retail Institutions Than Other Opioids*

While the estimated number of emergency department (ED) visits related to the nonmedical use of buprenorphine has been increasing (see *CESAR FAX*, Volume 20, Issue 25), the magnitude of these visits is small compared to that of other opioids. For example, there were 14,266 ED visits for nonmedical use of buprenorphine in 2009, compared to 86,258 for hydrocodone and 148,449 for oxycodone. However, after controlling for the number of dosage units (DUs) distributed to dispensing and retail institutions, buprenorphine ranks second only to fentanyl<sup>1</sup> in the rate of ED visits for nonmedical use. In 2009, there were 22.05 ED visits for nonmedical use of fentanyl for every 100,000 DUs of fentanyl distributed to dispensing and retail institutions, compared to 8.48 for buprenorphine<sup>2</sup>, 7.74 for methadone<sup>2</sup> and 5.45 for hydromorphone. All other opioids had rates of less than 5 per 100,000 DUs (see figure below).

### **Estimated Rate of Emergency Department (ED) Visits Related to Nonmedical Use of Eight Opioids (Rate per 100,000 Dosage Units Distributed to Dispensing or Retail Institutions), U.S., 2009**



<sup>1</sup>One possible reason for the higher rate of fentanyl ED visits may be that fentanyl used nonmedically is often clandestinely produced and/or mixed with heroin or cocaine (Source: [www.nida.nih.gov/drugpages/fentanyl.html](http://www.nida.nih.gov/drugpages/fentanyl.html)).

<sup>2</sup>One possible reason for the higher rate of buprenorphine and methadone ED visits may be that these drugs are frequently prescribed to opioid dependent persons, who are at a higher risk for drug misuse.

NOTES: Nonmedical use includes taking more than the prescribed dose; taking a drug prescribed for another individual; deliberate poisoning by another person; and documented misuse or abuse of a drug. Data on dosage units distributed to dispensing and retail institutions is from the DEA's Automated Reports and Consolidated Orders System (ARCOS), which requires manufacturers and distributors to report the number of grams of monitored substances distributed to dispensing and retail institutions. Dispensing and retail institutions include pharmacies, practitioners, hospitals, teaching institutions, and narcotics treatment programs. Dosage units are the standard unit in which a medication is prescribed (e.g., pill, tablet, patch).

SOURCES: Adapted by CESAR from data from Substance Abuse and Mental Health Services Administration (SAMHSA), Drug Abuse Warning Network (DAWN), *National Estimates of Drug-Related Emergency Department Visits, 2004-2009: Nonmedical Use of Pharmaceuticals Visits*, online at [https://dawninfo.samhsa.gov/data/ed/Nation/Nation\\_2009\\_NMUP.xls](https://dawninfo.samhsa.gov/data/ed/Nation/Nation_2009_NMUP.xls) (accessed 7/20/11); and U.S. Drug Enforcement Agency (DEA), Office of Diversion Control, Automation of Reports and Consolidated Orders System (ARCOS) 2009 data requests (4/13/2010).

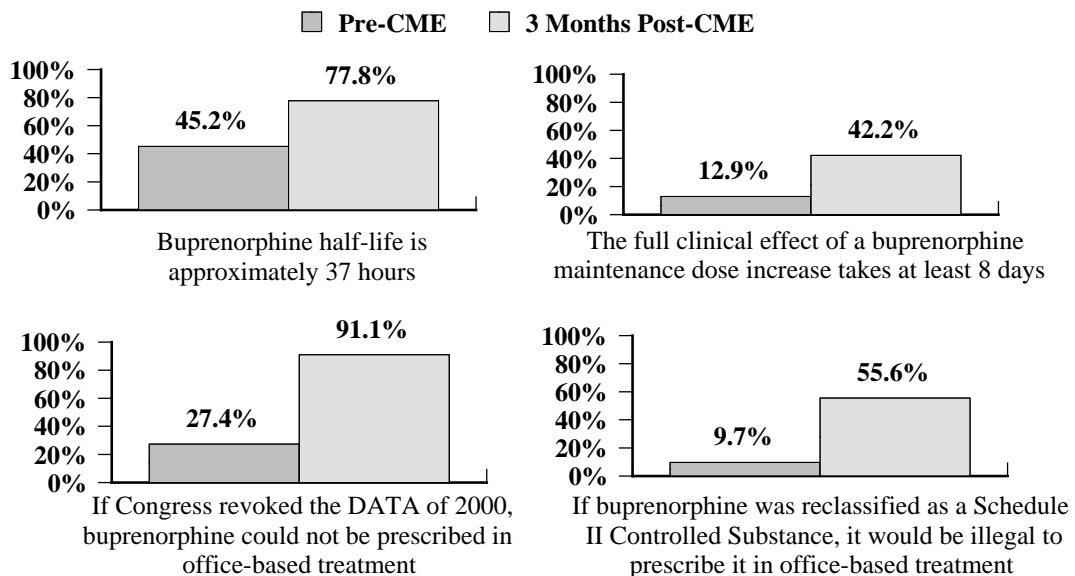
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Continuing Medical Education Improves Buprenorphine-Waivered Physicians' Knowledge and Practice Behaviors*

In order to prescribe buprenorphine for opioid addiction, a physician must complete an 8 hour class and receive a federally approved waiver. However, a recent study has found that waived physicians may have limited knowledge of buprenorphine pharmacology and legislative issues and that additional continuing medical education (CME) training might improve their understanding. Physicians in two U.S. regions with indicators of buprenorphine misuse/diversion were surveyed before and three months after attending a free CME on the best medical practices recommended for office-based buprenorphine treatment. Knowledge of buprenorphine pharmacology and legislative issues significantly increased after the CME. For example, the percentage of physicians who knew that the full clinical effect of a buprenorphine maintenance dose increase takes at least 8 days increased from 12.9% before the CME to 42.2% after the CME (see figure below). In addition, the doctors reported significant improvement in 10 clinical practice behaviors, including examination for track marks/intranasal erythema; performance of random pill counts; discussions of diversion with patients; and use of random urine drug testing (data not shown). According to the authors, "certification trainings in [office-based opioid dependence treatment], although essential and relevant to practice, typically occur before a doctor begins treating patients—before they have understood or had the opportunity to identify practice challenges or the limitations of their knowledge in the context of delivering the treatment themselves" (p. 8). They suggest that mandatory, ongoing buprenorphine education for buprenorphine-waivered physicians "has the potential to improve patient care and the public health" and "may decrease risk of buprenorphine misuse and diversion from practices" (p. 8; p. 1).

### **Percentage of Buprenorphine-Waivered Physicians Knowing the Correct Answer to Buprenorphine Pharmacology and Legislative Issues, Pre- and 3 Months Post-CME**



NOTE: All differences in the figure are significant at  $p < .05$ .

SOURCE: Adapted by CESAR from Lofwall, M.R., Wunsch, M.J., Nuzzo, P.A., and Walsh, S.L., "Efficacy of Continuing Medical Education to Reduce the Risk of Buprenorphine Diversion," *Journal of Substance Abuse Treatment*, In Press, 2011. For more information, contact Dr. Michelle Lofwall at michelle.lofwall@uky.edu.

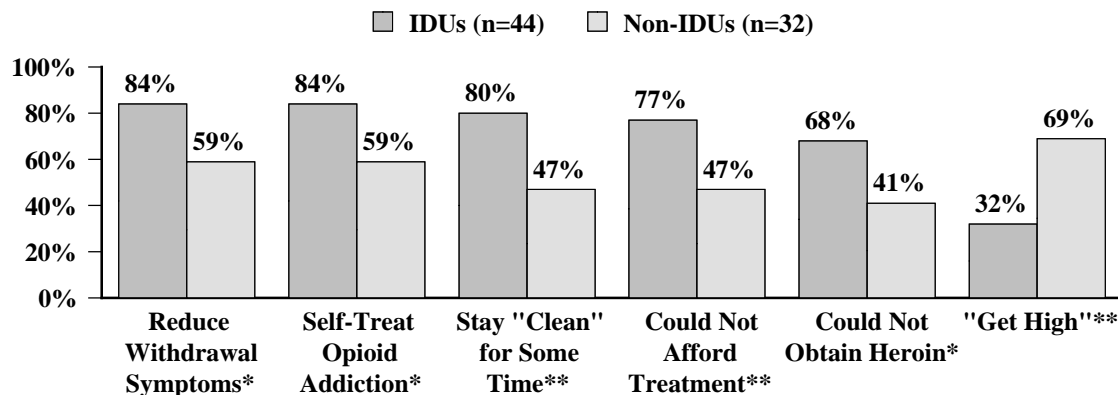
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Small Rhode Island Study Finds IDUs More Likely to Use Diverted Buprenorphine/Naloxone to Self-Medicate; Non-IDUs More Likely to Use to Get High*

The motivation for using diverted buprenorphine/naloxone varies significantly between injecting drug users (IDUs) and non-IDUs, according to data from a study of self-reported adult opioid users in Providence, Rhode Island. Overall, approximately three-fourths (76%) of opioid users reported obtaining buprenorphine/naloxone illicitly. IDUs were significantly more likely than non-IDUs to report using diverted buprenorphine/naloxone for self-medication reasons, such as to reduce withdrawal symptoms or to self-treat opioid addiction (see figure below). In contrast, non-IDUs were significantly more likely than IDUs to report using diverted buprenorphine/naloxone to get high (69% vs. 32%). The authors suggest that these differences may be because IDUs have a greater severity of dependence—they were more likely to report high frequency opioid use, a history of enrollment in methadone maintenance treatment, and utilization of detoxification services. The authors also note that “The number of opioid users in our sample who reported having ever used buprenorphine/naloxone to ‘get high’ is surprising, given that buprenorphine/naloxone is a partial opioid agonist that is not expected to produce euphoria in regular users with a tolerance to opioids. It is possible that some participants, particularly noninjecting opioid users, did not use opioids regularly enough to develop significant tolerance” (p. 5).

### Motivation for Using Diverted Buprenorphine/Naloxone Among Opioid Users, Rhode Island, 2009



\* P < 0.05; \*\* p < 0.01

*EDITOR'S NOTE: While these findings are limited by the fact that this study used a small convenience sample of opioid users from one area of Providence, we believe the results are noteworthy because they are the first to suggest that individual drug use patterns and the severity of opioid dependence may be related to an individual's motivation for using diverted buprenorphine.*

NOTE: Adults who self-reported opioid use in the previous 30 days were recruited in Providence between August and November 2009 from a fixed-site syringe exchange program and by outreach workers recruiting from areas they identified to have high concentrations of active opioid users.

SOURCE: Adapted by CESAR from data from Bazazi, A.R., Yokell, M., Fu, J.J., Rich, J.D., Zaller, N.D., "Illicit Use of Buprenorphine/Naloxone Among Injecting and Noninjecting Opioid Users," *Journal of Addiction Medicine*, Published Ahead-of-Print, 2011. For more information, contact Dr. Nickolas Zaller at nzaller@lifespan.org.

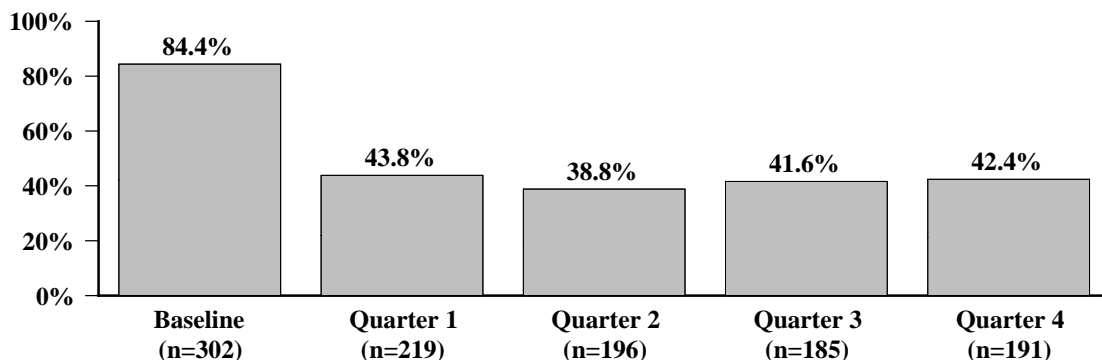
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## *Multisite Demonstration Project Finds Buprenorphine/Naloxone Effective in Treating Opioid Dependence in HIV-Infected Patients*

Buprenorphine/naloxone treatment provided to persons with coexisting opioid dependence and HIV-infection—a population often difficult to treat—can reduce opioid use when provided in HIV treatment settings, according to data from the Buprenorphine and Integrated HIV Care Model Demonstration Project (BHIVES). This multisite study provided an 8-hour buprenorphine training for physicians and clinical staff at all nine HIV treatment sites as well as other forms of support, including monthly technical assistance conference calls and a listserv for discussion of clinical issues and dissemination of clinical support materials, annual meetings, and site visits. The study found that 48% of HIV-infected persons continued to receive buprenorphine/naloxone treatment one year after beginning treatment (data not shown) and that self-reported\* illicit opioid use decreased from 84.4% at baseline (prior to treatment) to 42% one year later (see figure below). The authors conclude that while these results “demonstrate the feasibility of providing buprenorphine/naloxone treatment in a variety of HIV primary care settings,” further research on strategies to improve retention and the impact of varying intensities of urine toxicology monitoring are warranted (p. S37).

### **Percentage of HIV-Infected Persons Receiving Buprenorphine/Naloxone Treatment for Opioid Dependence Self-Reporting Illicit Opioid Use in the Year Post-Treatment Initiation, Nine U.S. BHIVES HIV Clinic Sites, 2005-2007**



\*Urinalysis data were not included as a measure of illicit opioid use because sites were not consistent in their timing or use of objective urine toxicology analysis. Current guidelines on the use of buprenorphine/naloxone in the treatment of opioid dependence recommend monthly urine screening for those with demonstrated abstinence, and more frequent screening in patients with ongoing illicit drug use. Despite the fact that all sites included protocols that planned for urine screening on a monthly basis, urinalysis was conducted less frequently than once a month after the first quarter of the study. According to the authors, these findings “raise possibility that there are structural or attitudinal barriers to conducting urine toxicology screening as planned and as is recommended” (p. S37).

SOURCE: Adapted by CESAR from data from Fiellin, D.A., et al., “Drug Treatment Outcomes Among HIV-Infected Opioid-Dependent Patients Receiving Buprenorphine/Naloxone,” *Journal of Acquired Immune Deficiency Syndromes* 56(S1):S33-S38, 2011. For more information, contact Dr. David A. Fiellin at david.fiellin@yale.edu.

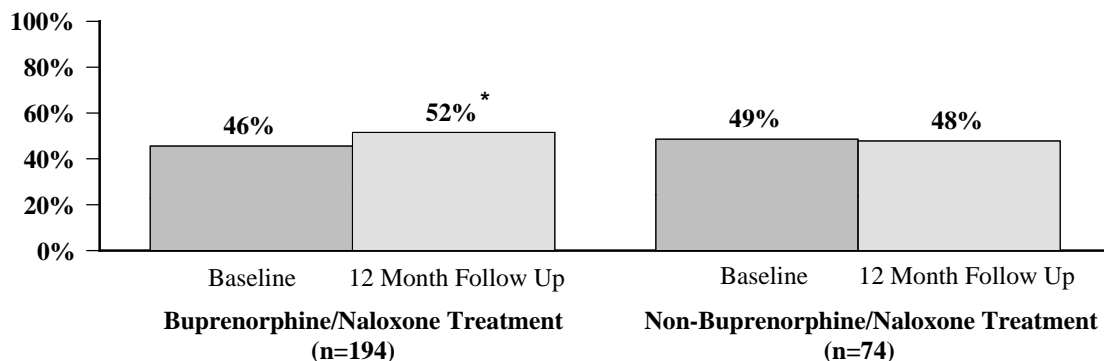
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

## ***Buprenorphine/Naloxone Treatment for Opioid Dependence in HIV-Infected Persons Improves Quality of HIV Care Received***

A recent multisite study found that buprenorphine can effectively treat opioid dependence in HIV-infected persons (see *CESAR FAX*, Volume 20, Issue 31). This same demonstration project also found that providing buprenorphine treatment for opioid dependence improves the quality of the HIV care received by these individuals. Quality of care indicators (QIs) at nine HIV clinics were evaluated at the initiation of and 12 months after treatment for opioid dependence. The study found that the mean percentage of QIs received (of those that could be received\*) increased from 46% to 52% among those being treated with buprenorphine/naloxone (see figure below). Specifically, participants receiving buprenorphine/naloxone increased their receipt of 6 of 16 HIV QIs, including hepatitis A and pneumococcal vaccination, CD4 and viral load monitoring, injection drug use risk reduction counseling, and HIV clinic visits. No differences were seen from baseline to follow up among those referred for other treatments\*\* and those receiving other treatments experienced increased receipt of only 3 of the 16 HIV QIs. Receiving buprenorphine/naloxone treatment was the only variable associated with improvement in quality of HIV care; other variables, such as age, race/ethnicity, gender, and opiate of choice, were not associated with changes in quality of care (data not shown). According to the authors, “integration of office-based [buprenorphine/naloxone] into HIV practices represents one innovation for closing this gap in the quality of HIV care by increasing engagement in and receipt of recommended HIV care” (p. 7).

**Mean Percentage of HIV Quality of Care Indicators Received at Baseline and 12 Month Follow Up in Nine U.S. HIV Clinics, by Type of Opioid Treatment, 2005-2007**



\*  $p < 0.001$

\*The mean percentage of QIs received was generated by dividing the number of instances in which recommended care was delivered by the number of times participants were eligible to receive recommended care multiplied by 100 and expressed as a percentage. For example, if a person was eligible to receive 10 HIV quality of care indicators over the 12-month period, yet received only 8, the summary quality score for that person was 80%.

\*\*Those who did not receive buprenorphine/naloxone treatment either chose or were assigned off-site methadone maintenance therapy or other treatment based on local site protocols.

SOURCE: Adapted by CESAR from data from Korthuis, P.T., et al., “Improving Adherence to HIV Quality of Care Indicators in Persons with Opioid Dependence: The Role of Buprenorphine,” *Journal of Acquired Immune Deficiency Syndromes*, 56(S1):S83-S90, 2011. For more information, contact Dr. P. Todd Korthuis at korthuis@ohsu.edu.

**A Weekly FAX from the Center for Substance Abuse Research**

**University of Maryland, College Park**

*2011 Media Reports of Buprenorphine Diversion and Misuse*

<b>Date</b>	<b>State</b>	<b>Subject</b>	<b>Description</b>
8/19/11	TN	jail/prison	Suboxone® strips and other drugs smuggled into jails in variety of ways ( <i>"Contraband Finds Its Way Into Regional Jails In a Variety of Ways," Bristol Herald Courier</i> )
8/4/11	WV	trafficking	Drug ring arrested for selling Oxycodone® and Suboxone ( <i>"Investigation Brings 25 Drug Arrests in West Virginia," Cumberland Times-News</i> )
8/1/11	IN	jail/prison	Suboxone smuggled into prison in bra ( <i>"Woman Accused of Smuggling Drugs Inside Her Bra at Pendleton Facility," WXIN-TV</i> )
7/27/11	VT	jail/prison, trafficking	Buprenorphine smuggled into prison & street diversion/trafficking ( <i>"Suboxone Succeeds in Aiding Opiate Addicts, but Too Many Are Abusing It Instead," Burlington Free Press</i> )
7/19/11	CA	diversion, trafficking	Doctor selling prescriptions for painkillers, including buprenorphine ( <i>"Doctor Faces Trial for Selling Prescriptions," City News Service</i> )
7/15/11	NM	jail/prison, trafficking	Law enforcement reports of buprenorphine diversion/trafficking & buprenorphine in jail ( <i>"Drug Meant to Treat Heroin Users Being Used to Get High," KOB Eyewitness News 4</i> )
7/13/11	MD	trafficking	Man charged with intent to distribute Suboxone, heroin, cocaine ( <i>"Heroin, Cocaine Seized in Traffic Stop," Frederick News-Post</i> )
6/21/11	ME	jail/prison	Suboxone smuggled into state prison ( <i>"Ex-Caseworker Fined \$4,500 for Giving Pills, Porn to Inmate," Portland Press Herald</i> )
6/7/11	PA	jail/prison	Inmate had Suboxone smuggled into federal prison ( <i>"Federal Inmate Sentenced to Additional 18 Months in Prison for Possessing Contraband," States News Service</i> )
6/5/11	U.S.	jail/prison	National reports of Suboxone smuggled into prisons ( <i>"Prison Official: Contraband Smugglers Can Get Creative," The Union Leader</i> )
5/26/11	U.S.	jail/prison	Buprenorphine smuggled into prison ( <i>"When Children's Scribbles Hide a Prison Drug," New York Times</i> )
5/26/11	WV	trafficking	Firefighter charged with selling Suboxone ( <i>"Firefighter Charged with Selling Drugs," Charleston Gazette</i> )
5/12/11	PA	jail/prison	Prison guard selling Suboxone to inmates ( <i>"Charges Against Ex-Prison Guard Forwarded to Court," The Citizens' Voice</i> )
4/7/11	MA	jail/prison	Buprenorphine smuggled into jail ( <i>"Deacon Admits Passing Contraband to Inmate," UPI</i> )
3/31/11	NJ	jail/prison	Buprenorphine smuggled into prison ( <i>"Final Suspect in Suboxone Investigation at Cape May County Correctional Center Arrested," Targeted News Service</i> )
3/30/11	ME	jail/prison	Buprenorphine smuggled into prison in waistband of pants ( <i>"2 Inmates, 2 Women Charged in Drug Operation," Bangor Daily News</i> )
3/22/11	NY	jail/prison	Possession of Suboxone by inmate in prison ( <i>"Man to Go Back to Prison After Admitting Drug Possession," Watertown Daily Times</i> )
3/21/11	PA	jail/prison	Suboxone smuggled into prison underneath postage stamps on letters ( <i>"Eleven Charged in Operation Postage Stamp," States News Service</i> )
3/16/11	NY	trafficking	Drug ring sold Suboxone and Lortab® to buy cocaine and other drugs ( <i>"10 Indicted in Scheme to Obtain Pain Pills to Buy, Sell Street Drugs," Buffalo News</i> )
3/8/11	MA	diversion	Pharmacist charged with stealing Vicodin® and Suboxone from workplace ( <i>"CVS Employee Charged with Drug Distribution," States News Service</i> )

SOURCE: CESAR search of LexisNexis Academic database for "All News" in the "United States" with the terms "buprenorphine," "Suboxone," or "Subutex." Only articles describing diversion or misuse were included. Only one article per news report/incident was included.

**A Weekly FAX from the Center for Substance Abuse Research**

**University of Maryland, College Park**

## ***Buprenorphine Availability, Diversion, and Misuse: A Summary of the CESAR FAX Series***

While research indicates that buprenorphine is an effective drug for treating opioid dependence, the potential for its nonmedical use and related unintended consequences may be going unnoticed. Our recent series of publications on buprenorphine were designed to highlight several indicators of the increased availability, diversion, and misuse of buprenorphine. Following is a summary of the key points of the recent *CESAR FAX* series on buprenorphine, followed by suggested policy changes that may decrease buprenorphine diversion and misuse.

### **Buprenorphine is an effective treatment for opioid dependence.**

In addition to being an effective treatment for opioid dependence in general, recent studies have also found that buprenorphine/naloxone treatment provided in HIV treatment settings to persons with coexisting opioid dependence and HIV-infection—a population often difficult to treat—can reduce opioid use as well as improve the quality of HIV care received. (*Source: CESAR FAX, Vol. 20, Iss. 31 & 32*)

### **The amount of buprenorphine legally available for distribution and sale has increased.**

Distribution of buprenorphine to retail and dispensing institutions (such as pharmacies, hospitals, practitioners, teaching institutions, researchers, analytical labs, and narcotic treatment programs) has increased from 13,475 in 2003 to 1,451,503 in 2010. The number of patients receiving a prescription for Subutex® or Suboxone® from U.S. outpatient retail pharmacies increased from slightly less than 20,000 in 2003 to more than 600,000 in 2009. (*Source: CESAR FAX, Vol. 20, Iss. 22 & 23*)

### **Buprenorphine diversion and nonmedical use appear to be increasing.**

The number of buprenorphine drug items secured in law enforcement operations and analyzed by state and local forensic laboratories has increased from 21 in 2003 to 8,172 in 2009. Buprenorphine has been smuggled into state prisons, including those in Maine, Massachusetts, New Jersey, New Mexico, Pennsylvania, and Vermont. More than one-half of buprenorphine-related emergency department (ED) visits are for the nonmedical use of the drug. The estimated number of ED visits related to the nonmedical use of buprenorphine has more than tripled, from 4,440 in 2006 to 14,266 in 2009. A recent study found that injecting drug users (IDUs) in Rhode Island were more likely to use diverted buprenorphine/naloxone to self-medicate while non-IDUs were more likely to use the diverted drug to get high. Regardless of whether diverted buprenorphine is being used nonmedically to self-treat opiate addiction or to get high, unmonitored use of diverted buprenorphine places users at serious risk for potential adverse health effects, especially when taken in combination with other opioids or with depressants such as sedatives, tranquilizers, or alcohol. (*Source: CESAR FAX, Vol. 20, Iss. 22, 24, 25, 26, 30, & 33*)

### **Policy changes that may decrease buprenorphine diversion and misuse**

The apparent increase in buprenorphine availability, diversion, and nonmedical use suggest the need for buprenorphine policy changes. First, current testing protocols, including those of medical examiners and drug testing programs, should include routine testing for buprenorphine to estimate the full magnitude of and to monitor buprenorphine diversion and misuse. Second, physician education programs for prescribing buprenorphine, especially strategies to detect and deter diversion and misuse, need to be strengthened. A recent study found that waived physicians had limited knowledge of buprenorphine pharmacology and legislative issues, suggesting that the mandatory 8-hour training required to obtain a waiver to prescribe buprenorphine may be inadequate (*See CESAR FAX, Volume 20, Issue 29*). CESAR will continue to monitor the diversion and abuse of buprenorphine and report on developments as they arise.

A Weekly FAX from the Center for Substance Abuse Research

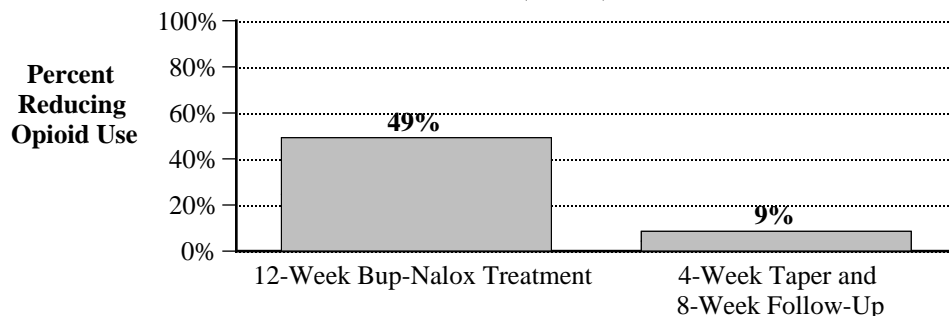
University of Maryland, College Park

## ***Clinical Trial Finds That While Buprenorphine-Naloxone Maintenance Reduced Other Opioid Use Among Those Dependent on Prescription Opioids, 91% Were Not Opioid-Free at Follow-Up***

*“Patients dependent on prescription opioids . . . are most likely to reduce their opioid use during the first several months of treatment while receiving buprenorphine-naloxone; if tapered off this medication, the likelihood of relapse to opioid use or dropout from treatment is overwhelmingly high” (p. E7).*

Long-term buprenorphine-naloxone treatment reduces opioid use by those dependent on prescription painkillers, according to the first randomized, controlled trial using a medication for the treatment of prescription opioid dependence. Nearly one-half (49%) of those receiving 12 weeks of treatment with the opioid buprenorphine-naloxone reduced their use of other opioids.\* However, eight weeks after the buprenorphine-naloxone treatment was tapered off and discontinued in accordance with the study protocol, only 9% had reduced their opioid use. Thus 91% of the study participants were not opioid-free at follow-up. According to the authors, “The high rate of unsuccessful outcomes after buprenorphine-naloxone taper is notable in light of the good prognostic characteristics of the population (i.e., largely employed, well educated, relatively brief opioid use histories, and little other current substance abuse) and previous research suggesting that patients dependent on prescription opioids might have better outcomes than those dependent on heroin” (p. E7). The authors suggest that future research look at “what length of buprenorphine-naloxone treatment, if any, would lead to substantially better outcomes after a taper” (p. E7). [Editors Note: The findings of likely relapse after cessation of buprenorphine-naloxone treatment are not surprising to us, as buprenorphine-naloxone treatment consists primarily of replacing one opioid with another and continuing the dependence.]

### **Percentage of Prescription Opioid-Dependent Persons Reducing Opioid Use After 12 Weeks of Buprenorphine-Naloxone Treatment and 12 Weeks of Taper/Follow-Up (N=360)**



\*Reduced opioid use was defined as abstaining from other opioids during the final week and during at least 2 of the previous 3 weeks of treatment or taper/follow-up. Abstinence was determined by urine test-verified self-reports; missing urine samples were considered positive for opioids. Opioids tested for included oxycodone, hydrocodone, hydromorphone, morphine, codeine, propoxyphene, and methadone.

SOURCE: Adapted by CESAR from Weiss, R.D., et. al., “Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence.” Archives of General Psychiatry, Online First November 7, 2011. Available online at <http://archpsyc.ama-assn.org/cgi/content/full/archgenpsychiatry.2011.121v1>. For more information, contact Dr. Roger Weiss at [rweiss@mclean.harvard.edu](mailto:rweiss@mclean.harvard.edu).

### ***CESAR FAX Special Series on Buprenorphine***

While research indicates that buprenorphine is an effective drug for treating opioid dependence, the potential for its nonmedical use and related unintended consequences may be going unnoticed. This series of publications, available at [www.cesar.umd.edu](http://www.cesar.umd.edu), was designed to highlight several indicators of the increased availability, diversion, and misuse of buprenorphine.

## *Drug Users, Treatment Providers, and Law Enforcement Officers Describe Increasing Suboxone<sup>®</sup> Misuse in Ohio*

Since 1999, the Ohio Substance Abuse Monitoring Network (OSAM) has been monitoring local substance abuse trends. Their most recent report, covering January to June 2011, indicates that the “availability of Suboxone<sup>®</sup> remains high in all regions, with the exception of Toledo where it remains moderately available” (p. 4). Obtaining Suboxone is described by another user as “super easy; Like candy machines, a dime a dozen” (p. 33). According to a treatment provider, Suboxone “is becoming easier to get than methadone” (p. 17). Following is a summary of Suboxone use in Ohio, in the words of users (U), treatment providers (TP), and law enforcement officers (LE). For more information on Suboxone (buprenorphine), see the *CESAR FAX Special Series: Buprenorphine*, available online at <http://www.cesar.umd.edu>.

**How Is Suboxone Obtained?** “You’ve got people at [12-step] meetings handing them [Suboxone] off. They’re being sold like any other drug” (TP, p. 4). “When they prescribe it . . . , they prescribe a lot of it, and people don’t use the whole prescription. They [users] would then sell it on the street” (LE, p. 82). “They’re [heroin addicts] getting Suboxone and turning around and selling it” (U, p. 66). “People pick up prescriptions [for Suboxone] and call [their dealer] and sell them” (U, p. 66). “The dealers will give them [users] a free Suboxone with their heroin. Customer satisfaction.” (TP, p. 82).

### **Why Is Suboxone Used?**

**Fight Withdrawal:** “[Some users] don’t want to get off [opioids] for good. They just want to not be sick, so they have Suboxone stashed away for when they feel sick” (TP, p. 115). “They [opiate addicts] use it . . . like Tylenol 3<sup>®</sup>, to use till they can get a fix. [Suboxone is] a drug of convenience” (TP, p. 83). “Some start off using it . . . to assist with withdrawal, but find that they like how it feels and become addicted” (TP, p. 34). “I quartered them [Suboxone] . . . to take the bare minimum, so I wouldn’t be sick, but that way I could still use an opiate; I would buy them . . . to come off other stuff, but it never worked that way. ‘Cuz you could get high off Suboxone if you hadn’t had any opiates in a couple of days . . . If you are addicted to opiates, you take the smallest piece of Suboxone—it makes you feel normal” (U, p. 133).

**Get High:** “If you are clean [opioid free], you will get very high from Suboxone” (U, p. 17). “For a buzz . . . can snort Suboxone, as long as you don’t have other opiates in the system” (U, p. 50). “If you are not addicted to opiates and you take a Suboxone, it’s very, very strong. It can make you high for three days” (U, p. 133). “People . . . will use Xanax<sup>®</sup> a half-hour before Suboxone and will get high. Some clients say the effects are as good as, or better than, that of OxyContin<sup>®</sup>” (TP, p. 17). “[A] lot of people are being introduced to opioids through Suboxone now because, if they were not Suboxone users, the buprenorphine . . . the active agent in Suboxone is giving them the opiate effect, and now they’re looking for stronger opioids. So now it’s . . . a gateway drug to opioid addiction” (TP, p. 133).

**Avoid Detection:** “Participants also reported that individuals who need to avoid detection of drug use on urine drug screens (probationers) use Suboxone because it is often not screened” (Report, p. 4). “[Suboxone is] the institutional drug of choice” (U, p. 17).

**How Is Suboxone Being Used?** “People typically put them . . . under their tongue, or they chew them up. I’ve actually witnessed a couple people shoot [inject] them up; I would eat the full 8 mg Suboxone” (U, p. 132). “I snorted it . . . when I would take it. It made me not sick” (U, p. 132). “Well, I shoot [Suboxone] in my neck, so, um, it goes straight to you, you know” (U, p. 133). “I do know a few people that when switched to the films [Suboxone strips], they say that those are a lot easier to shoot up [inject]. Yeah, ‘cause they dissolve in water; they dissolve completely, and I’ve heard people say that those actually work really well” (U, p. 133).

SOURCE: Adapted by CESAR from Ohio Department of Alcohol and Drug Addiction Services, *Ohio Substance Abuse Monitoring Network: Surveillance of Drug Abuse Trends in the State of Ohio, January-June 2011*, 2011. Available online at <http://www.odadas.state.oh.us/public/OsamHome.aspx>.