

CESAR *FAX* →

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

***CESAR FAX* Buprenorphine Series**

March 31, 2003 to December 15, 2014

(updated January 9, 2015)

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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 *CESAR FAX* issues on buprenorphine were designed to highlight 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 Buprenorphine Series
(updated 1/9/2015)

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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).

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.

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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. 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>.

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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. For more information, contact Erin Artigiani at erin@cesar.umd.edu or 301-405-9794.

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“Buprenorphine Treatment for Opioid Dependence”

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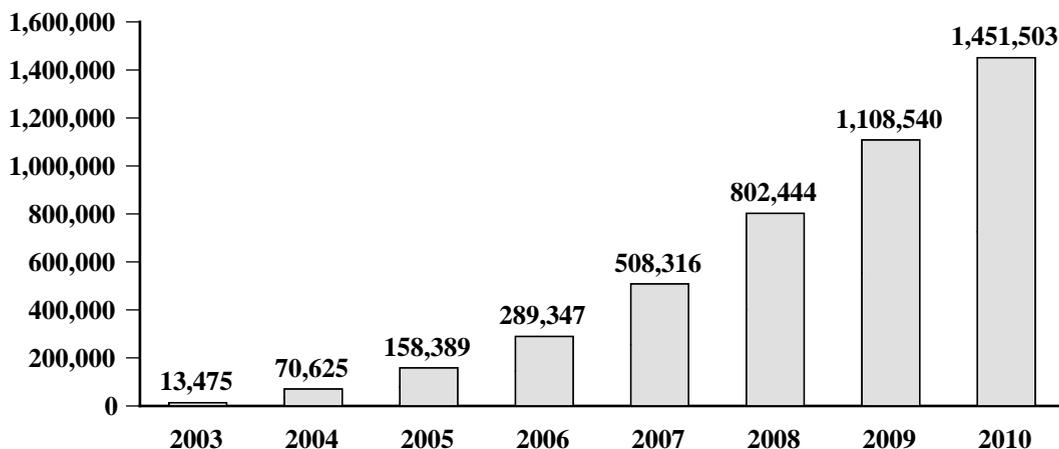
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U.S. Retail Distribution of Buprenorphine Approaches 1.5 Million Grams

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.

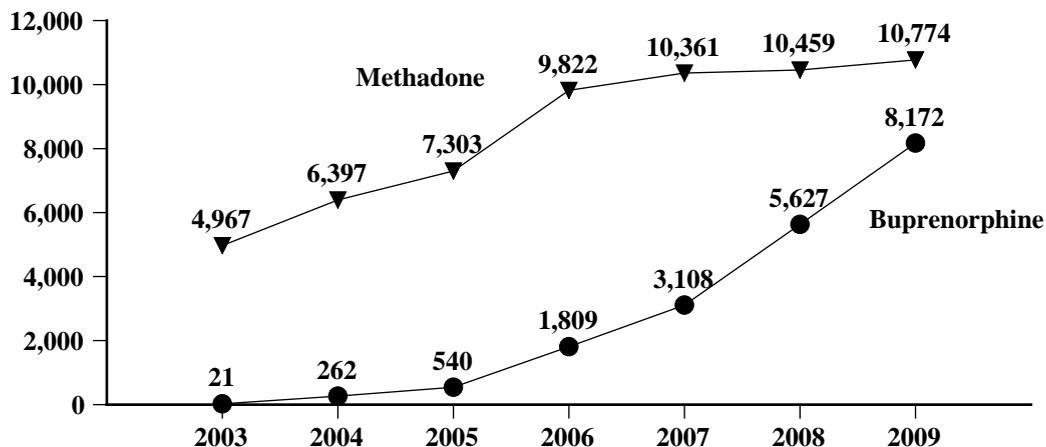
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Number of Law Enforcement-Seized Buprenorphine Items Analyzed by U.S. Labs Increases Dramatically

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); 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).

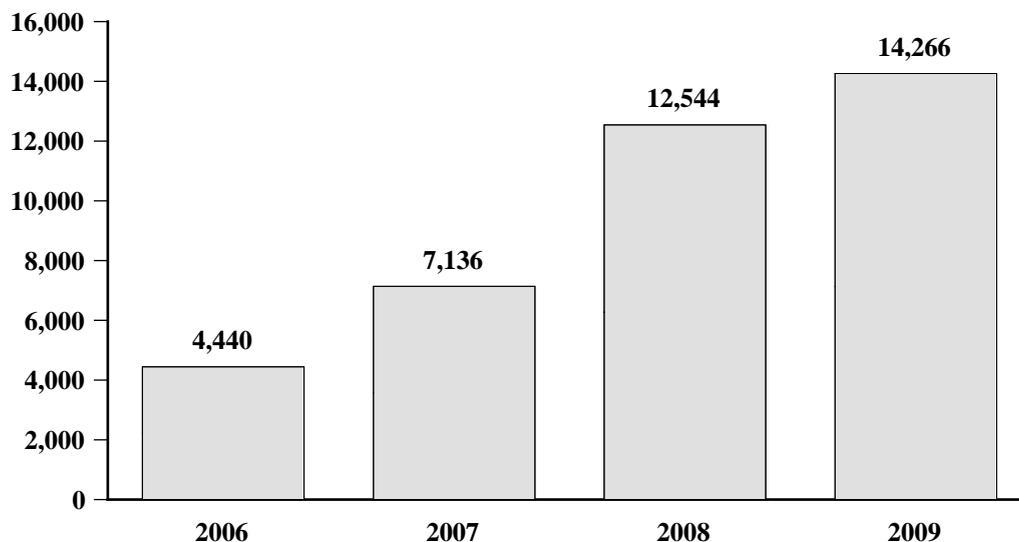
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Number of U.S. Emergency Department Visits Related to the Nonmedical Use of Buprenorphine More Than Triples Since 2006

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 (accessed 6/23/11).

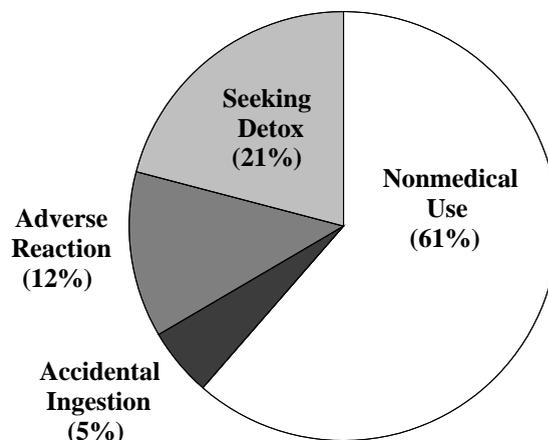
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61% of Buprenorphine-Related Emergency Department Visits for Nonmedical Use

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).

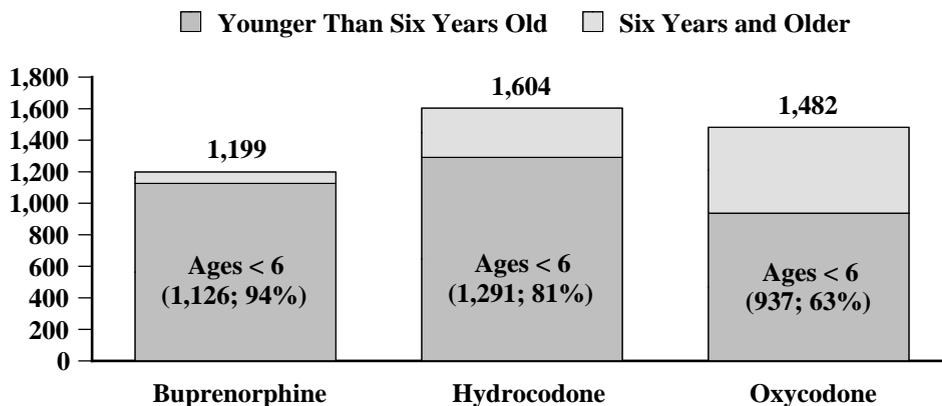
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Nearly All Emergency Department Visits for the Accidental Ingestion of Buprenorphine Occur in Children Under the Age of Six

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 oxycodone¹ (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 States² 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



¹Estimates 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.

²Pedapati, 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 (accessed 7/11/11).

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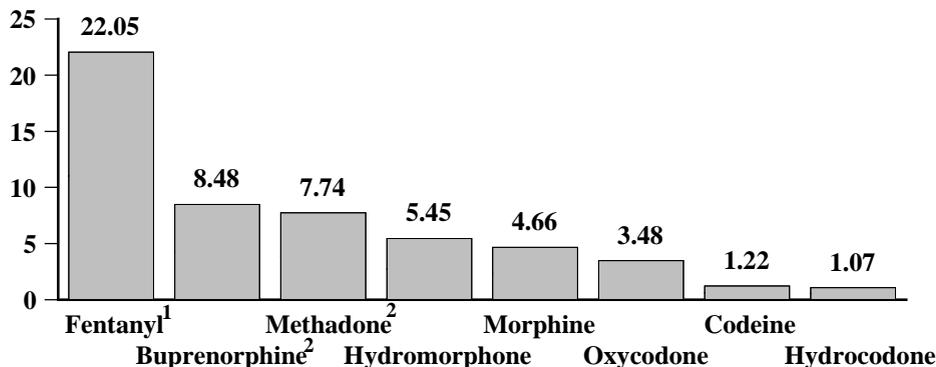
A Weekly FAX from the Center for Substance Abuse Research

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 fentanyl¹ 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 buprenorphine², 7.74 for methadone² 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



¹One 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).

²One 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 (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).

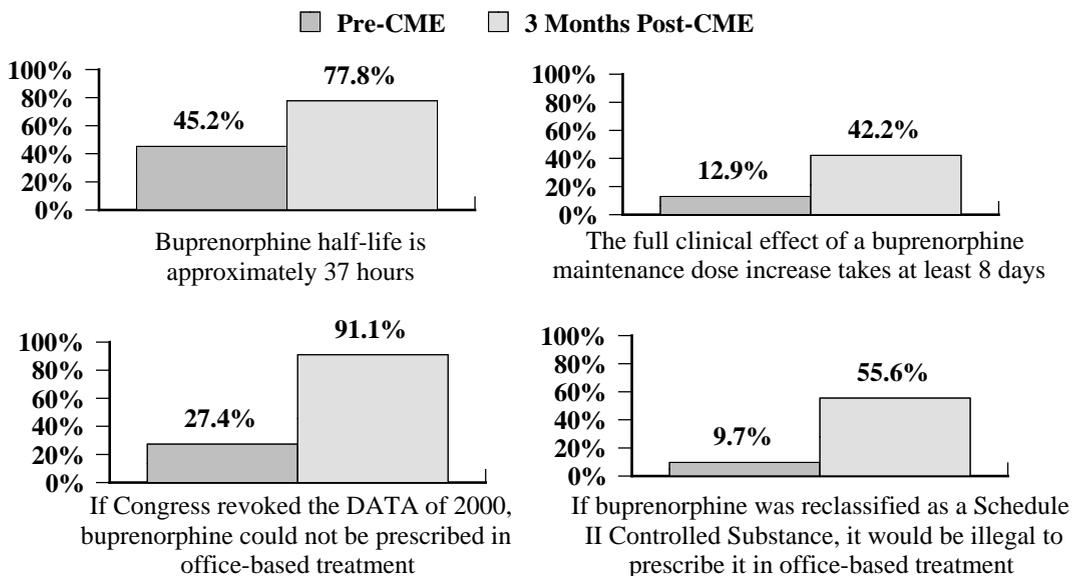
A Weekly FAX from the Center for Substance Abuse Research

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.

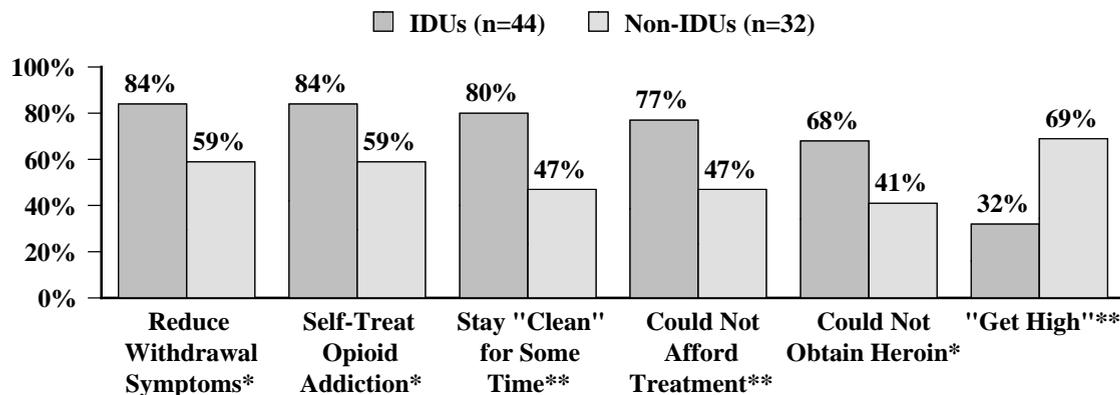
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Small Rhode Island Study Finds IDUs More Likely to Use Diverted Buprenorphine/Naloxone to Self-Medicate; Non-IDUs More Likely to Use to Get High

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.

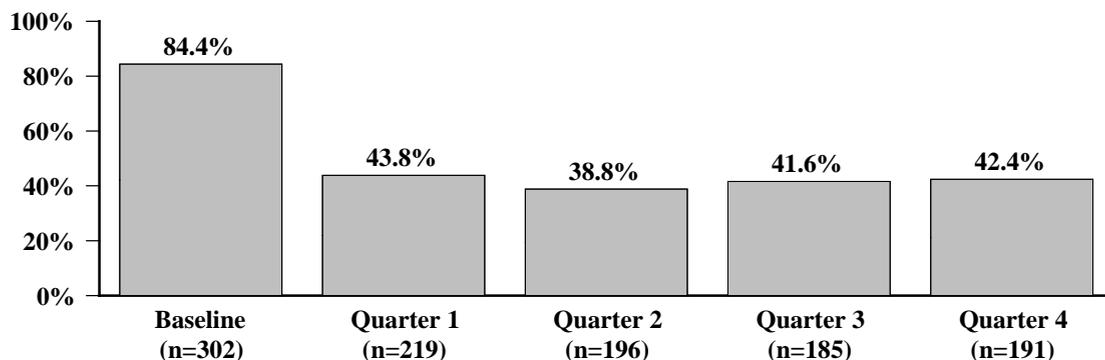
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University of Maryland, College Park

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.

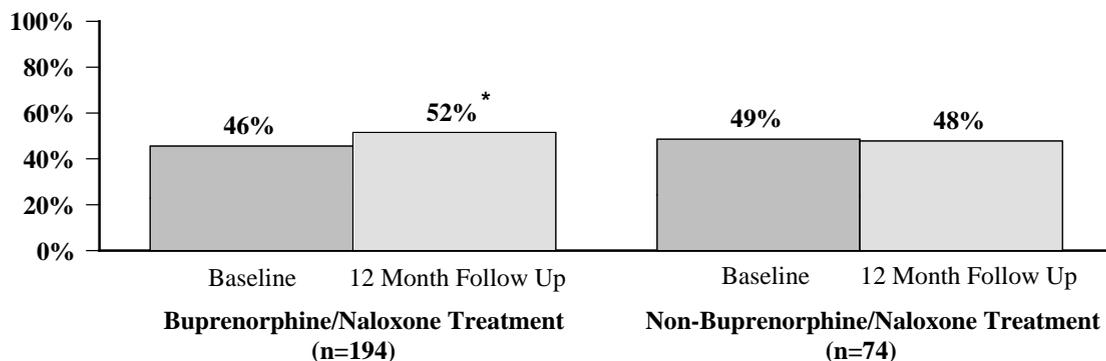
A Weekly FAX from the Center for Substance Abuse Research

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.

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University of Maryland, College Park

2011 Media Reports of Buprenorphine Diversion and Misuse

Date	State	Subject	Description
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

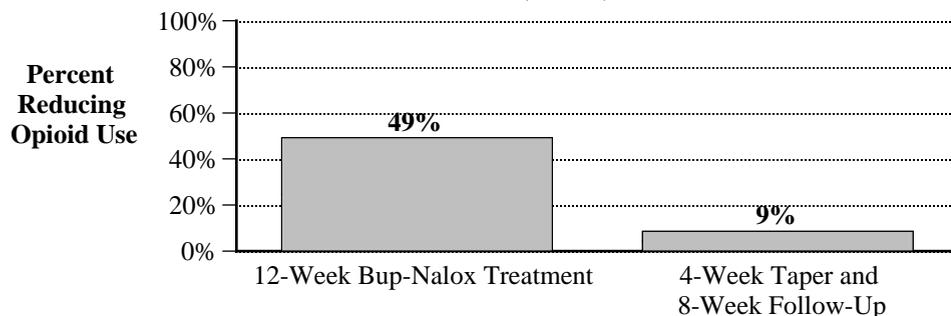
University of Maryland, College Park

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.

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, was designed to highlight several indicators of the increased availability, diversion, and misuse of buprenorphine.

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Drug Users, Treatment Providers, and Law Enforcement Officers Describe Increasing Suboxone[®] 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[®] 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[®], 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[®] a half-hour before Suboxone and will get high. Some clients say the effects are as good as, or better than, that of OxyContin[®]” (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>.

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

CESAR Publishes Report Warning of Emerging Epidemic of Buprenorphine Misuse

“Although the therapeutic benefits of buprenorphine treatment are well substantiated, it is important to recognize the unintended consequences of newly introduced analgesics, which have historically taken years to address. We need to act quickly to avoid suffering such consequences again” (p. 6-7).

Prior research has shown that criminal offenders’ drug test results can help identify emerging drug epidemics well before they become evident in surveys and other community indicators. CESAR staff recently pilot tested the Adult Offender Population Urine Screening (OPUS) Program in Maryland as a rapid, low-cost tool for detecting and assessing emerging local drug trends. In 2008, 1,061 urine specimens* originally collected and screened for 5 or fewer drugs by Maryland Division of Parole and Probation (DPP) agents were systematically sampled and sent to an independent laboratory for expanded testing for 31 drugs. The results showed an increase in the percentage of persons testing positive for buprenorphine since a smaller 2005 pilot study, and that these specimens often contained other drugs, suggesting possible misuse. Of the 98 specimens that tested positive for buprenorphine, 45% also contained two or more additional drugs and more than 60% contained other opioids (data not shown). The drugs most frequently found were morphine (45%), cocaine (27%), marijuana (19%), and benzodiazepines (19%; see figure below). Both other opioids and benzodiazepines could have lethal consequences if used with buprenorphine¹.

A unique benefit of OPUS is that it enables the identification of local areas where drug misuse may be emerging. Once specific hot spots are identified, follow-up interviews can provide concrete details about substance use that can be used to guide criminal justice and public health efforts. CESAR staff conducted interviews in 2010 with 15 supervisees in one of the six probation offices close to Baltimore that submitted a high percentage of buprenorphine-positive specimens. The supervisees reported wide-spread availability of buprenorphine in the street and in prisons. While the most frequently mentioned reason for using buprenorphine was for self-medication to manage withdrawal symptoms, several participants mentioned that buprenorphine could be used to get high or to enhance the effects of other drugs. Additional reports of the smuggling of buprenorphine into jails and diversion of the drug to the street have also been reported across the country².

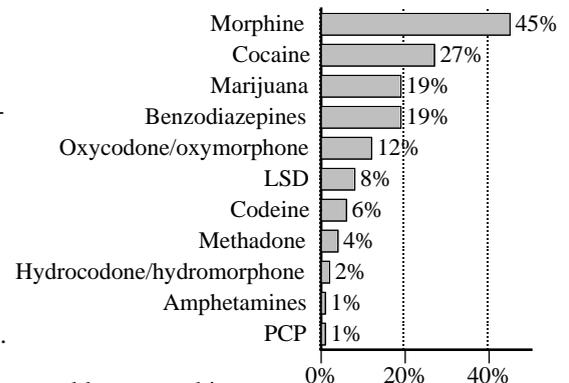
The Maryland Adult OPUS findings, combined with national indicators of increased buprenorphine availability, diversion, and nonmedical use, suggest that there may be an epidemic of buprenorphine misuse emerging across the U.S. Unfortunately, “current testing protocols do not routinely include buprenorphine and cannot inform us of the magnitude and scope of buprenorphine misuse. Thus, offenders smuggle the drug into jails and prisons because its use will go undetected and buprenorphine-related deaths cannot be tracked because medical examiners and coroners do not routinely test for the drug in most states” (p. 6). The authors recommend that “buprenorphine be added to all relevant drug testing regimens, if only to gauge the extent of diversion and misuse” (p. 6). In addition, the authors suggest that physician education programs “redouble their efforts to teach strategies to deter diversion and misuse of the drug” (p. 3) and that doctors closely monitor dosing “to ensure that the appropriate amount is prescribed, thereby reducing the likelihood of diversion” (p. 6). The OPUS model could be easily replicated in other states interested in tracking emerging prescription and other drug problems.

*To enhance the likelihood of detecting less commonly used drugs, we targeted random samples of 15 drug-positive specimens and 5 drug-negative specimens submitted by each DPP office.

¹Reckitt Benckiser Pharmaceuticals Inc., *Suboxone Tablet Product Information*, 2012. Available online at http://www.suboxone.com/pdfs/SuboxonePI_tablet.pdf. ²CESAR FAX, Volume 20, Issue 33 and *CESAR FAX Buprenorphine Series*, 2012. Available online at www.cesar.umd.edu.

SOURCE: Adapted by CESAR from Wish, ED, Artigiani, E, Billing, A, Hauser, W, Hemberg, J, Shippet, M, and DuPont, R, “The Emerging Buprenorphine Epidemic in the United States,” *Journal of Addictive Diseases* 31(1):3-7, 2012. Available online at <http://www.tandfonline.com/doi/abs/10.1080/10550887.2011.642757>. For more information, contact CESAR at cesar@umd.edu.

Percentage of Buprenorphine-Positive Specimens Testing Positive for Other Drugs, 2008 (N=98)



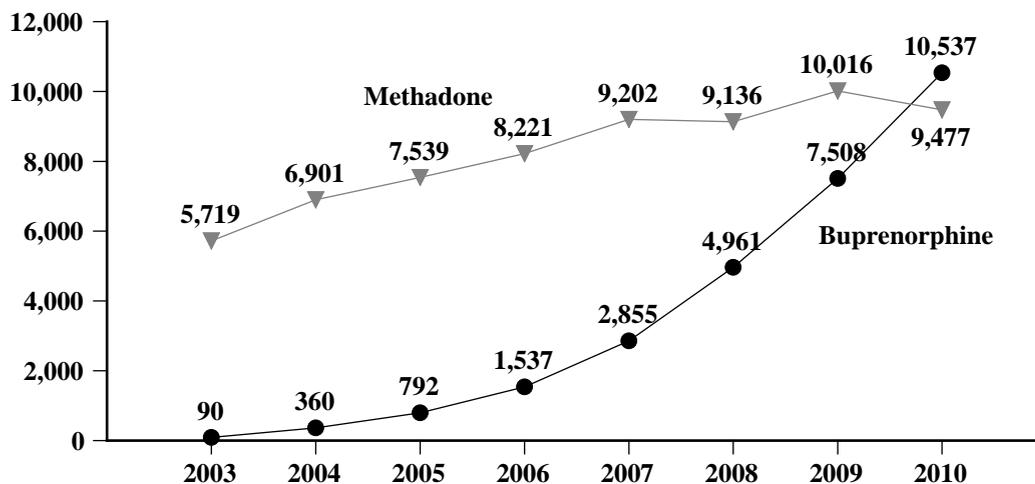
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Buprenorphine Now More Likely Than Methadone to Be Found in U.S. Law Enforcement Drug Seizures

Buprenorphine is now more likely than methadone to be found in law enforcement drug seizures that are submitted to and analyzed by forensic laboratories across the country, according to data from the National Forensic Laboratory Information System (NFLIS). NFLIS monitors illicit drug abuse and trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. From 2003 to 2009, the number of methadone reports increased gradually, reaching a peak of 10,016 in 2009, and then decreased slightly to 9,477 in 2010. In contrast, the number of buprenorphine reports has increased dramatically, from 90 in 2003, to 10,537 in 2010. Regardless of whether diverted buprenorphine is being used nonmedically to self-treat opiate addiction or to get high, unsupervised 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. The next issue of the *CESAR FAX* will discuss regional trends in buprenorphine drug seizures.

**Estimated Number of Total Methadone and Buprenorphine Reports,
U.S. Law Enforcement-Seized Drug Exhibits Analyzed by Forensic Laboratories, 2003-2010**



NOTES: Estimates are calculated using the National Estimates Based on All Reports (NEAR) methodology (see www.nflis.deadiversion.usdoj.gov/Reports.aspx). Annual data are based on drugs submitted to laboratories during the calendar year and analyzed within three months of the end of the calendar year. Up to three drugs can be reported for each drug item or exhibit analyzed by a laboratory. 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 data provided by the U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, Drug and Chemical Evaluation Section, Data Analysis Unit on 3/21/2012.

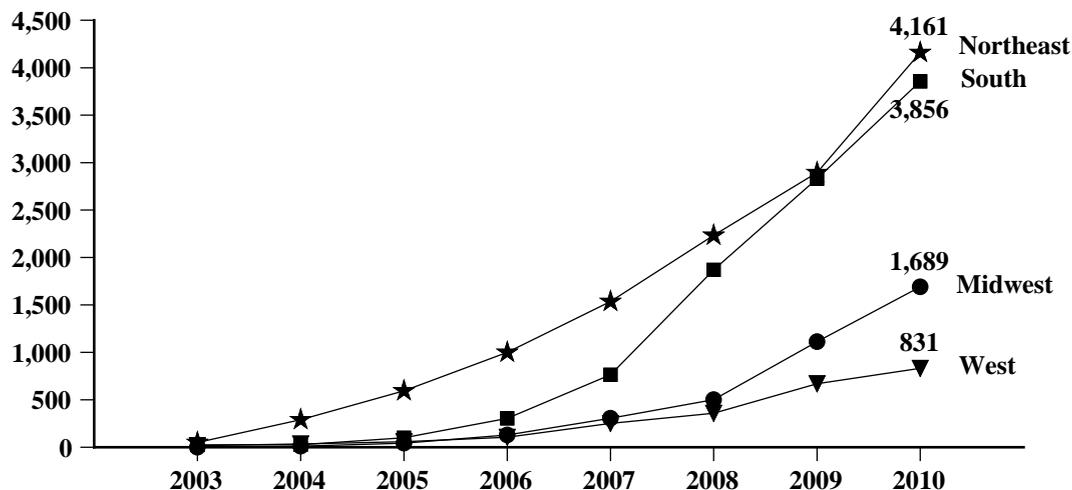
A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Northeastern and Southern Regions of Country Account for Largest Increases in Buprenorphine Found in Law Enforcement Drug Seizures

Since 2003, the amount of U.S. law enforcement-seized buprenorphine analyzed by state and local laboratories has increased dramatically, surpassing that of methadone (see *CESAR FAX*, Volume 21, Issue 13). According to data from the Drug Enforcement Administration (DEA)'s National Forensic Laboratory Information System (NFLIS), the largest increases have occurred in the Northeast (from 49 in 2003 to 4,161 in 2010) and the South* (from 25 to 3,856). The estimated number of buprenorphine reports in the Midwest and West have also increased, but at a slower pace and at lower levels. In 2010, there were an estimated 1,689 buprenorphine reports in the Midwest and 831 in the West.

**Estimated Number of Buprenorphine Reports,
U.S. Law Enforcement-Seized Drug Exhibits Analyzed by Forensic Laboratories,
by U.S. Census Region*, 2003-2010**



*Northeast: CT, MA, ME, NH, NJ, NY, PA, RI, VT

South: AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA WV

Midwest: IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI

West: AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY

Buprenorphine estimates for the South and West regions do not meet the DEA's standard of precision and reliability.

NOTES: Estimates are calculated using the National Estimates Based on All Reports (NEAR) methodology (see www.nflis.deadiversion.usdoj.gov/Reports.aspx). Annual data are based on drugs submitted to State and local laboratories during the calendar year and analyzed within three months of the end of the calendar year. Up to three drugs can be reported for each drug item or exhibit analyzed by a laboratory. 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 data provided by the U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, Drug and Chemical Evaluation Section, Data Analysis Unit on 3/21/2012.

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Study Describes Illicit Use of Buprenorphine Among Nonmedical Users of Opioids in Ohio

“Our study clearly indicates that non-medical use of buprenorphine has found a niche in the streets among illicit users of pharmaceutical opioids” (p. 206).

While buprenorphine misuse has been reported in many states, most studies have focused on opioid-dependent individuals, heroin users, and/or those in treatment. For example, an Ohio study of treatment providers, law enforcement officials, and drug users recruited through treatment programs found evidence of increasing buprenorphine misuse (see *CESAR FAX*, Volume 21, Issue 2). New research in Ohio now provides evidence of illicit use of buprenorphine among a population not previously studied—young adults not involved with heroin or injection drug use nor dependent on pharmaceutical opioids. Following are findings from this community-recruited sample* of young adults from the Columbus, Ohio area:

Knowledge About Buprenorphine: The majority of users reported that when they were first introduced to buprenorphine they had limited knowledge about the drug. Some had no idea it was used to treat opioid dependence and were told that it would work like any other pain pill.

Street Availability: While the majority of respondents reported that buprenorphine was more difficult to obtain than more commonly used prescription opioids (such as oxycodone or hydrocodone), several respondents reported that they felt the popularity of and demand for buprenorphine has been rising. Friends or acquaintances who were addicted to prescription opioids or heroin and networks of users with legitimate prescriptions were the most common sources of illicitly used buprenorphine. In fact, some users “expressed a belief that buprenorphine doses prescribed by physicians were too high for most patients who needed much lower amounts to control their withdrawal symptoms” (p. 205).

Use to Get High: While approximately one-half said that they took buprenorphine to get high, the reported effects ranged from no effect to too intense. Those who used buprenorphine to get high typically used it on very few occasions, either because the street availability was limited or they did not get the euphoric effects they expected or wanted. Some believed that you need to inhale buprenorphine and/or have a low tolerance to opiates to get high.

Use to Self-Medicate: About one-half reported using buprenorphine to self-medicate withdrawal symptoms*, using the drug regularly to replace their preferred opiates, to reduce their illicit pain pill use, or to quit altogether. Self-medication was preferred to going to a substance abuse treatment program because of the high cost of buprenorphine-based treatment at primary care, waiting lists at publicly-funded facilities, and the stigma related to seeking drug treatment.

*A total of 396 nonmedical users of pharmaceutical opioids ages 18-23 years old who were living in the Columbus, Ohio area were recruited using respondent-driven sampling. Participants had to 1) self-report the nonmedical use of prescription opioids at least 5 times in the past 90 days; 2) have no lifetime dependence on opioids; 3) have no history of heroin or injection drug use; 4) not have been in formal treatment in the last 30 days; 5) intend to use again nonmedically; and 6) not currently be awaiting trial or have pending criminal charges. Quantitative data were collected on all participants, qualitative data was collected on a subset of 51 individuals, and 20 of these were also interviewed 12-18 months after baseline.

SOURCE: Adapted by CESAR from Daniulaityte, R., Falck, R., and Carlson, R.G., “Illicit Use of Buprenorphine in a Community Sample of Young Adult Non-Medical Users of Pharmaceutical Opioids,” *Drug and Alcohol Dependence* 122(3):201-207, 2012. For more information, contact Raminta Daniulaityte at raminta.daniulaityte@wright.edu.

CESAR FAX Buprenorphine Series Updated Regularly and Available Online

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. CESAR has been closely following indicators of increased availability, diversion, and misuse of buprenorphine. The compilation of *CESAR FAX* issues related to buprenorphine is regularly updated as new issues are published and can be found online at www.cesar.umd.edu.

A Weekly FAX from the Center for Substance Abuse Research

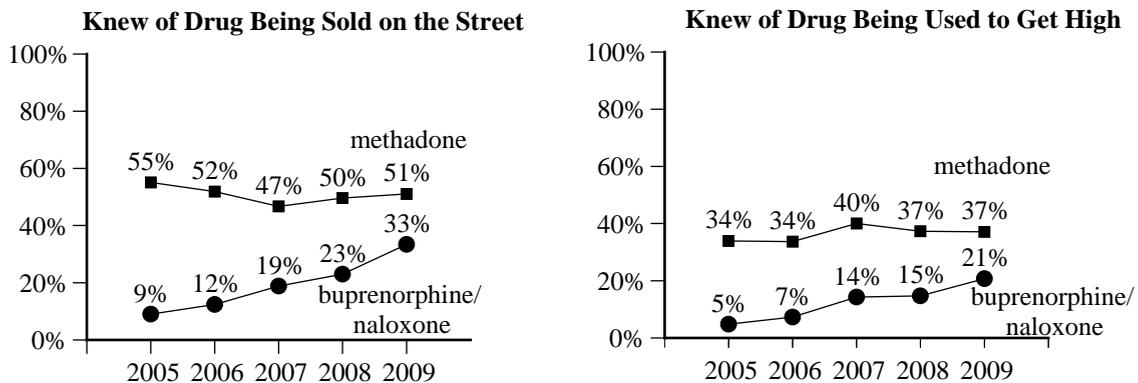
University of Maryland, College Park

One-Third of U.S. Treatment Applicants Report Buprenorphine/Naloxone Sold on Street; One-Fifth Report the Drug Is Used to Get High

“Diversion and abuse of buprenorphine/naloxone have steadily increased since 2005 through 2009,” according to data from a national post-marketing surveillance program* funded by the manufacturer. One of the indicators of diversion and abuse utilized by the surveillance program is a survey of nearly 19,000 applicants to 86 substance abuse treatment programs in 30 states. Both the percentage of applicants who reported knowing that buprenorphine/naloxone, which has been approved for opioid therapy since 2002, was sold on the street and those that reported knowing that the drug was used to get high increased from 2005 to 2009, reaching 33% and 21%, respectively. In comparison, the percentage who reported that methadone, which has been used since the 1950s for opioid therapy, was sold on the street or used to get high has remained relatively stable over the past three years (see figure below). The authors note that “the increases in diversion and abuse measures indicate the need to take active attempts to curb diversion and abuse as well as continuous monitoring and surveillance of all buprenorphine products” (p. 190).

Percentage of Applicants to U.S. Treatment Programs Who Knew of Methadone and Buprenorphine/Naloxone Being Sold on the Street or Being Used to Get High, 2005-2009

(n=18,956 from 2005 to 2009)



*Conducted for Reckitt Benckiser Pharmaceuticals by an independent contractor, the Surveillance of Diversion and Abuse of Therapeutic Agents (SODATA) utilizes several national indicators of diversion and abuse combined with a survey of applicants to substance abuse treatment programs and a survey of CSAT-certified physicians.

**Surveys were conducted at 86 treatment programs (both providing and not providing pharmacotherapy) from 30 states providing a total of 18,956 completed surveys from 2005 to 2009. While the treatment applicant survey was not a probability sample, the demographic characteristics of the applicant sample were similar to that of the national census of publicly-funded treatment admissions. The applicant survey does not estimate either the incidence or the prevalence of diversion/abuse, but it is an indication of changes in perception of diversion/abuse among a population likely to be knowledgeable about illegal markets through their own experiences, that of others, and direct observations.

See Wish, ED, Artigiani, E, Billing, A, Hauser, W, Hemberg, J, Shilet, M, and DuPont, R, “The Emerging Buprenorphine Epidemic in the United States,” *Journal of Addictive Diseases* 31(1):3-7, 2012 for more information on buprenorphine diversion and abuse.

SOURCE: Adapted by CESAR from Johanson, C-E; Arfken, C. L.; di Menza, S.; and Schuster, C. R., “Diversion and Abuse of Buprenorphine: Findings from National Surveys of Treatment Patients and Physicians,” *Journal of Drug and Alcohol Dependence* 120:190-195, 2012. For more information, contact Chris-Ellyn Johanson at cjohans@med.wayne.edu.

A Weekly FAX from the Center for Substance Abuse Research

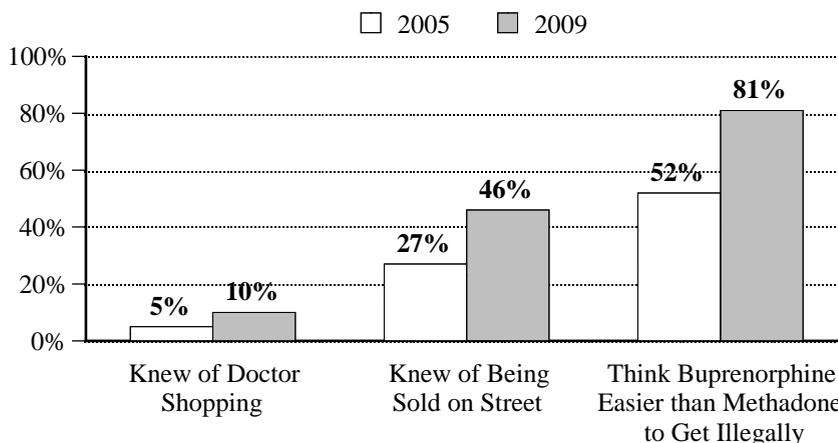
University of Maryland, College Park

Majority of Buprenorphine-Certified Physicians Think Buprenorphine Is Easier to Get Illegally Than Methadone

Physicians who are certified to prescribe buprenorphine are increasingly likely to perceive diversion and abuse of the drug, according to a survey funded by the manufacturer as part of a national post-marketing surveillance program*. Nearly one-half (46%) of physicians certified to prescribe buprenorphine in 2009 knew of buprenorphine products being bought or sold on the street, compared to 27% in 2005. In addition, a majority (81%) of the physicians surveyed believed that buprenorphine was easier than methadone to buy on the street in their community in 2009, a 56% increase from 2005 (see figure below). Forty-four percent reported that they knew someone who used illegal buprenorphine/naloxone to manage opioid withdrawal, 34% for maintenance until entering treatment, 17% to try out its effect, and 7% to get high (data not shown). The authors suggest that “the increase in diversion may be driven by the increase in abuse” (p. 194), as evidenced by the increasing percentage of treatment applicants who said they knew of buprenorphine being used to get high (from 5% in 2005 to 21% in 2009; see *CESAR FAX*, Volume 21, Issue 25). However, the increase in diversion may also “be driven by therapeutic demand, suggesting treatment expansion may be necessary. Finding a balance between diversion and abuse of a medication versus expanded treatment remains a challenge” (p. 194).

Perceptions of Buprenorphine Diversion/Misuse, Physicians Federally Certified to Prescribe Buprenorphine

(n=8,194 from 2005 to 2009)



*Conducted by an independent contractor for Reckitt Benckiser Pharmaceuticals, the Surveillance of Diversion and Abuse of Therapeutic Agents (SODATA) utilizes several national indicators of diversion and abuse combined with a survey of applicants to substance abuse treatment programs and a survey of CSAT-certified physicians. A total of 8,194 quarterly surveys were conducted with randomly-selected physicians federally-certified to prescribe buprenorphine from 2005 to 2009.

See Wish, ED, Artigiani, E, Billing, A, Hauser, W, Hemberg, J, Shilet, M, and DuPont, R, “The Emerging Buprenorphine Epidemic in the United States,” *Journal of Addictive Diseases* 31(1):3-7, 2012 for more information on buprenorphine diversion and abuse.

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A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Estimated Number of Buprenorphine- and Hydromorphone-Related ED Visits More Than Doubles from 2006 to 2010

The estimated number of emergency department (ED) visits related to the nonmedical use of opioid pain killers increased 79% from 201,280 in 2006 to 359,921 in 2010, according to the most recent data from the Drug Abuse Warning Network (DAWN). The greatest increases were seen in buprenorphine- and hydromorphone-related ED visits. In 2006, the nonmedical use of buprenorphine was involved as either a direct cause or a contributing factor in an estimated 4,440 ED visits, compared to 15,778 in 2010—an increase of 255%. The estimated number of visits related to the nonmedical use of hydromorphone increased 161% over the same 5-year period (see figure below). While the number of ED visits for the nonmedical use of buprenorphine and hydromorphone is relatively small compared to other opioid pain relievers, the magnitude of the increase suggests that there may be emerging problems with the nonmedical use of these drugs that warrant the monitoring of their use and related consequences.

Estimated Number of U.S. Emergency Department Visits Related to the Nonmedical Use of Opioid Pain Relievers, 2006 to 2010

Drug Name (Common Brand Names)	Number of ED Visits for Nonmedical Use		Percent Change 2006 to 2010
	2006	2010	
Buprenorphine (Suboxone, Subutex, Temgesic, Buprenex)	4,440	15,778	+255%
Hydromorphone (Palladone, Dilaudid)	6,780	17,666	+161%
Oxycodone (Oxycontin, Percodan, Percocet)	64,891	146,355	+126%
Hydrocodone (Vicodin, Lorcet, Lortab)	57,550	95,972	+67%
Methadone (Methadose)	45,130	65,945	+46%
Morphine (MS Contin, Morphine IR)	20,416	29,605	+45%
Propoxyphene (Darvon)	6,220	8,832	+42%
Fentanyl (Actiq, Duragesic)	16,012	21,196	+32%
Codeine (Tylenol with Codeine)	6,928	7,928	+14%
Meperidine (Demerol)	1,440	1,151	-20%
Total Opioid Pain Relievers	201,280	359,921	+79%

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. Five categories of opioid pain relievers (dihydrocodeine, opium, pentazocine, phenacetin, and all other narcotic analgesics) were not included in the above table because the estimate for either 2006 and/or 2010 did not meet standards of precision (relative standard error greater than 50% or an unweighted count or estimate less than 30).

SOURCE: Adapted by CESAR from Substance Abuse and Mental Health Services Administration (SAMHSA), *National Estimates of Drug-Related Emergency Department Visits, 2004-2010 - Nonmedical Use of Pharmaceuticals*, 2012. Available online at <http://www.samhsa.gov/data/DAWN.aspx#DAWN%202010%20ED%20Excel%20Files%20-%20National%20Tables>.

CESAR Responds to NPR's Story on Suboxone

CESAR's Director was recently interviewed for NPR's July 31st Planet Money episode, "The Anti-Addiction Pill That's Big Business For Drug Dealers." A podcast of the episode and CESAR's expanded comments about the segment are available at <http://www.npr.org/blogs/money/2012/07/31/157665908/episode-391-the-anti-addiction-pill-thats-big-business-for-drug-dealers> (sort comments by "oldest first" and CESAR's is the fourth comment).

A Weekly FAX from the Center for Substance Abuse Research

University of Maryland, College Park

Thus Far in 2012 More Than One-Half of U.S. States Have Had Media Reports of Buprenorphine Misuse or Diversion

There were a total of 186 media reports of buprenorphine misuse or diversion from January 1 to August 31, 2012, according to an update of an informal analysis first conducted by CESAR in 2011 (see *CESAR FAX*, Volume 20, Issue 33). The most common types of media reports were of persons possessing (56%) or selling (25%) buprenorphine, often along with other drugs such as prescription opioids and benzodiazepines, marijuana, heroin, and cocaine. There were also reports of smuggling into correctional institutions (14%), diversion by theft and fraud (8%), and use by children (3%). More than one-third (35%) of the media reports involved other drugs and approximately one-fifth (19%) involved other crimes, including trafficking of other drugs, burglary, and robbery. Massachusetts had the highest number of media reports (39), followed by New York (24), Maine (19), Pennsylvania (15), Kentucky (14), and New Hampshire (14). Below is a list of the 27 states and one territory that had at least one buprenorphine media report in the first eight months of 2012, the total number of media reports per state, and a brief description of one of the media reports. The full list of media reports is available online at www.cesar.umd.edu.

Selected Articles from U.S. States Reporting on Buprenorphine Misuse or Diversion, January-August 2012

(N=186 media reports in 27 States and 1 Territory)

State	Total # of Articles	Example Article Subject	Example Article Description
AK	1	possession	Man arrested for possession of methadone, Xanax, and Suboxone. <i>("Alaska Department of Public Safety Issues Trooper Dispatches," Targeted News Service, 6/6/12)</i>
AL	1	possession	Woman found in possession of Suboxone when arrested for distribution of methadone and hydrocodone to undercover officer. <i>("Woman Arrested on Drug Counts," Chattanooga Times Free Press, 1/21/12)</i>
CA	5	possession	Two people found to be in possession of Suboxone pills after being arrested for felony drug sales. ("Meth, Pot, Heroin Found at Eureka Home Today," <i>Eureka Times Standard</i> , 4/11/12)
CO	1	death	Man died with cocaine, Xanax, Subutex and alcohol in his system; buddies drove around with him dead in car and used his credit cards. <i>("2 Colo. Men Get Probation in Real-Life 'Weekend at Bernie's' Case," Gannett News Service, 3/9/12)</i>
CT	3	possession, selling	Man charged with possession of 40 grams of powdered cocaine, 4 oxycodone tablets, 1 Suboxone tablet, and 3 Suboxone strips. <i>("Drug Probe Leads to Arrest of West Haven Man," New Haven Register, 7/11/12)</i>
DE	1	possession	Two men charged with possession of 125 grams of heroin, 10 Suboxone films, 40 hydroxyzine pills, 19 grams of marijuana, and three shotguns. <i>("Drug Arrests In Angola by The Bay," Cape Gazette, 6/1/12)</i>
FL	1	use by child	Two persons charged with giving two children Buprenorphine. <i>("Two Charged with Giving Drugs to Children," Northwest Florida Daily News, 6/7/12)</i>
IN	6	smuggling into jail/prison	Correctional officer smuggled 80 Suboxone strips and 280 grams of marijuana into prison. <i>("Prison Guard Catches Coworker Trying to Smuggle Drugs," The Herald Bulletin, 2/24/12)</i>
KY	14	diversion	Home burglary in which a wallet, cell phone and Suboxone strips were stolen. <i>("Brief: Woman Reports Assaults, Thefts," The Daily Independent, 8/13/12)</i>
MA	39	possession	Woman charged with drug trafficking and possession of marijuana, heroin, and Suboxone. <i>("DA: Falmouth Woman Deals Drugs with Baby in Car," The Associated Press State & Local Wire, 2/7/12)</i>

Table continued on second page.

SOURCE: CESAR search of LexisNexis Academic database for "All News" in the "United States" with the terms "buprenorphine," "Suboxone," "Subutex," "Butrans," or "Buprenex." Only articles describing misuse or diversion were included. Only one article per news report/incident was included. If two unrelated incidents were reported in one article (e.g., "Police Beat" articles), each incident was counted individually. The state listed is the state in which the incident occurred.

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University of Maryland, College Park

Selected Articles from U.S. States Reporting on Buprenorphine Misuse or Diversion, January-August 2012

(N=186 media reports in 27 States and 1 Territory)

Table Continued

State	Total # of Articles	Example Article Subject	Example Article Description
MD	3	selling	Man arrested for drug distribution; hundreds of pills found in home, including Suboxone, methadone, Xanax, and oxycodone. ("Police Beat," <i>The Capital</i> , 1/11/12)
ME	19	selling	Suboxone tablets, heroin, and drug paraphernalia found in home of man arrested for drug trafficking. ("Southwest Harbor Man Gets 9 Years for Dealing Drugs," <i>Bangor Daily News</i> , 6/7/12)
MN	1	possession	Woman charged with possession of 8 tablets of Suboxone and methamphetamine. ("Minneapolis Firefighter from Coon Rapids Sold Meth Out of Fire Station, Court Papers Say," <i>St. Paul Pioneer Press</i> , 3/28/12)
MS	5	selling	Man sold Suboxone to an undercover police officer. ("Two Arrested for Separate Drug Sale Cases," <i>Picayune Item</i> , 3/28/12)
NC	1	possession, selling	Three women arrested on prostitution charges also charged with possession and selling of marijuana, morphine, alprazolam and Suboxone. ("Police Bring Prostitution Charges," <i>Times-News</i> , 5/14/12)
NH	14	selling	Man charged with sale of Suboxone. ("8 Arrests Made in Nashua Drug Sweep in Wake Of Probe," <i>The Union Leader</i> , 5/31/12)
NJ	2	possession	Man charged with possession of Suboxone and heroin after motor vehicle stop. ("Police Blotter," <i>Glen Rock Gazette</i> , 8/31/12)
NM	6	smuggling into jail/prison	Woman charged with attempting to smuggle 59 strips and 5 tablets of Suboxone to an incarcerated individual. ("Woman Charged with Attempt to Smuggle Drugs at Las Cruces Prison," <i>Las Cruces Sun-News</i> , 8/27/12)
NY	24	selling	Woman charged with selling Suboxone and oxymorphone, for which she was prescribed. ("Niagara Police & Courts," <i>Buffalo News</i> , 6/22/12)
OH	3	possession	Man in possession of 6 grams of marijuana, 11 Xanax pills and 1 Suboxone pill after intoxicated driving traffic stop. ("Police: Children, Drugs Inside Car During OVI Stop," <i>Dayton Daily News</i> , 7/28/12)
PA	15	possession, selling	Man arrested for possession and sale of Suboxone and DMT. ("Erie County Man Arrested Following Search of Suspected 'DMT' Drug Lab in Girard," <i>States News Service</i> , 1/11/12)
Puerto Rico	1	smuggling into jail/prison	Woman attempted to smuggle 30 Suboxone pills, 100 Suboxone strips, and 13 grams of marijuana into federal detention center. ("Visitor Arrested for Attempting to Smuggle Contraband into Metropolitan Detention Center," <i>Justice Department Documents and Publications</i> , 3/19/12)
RI	4	possession	Two charged with possession of Suboxone, as well as possession of heroin, marijuana, and receiving stolen goods. ("Detective Bureau," <i>US State News</i> , 3/9/12)
TN	2	diversion, selling	Woman charged with using TennCare benefits to purchase Suboxone and then selling to an undercover agent. ("Overton County Drug Round-Up Includes TennCare Fraud Charges," <i>States News Service</i> , 2/14/12)
VA	7	selling	Two charged with distribution of Suboxone and crack cocaine. ("Bristol, VA Grand Jury Returns More Than 100 Drug Charges," <i>Bristol Herald Courier</i> , 5/23/12)
VT	1	use by child	Man pled guilty to child cruelty after one-year-old daughter swallowed Suboxone pill that he had bought illegally. ("Vt. Dad Admits He Left Out Pill, Baby Swallowed It," <i>The Associated Press State & Local Wire</i> , 3/12/12)
WA	3	possession	Man arrested on drug charges and trafficking in stolen property after his home was searched and police found Suboxone, heroin, marijuana, mushrooms, firearms and stolen property. ("Drug Trade Cleaned Up in S-W," <i>Skagit Valley Herald</i> , 3/23/12)
WV	3	possession	90 Suboxone pills found as part of seizure of more than 7,100 prescription pills. ("Officers Seize Cache of Pills: Drug Unit Detectives Nab More Than 7,100 Prescription Pills in Separate Traffic Stops," <i>Charleston Daily Mail</i> , 2/23/12)

SOURCE: CESAR search of LexisNexis Academic database for "All News" in the "United States" with the terms "buprenorphine," "Suboxone," "Subutex," "Butrans," or "Buprenex." Only articles describing misuse or diversion were included. Only one article per news report/incident was included. If two unrelated incidents were reported in one article (e.g., "Police Beat" articles), each incident was counted individually. The state listed is the state in which the incident occurred.

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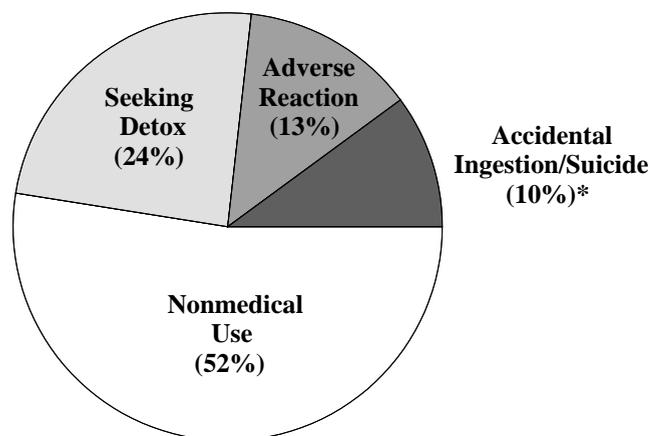
University of Maryland, College Park

One-Half of Buprenorphine-Related Emergency Department Visits for Nonmedical Use

Slightly more than one-half (52%) of the estimated 30,135 buprenorphine-related emergency department visits in the U.S. in 2010 were for nonmedical use of the drug, according to data from the Drug Abuse Warning Network (DAWN). Approximately one-fourth of these visits, in which buprenorphine was involved as either a direct cause or a contributing factor, were related to seeking detoxification and 13% were for adverse reactions. The estimated number of emergency department visits related to the nonmedical use of buprenorphine has more than tripled since 2006 (see *CESAR FAX*, Volume 21, Issue 31).

Types of U.S. Buprenorphine-Related Emergency Department Visits, 2010

(N=30,135)



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. *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. *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. *Suicide* includes visits for overdoses, as well as suicide attempts by other means if drugs were involved or related to the suicide attempt.

*The number of buprenorphine-related ED visits categorized as accidental ingestion and 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). For this analysis, the two categories were combined and the percentage derived from the difference remaining after accounting for the categories that were known. Percentages do not sum to 100 due to rounding.

SOURCE: Adapted by CESAR from data from the Substance Abuse and Mental Health Services Administration (SAMHSA), *Drug Abuse Warning Network, 2010: Selected Tables of National Estimates of Drug-Related Emergency Department Visits*, online at <http://www.samhsa.gov/data/DAWN.aspx#DAWN%202010%20ED%20Excel%20Files%20-%20National%20Tables> (accessed 11/19/12).

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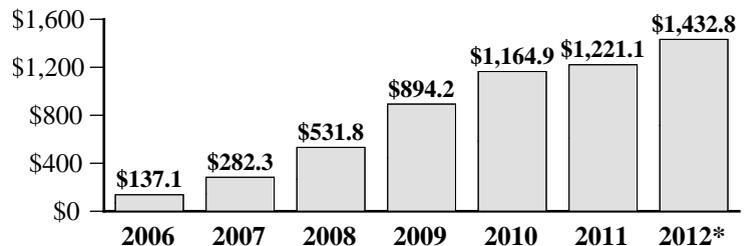
Suboxone® Sales Estimated to Reach \$1.4 Billion in 2012—More Than Viagra® or Adderall®

Sales data from the first three quarters of 2012 indicate that Suboxone retail sales in the U.S. will likely reach \$1.4 billion* this year—nearly a ten-fold increase over the \$137.1 million in sales in 2006 (see figure below). Suboxone currently has the 28th highest retail sales of all prescription drugs¹ in the U.S., up from 198th in 2006. Suboxone sales will likely continue to increase in light of new SAMHSA regulations allowing Opioid Treatment Programs (OTPs) to dispense a multiple days' supply of take-home buprenorphine, the main ingredient in Suboxone, to eligible patients without having to adhere to previous length of time in treatment requirements.² The steady and rapid increase in Suboxone sales suggests that the drug is being widely adopted in the treatment of opioid dependence, likely because of its effectiveness³ and because it can be prescribed in both private physicians' offices and OTPs.

While increased availability means that more opioid dependent persons are being treated, it is also likely that diversion and nonmedical use will increase. Prior issues of the *CESAR FAX* have indicated that buprenorphine is being diverted for use by those who do not have a prescription and that there has been an increase in the health-related consequences of nonmedical use of buprenorphine.³ Furthermore, a recent State of Florida medical examiner report⁴ found that the number of buprenorphine-related deaths had increased from 6 in 2009 to 27 in 2011 (compared to 62 heroin-related deaths in 2011). These figures likely underestimate buprenorphine-related deaths because, unlike heroin, buprenorphine is not systematically tested for by State of Florida medical examiners.

U.S. Retail Sales of Suboxone, 2006-2012*

(in millions of dollars)



*Sales for the 4th quarter of 2012 were estimated using the average of the first three quarters of 2012 (Q1: \$338.8; Q2: \$342.8; Q3: \$393.0)

Editor's Note: The true magnitude and scope of buprenorphine diversion, misuse, and adverse consequences is unknown because current epidemiologic measures do not systematically monitor buprenorphine. Routine drug testing protocols used by workplaces and the criminal justice system may not include buprenorphine. Similarly, buprenorphine-related deaths are not accurately tracked because medical examiners and coroners do not routinely test for the drug. *We believe that in order to maximize the effectiveness and legitimacy of buprenorphine as a treatment for opioid dependence, it is essential that adequate systems for monitoring potential diversion, misuse, and adverse consequences be put in place throughout the country.* According to the manufacturer, Suboxone “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.”⁵ Failure to adequately assess the potential risks of diversion and misuse could result in serious public health consequences and more limitations on the drug's use.

¹As ranked in the 3rd quarter of 2012. To put Suboxone sales in perspective with other commonly prescribed drugs, OxyContin was ranked 13th in the 3rd quarter of 2012, Viagra 48th, and Adderall XR 81st. Methadone did not rank in the top 100 in any year examined. Figures include sales through both retail and hospital channels. ²See http://www.ofr.gov/OFRUpload/OFRData/2012-29417_PI.pdf. ³See the *CESAR FAX Buprenorphine Series* (online at www.cesar.umd.edu). ⁴Florida Department of Law Enforcement, Medial Examiners Commission, *Drugs Identified in Deceased Persons by Florida Medical Examiners: 2011 Report*, October 2012. Online at http://www.fdle.state.fl.us/Content/getdoc/fa86790e-7b50-45f3-909d-c0a4759fefa8/2011-Drug-Report_Final.aspx (accessed 12/7/12). ⁵Reckitt Benckiser Pharmaceuticals Inc., “Suboxone Important Safety Information,” undated. Online at www.suboxone.com/patients/safety/Default.aspx (accessed 12/10/12).

SOURCE: Drugs.com, *Suboxone Sales Data*, November 2012. Online at <http://www.drugs.com/stats/suboxone> (accessed 12/7/12).

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Study Finds Persons Who Fill Buprenorphine Prescriptions Have Higher Rates of Medical Conditions Associated with Pain and Comorbid Psychiatric Disorders

Patients who fill buprenorphine prescriptions have higher rates of medical conditions associated with acute and chronic pain, according to a study of three large insurance claims databases. The most frequently diagnosed medical disorders among patients who filled buprenorphine prescriptions for Subutex®, Suboxone®, or buprenorphine hydrochloride sublingual were back problems (42%), other connective tissue disease (24%), and other non-traumatic joint disorders (20%), compared to less than 10% for each of these disorders among patients not filling a prescription for buprenorphine. In addition, buprenorphine patients were significantly more likely to fill prescriptions for other opiate agonists, antidepressants, benzodiazepines, muscle relaxants, and non-steroidal anti-inflammatory drugs in the 6 months prior to their buprenorphine initiation and had significantly higher rates of mood and anxiety disorders (see figure below). According to the authors, these findings suggest that “the population currently receiving buprenorphine treatment is complex” and that “these patients would benefit from integrated treatment that addresses their needs in a coordinated and comprehensive manner” (p. 6).

Editors Note: *It is unknown how many of the patients prescribed buprenorphine were being treated for opioid dependence, off-label for pain, or for comorbid opioid addiction and pain. However, the study also found that only 53% of buprenorphine recipients had a recorded diagnosis of opioid abuse/dependence in 6 months prior to their buprenorphine initiation, and only 62% had a recorded diagnosis of any substance abuse disorder (alcohol or other drugs). While the authors note that this “most likely reflects concerns about stigma and reimbursement, rather than lack of an actual substance abuse diagnosis” (p. 6), it is also possible that these patients received buprenorphine prescriptions for conditions other than opioid abuse and dependence.*

Comparison of Patients Who Received and Filled a Buprenorphine Prescription Through Private Insurance or Medicare to Patients Who Did Not Receive and Fill a Buprenorphine Prescription, 2007-2009*

Most Frequent:		Buprenorphine Prescription (n=8,715)	No Buprenorphine Prescription* (n=23,115)
Medical Diagnoses	Spondylosis, Intervertebral Disc Disorders, Other Back Problems	42%	7%
	Other Connective Tissue Disease	24%	7%
	Other Non-Traumatic Joint Disorders	20%	6%
Other Prescriptions Filled*	Other Opiate Agonists	69%	12%
	Antidepressants	47%	11%
	Benzodiazepines	47%	6%
	Muscle Relaxants (skeletal central)	28%	4%
	Non-Steroidal Anti-Inflammatory Drugs	25%	9%
Psychiatric Diagnoses	Mood Disorders	39%	5%
	Anxiety Disorders	23%	3%

*Patients with no buprenorphine prescription filled were an age/gender matched random sample. The most frequent prescriptions filled were filled in the six months prior to the date of the first buprenorphine prescription fill or the same time period for the comparison group. Similar results for all data were found for the Medicaid population but are not included in this publication. All differences were significant at p <.0001.

NOTES: Data were obtained from three insurance databases encompassing private, Medicare, and Medicaid insurance claims from 2007 to 2009. Each database captures all billed services, including prescription drugs, outpatient and inpatient care, and mental health and substance abuse services that are carved out to separate management companies.

SOURCE: Adapted by CESAR from Mark, T. L., Dilonardo, J., Vandivort, R., and Miller, K., “Psychiatric and Medical Comorbidities, Associated Pain, and Health Care Utilization of Patients Prescribed Buprenorphine,” *Journal of Substance Abuse Treatment* (In Press, Corrected Proof), available online 12/20/2012. For more information, contact Dr. Tami Mark at tami.mark@truvenhealth.com.

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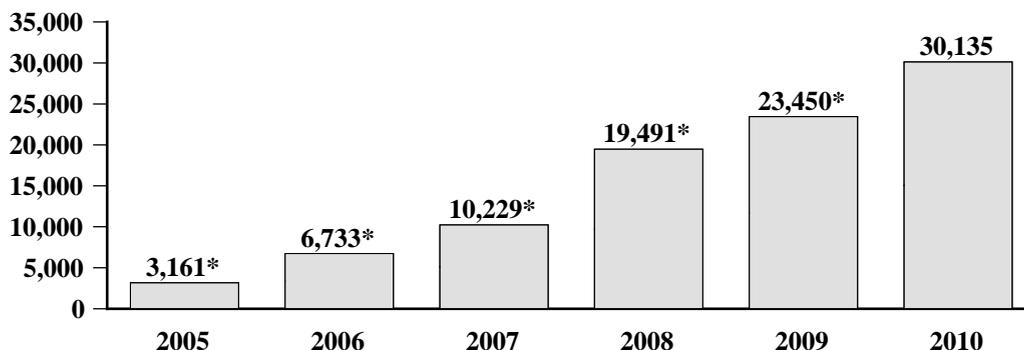
Number of U.S. Emergency Department Visits Involving Buprenorphine Increases Nearly Ten-Fold from 2005 to 2010

“Availability of buprenorphine is less restricted than other treatments for opioid dependence, such as methadone, which can only be administered in specialized clinics. Although this availability can increase access to treatment, it can also increase the potential for diversion and misuse by those who are not opioid dependent.

Such use can lead to buprenorphine dependence or abuse” (SAMHSA, p. 1).

The estimated number of emergency department visits in which buprenorphine was involved as either a direct cause or a contributing factor increased from 3,161 in 2005 to 30,135 in 2010, according to a recently released report from the Substance Abuse and Mental Health Services Administration (SAMHSA). More than half (52%) of these buprenorphine-related emergency department (ED) visits were for the nonmedical use of pharmaceuticals (see *CESAR FAX*, Volume 21, Issue 47). According to the authors, “the buprenorphine in these visits may have been misused or abused, either for psychoactive effects or in an attempt to self-treat for opioid dependence (without a prescription), or the buprenorphine may have been used appropriately but mixed with other drugs that were being abused or misused” (p. 3-4). The authors also suggest that “for patients who may be attempting to self-treat opioid dependence using buprenorphine without a prescription, expanding access to treatment and putting these patients in the care of a certified physician may help reduce the nonmedical use of buprenorphine and subsequent ED visits” (p. 6).

Estimated Number of U.S. Emergency Department Visits Involving Buprenorphine, 2005-2010



*The estimate was statistically significantly different from the estimate for 2010 at the .05 level.

NOTES: Emergency department visits involving buprenorphine are those in which buprenorphine was involved as either a direct cause or a contributing factor to the visit. Nonmedical use includes taking more than the prescribed dose of a prescription medication or more than the recommended dose of an over-the-counter (OTC) medication or supplement, taking a prescription medication prescribed for another individual, being deliberately poisoned with a pharmaceutical by another person, or misusing or abusing a prescription medication, an OTC medication, or a dietary supplement. In this report, buprenorphine refers to both buprenorphine alone and the buprenorphine-naloxone formulation.

SOURCE: Adapted by CESAR from data from Substance Abuse and Mental Health Services Administration (SAMHSA), “Emergency Department Visits Involving Buprenorphine,” *The DAWN Report*, January 29, 2013. Available online at <http://www.samhsa.gov/data/2k13/DAWN106/sr106-buprenorphine.pdf>.

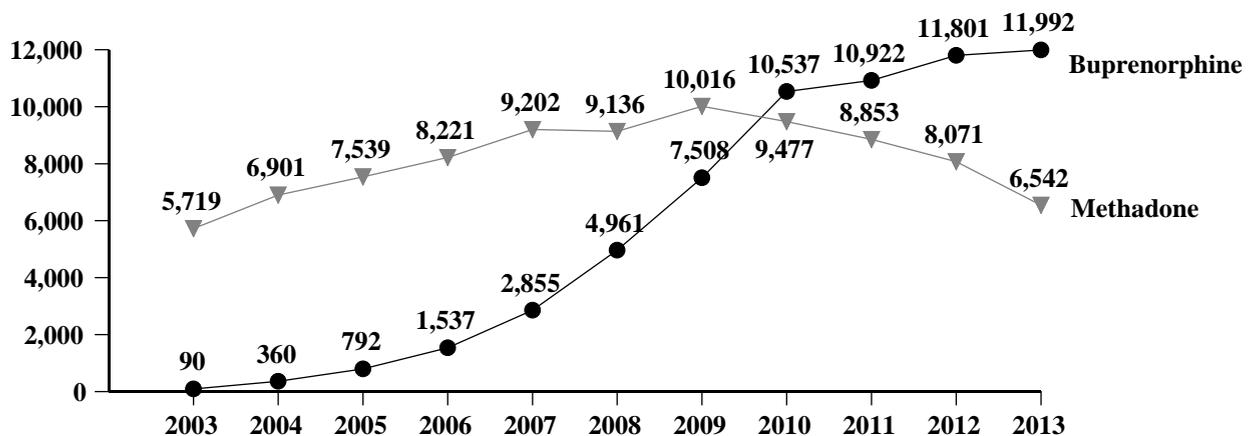
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More Buprenorphine Than Methadone Reports in 2013 NFLIS

The National Forensic Laboratory Information System (NFLIS) collects results from law enforcement-encountered drug items submitted to and analyzed by state and local forensic laboratories across the country. From 2003 to 2009, the number of methadone reports in NFLIS increased gradually, reaching a peak of 10,016 in 2009, and then decreased each year, reaching a low of 6,542 in 2013. In contrast, the number of buprenorphine reports increased from 90 in 2003 (one year after buprenorphine was approved to treat opioid dependence) to 10,537 in 2010, but has increased slowly each year since then, reaching a high of 11,992 in 2013. In 2013, the majority of buprenorphine reports were from the Northeast U.S. census region (8.10 per 100,000 population), while the West had the lowest number (1.8 per 100,000). More information about buprenorphine can be found in the *CESAR FAX Buprenorphine Series*, available online at <http://ter.ps/cesarbusp>.

Estimated Number of Total NFLIS Methadone and Buprenorphine Reports, 2003-2013



NOTES: Estimates are calculated using the National Estimates Based on All Reports (NEAR) methodology, which has strong statistical advantages for producing national and regional estimates. Estimates are based on drug cases and items submitted to participating state and local laboratories during the calendar year and analyzed within three months of the end of the calendar year. Up to three drugs can be reported for each drug item (or exhibit) analyzed by a laboratory. State and local policies related to the enforcement and prosecution of specific drugs may affect drug item submissions to laboratories for analysis. Laboratory policies and procedures for handling drug evidence may also vary. For example, some analyze all items submitted, while others analyze only selected items. Many laboratories do not analyze drug evidence if the criminal case was dismissed from court or if no person could be linked to the item. Thus, NFLIS data might underestimate the availability of drugs in the illicit market that state or local labs do not systematically identify.

SOURCES: Adapted by CESAR from data provided by the U.S. Drug Enforcement Administration (DEA), Office of Diversion Control, Drug and Chemical Evaluation Section, Data Analysis Unit and from NFLIS Annual Reports (available online at <https://www.nflis.deadiversion.usdoj.gov/Reports.aspx>).

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