

## **Prescription Drug Diversion Literature**

This is a summary of the results of a search for the terms ‘diversion’, ‘drug’, and/or ‘illicit’ in PubMed. The purpose of this summary is to prepare for research or articles relating to the diversion of drugs from their intended purpose to illicit use. This is a general review, no specific project is in mind.

Three primary areas of interest are found in the literature; background, including definition and extent of problem, control methods, and discussions of specific drugs or drug classes. We address each of these below. Following the review sections are listings of the abstracts cited.

### **Background**

The background section contains information about articles that address definitions, extent/prevalence, why drugs are diverted and who is involved. The latest article presented deals with a related topic: sharing.

### **Definition**

Many similar definitions are found in the literature. We find the one used by Inciardi et al. to be the most complete. “Prescription drug diversion involves the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace, and can occur along all points in the drug delivery process, from the original manufacturing site to the wholesale distributor, the physician's office, the retail pharmacy, or the patient.”[1]

### **Extent**

Data from recent national surveys and other published reports in a 2008 article indicate that the lifetime prevalence of non-medical prescription drugs use/abuse in the United States is approximately 20% (48 million persons aged  $\geq$  12 years). Public health concern is further heightened by a significant increase in past-month use among adolescents (3.3% of 12-17 year olds) and young adults (6.4% of 18-25 year olds) and the vulnerability of a growing elderly population.[2] In 1978 Goldman and Thistel reported on applicants to two metropolitan drug abuse programs and found a significant percentage of applicants had used illicit methadone prior to seeking treatment and that for the most part they were using “program methadone” presumably diverted from take-home medication from patients active in treatment programs.[3] In 1982 Piklis

found that pentazocine/tripelennamine combination is available to the illicit trade through theft or diversion from legitimate sources.[4] Smith and Woody report the nonmedical use of scheduled medications commonly prescribed for pain, pain-related symptoms, and psychiatric disorders began rising in the mid-1990s.[5] In 2004, Brushwood and Kimberline noted “Leaks of controlled substances from the closed system of distribution seem to be increasing as rapidly through theft and loss as through inappropriate prescribing and dispensing.”[6] Barrett et al. reported on methylphenidate misuse in a university student sample. One finding was that “Most of those who reported their source of methylphenidate obtained it from an acquaintance with a prescription.”[7] Also in 2005 Cicero et al. studied abuse of Oxycontin in the United States. They noted “Over the past 5 years, there have been reports, frequently anecdotal, that opioid analgesic abuse has evolved into a national epidemic. In this study, we report systematic data to indicate that opioid analgesic abuse has in fact increased among street and recreational drug users, with OxyContin and hydrocodone products the most frequently abused.”[8] Coleman et al. found a recent federal report indicates that prescription drug abuse is now the second leading category of illicit drug use, following marijuana use.[9] McCabe and Boyd investigate the sources of prescription drugs for illicit use and stated “The majority of respondents who were illicit users obtained their prescription drugs from peer sources.”[10] In another article on that study, McCabe found the leading sources of prescription stimulants for illicit use were friends and peers.[11] In a third article regarding that study, McCabe et al. found “The prevalence rate for illicit use within the past year was highest for pain medication, followed by stimulant medication, sedative or anxiety medication, and sleeping medication.”[12] Other statements regarding the extent of drug diversion include

- With the high rates of prescription drug abuse among teenagers in the United States, a particularly urgent priority is the investigation of best practices for effective prevention and treatment for adolescents, as well as the development of strategies to reduce diversion and abuse of medications intended for medical use.[13]
- Designer drugs and high content modified release formulations have been exploited both in casual recreational drug abuse as well as, on a much larger scale, by the criminal diversion of these products for profit.[14]
- However, because these are attractive, addicting drugs, diversion from sources such as physicians and pharmacists can lead to serious health problems. Of importance is that addiction to opiate medications can interfere with treatment of the original pain condition, and can lead to life threatening states because of poor judgment and depressed mood in the users.[15]
- data on this population's mechanisms of access to prescription opioids clearly suggest that there is an active black market for these drugs.[16]

- Sources of abused prescription drugs cited by focus group participants were extremely diverse, including their physicians and pharmacists; parents and relatives; "doctor shopping"; leftover supplies following an illness or injury; personal visits to Mexico, South America and the Caribbean; prescriptions intended for the treatment of mental illness; direct sales on the street and in nightclubs; pharmacy and hospital theft; through friends or acquaintances; under-the-door apartment flyers advertising telephone numbers to call; and "stealing from grandma's medicine cabinet"[1]
- While antipsychotic medications are not typically thought of as drugs with an abuse potential, reports of the use and diversion of intranasal quetiapine among prison inmates, i.v. quetiapine abuse, and this case report indicate otherwise[17]

### **Why drugs are abused and diversion occurs**

The reasons for using diverted drugs were not addressed in the medical literature until recently. Motives were studied by McCabe et al. in 2007. The three most common motives associated with the nonmedical use of prescription opioids were to relieve pain, get high, and experiment.[18] In a study of attention-deficit-hyperactivity disorder (ADHD) drugs, Arria et al. found among 225 nonmedical users, nonmedical use was infrequent and mainly associated with studying, although 35 (15.6%) used prescription stimulants to party or to get high.[19]

### **Who is diverting drugs?**

There is no specific class or type of people who can be blamed for the rise of diversion. The literature, however, has reported extensively on abusers, students and health care workers. Research, primarily descriptive, initiated with drugs abusers included nine articles.[1, 16, 20-27] Studies of student misuse of drugs were reported in ten research studies.[7, 10-12, 18, 28-32] The author responsible for most of these is Sean McCabe and others at the Substance Abuse Research Center, University of Michigan, Ann Arbor. A third focus of research studies in the literature is health care workers which accounted for fifteen articles.[33-47] In addition to these major groups, research includes a literature search for ADHD diversion. [48] A random-digit dialed telephone survey combined with the National Survey on Drug Use and Health [49] also focused on ADHD. In 2007 Boeuf and Lapryere-Mestre analysis 1,710 abnormal prescription forms to describe patterns of drug diversion.[50]

### **Sharing**

Goldsworthy et al. discuss a relatively new topic: prescription-medication sharing.[51] They note that sharing may be associated with two distinct and not mutually exclusive classes of consequences: those that arise from abuse and illegal use and those that arise from loss of warnings and instructions. Their survey revealed 22.9% reported having loaned their medications to someone else and 26.9% reported having borrowed someone else's prescription

## **Control**

A major topic in the literature is control of drugs to prevent diversion. In 1983 Feldman et al. conducted a survey of 100 randomly selected Massachusetts hospital pharmacies and found, similar to the findings of a nationwide study, many respondents reported selective inclusion of those Schedule III, IV, and V drugs possessing an increased risk of illicit diversion into a more controlled distribution system.[22] In 1990 Angarola discussed success of national and international regulation of opioid drugs in preventing diversion and noted a reduction of opioid abuse and related illegal activities. However, this may have limited availability to those who the drugs.[52] For more on this concern see Double Edge section below.

In 1991, Weissman and Johnson propose that existing multiple prescription regulations are effective in reducing drug abuse and diversion.[53] In 1992, Klein et al. found that hospitals with surgical satellite pharmacies had better accountability than in hospitals without them.[54] In 1993, Schmidt and Schlesinger describe a system that involves participation by anesthesiologists, operating room nurses, and pharmacists to accurately record amount and type of drugs dispensed, used, wasted, and returned. Periodic, random, qualitative, and quantitative analyses of drugs returned for wastage are performed. In the first 6 months in which the system was used, 6,336 patients were treated and no cases of drug diversion were discovered or suspected.[41] In 1994 McNutt et al. report on a system that required all benzodiazepines prescriptions in New York State to be reported. They found reduced prescriptions for this class of drug among elderly patients. In 2001 Forgione et al. describe various ways prescription drugs are diverted to the black markets, some monitoring programs employed by the states, and guidelines that doctors, pharmacists, and other providers can use to protect themselves against possible liabilities arising from the diversion of prescription drugs.[55]

Specific control systems are described in the literature. Smiledge and Davern report an anesthesia controlled substance dispensing system in 1984. Drug kits are dispensed by the pharmacy to the operating room and then to individual anesthetists. The system limits quantities of drugs available at one time and provides for clear individual account for drugs and the rapid detection and reconciliation of discrepancies.[36] A similar method was described by Maltby et al. in 1994.[56] They reported one case of drug diversion by a staff anesthetist in seven years. In 1993, Dodd describes OSTAR – Oklahoma Schedule II abuse reduction; an electronic point of sale diversion control system.[57] Also in 1993, Mirro et al. describe the Indiana system of multiple copy prescriptions that allow information to be gathered in a central location to track illicit drug use.[58] As part of their requirements for accreditation, the Joint Commission for Accreditation of Hospital Organization (JCAHO) includes include counting, checking and locking a methods to avoid diversion.[59] In 2001, Simoni-Wastila and Tomplins compare two specific control programs: multiple copy prescriptions and electronic data transfer systems.[60] In 2002 Manchikant and Singh discuss the National All Schedules Prescription Electronic Reporting Act (NASPER) as proposed by the American Society of Interventional Pain Physicians. Cicero et al. in 1005, describe a method to review use of Tramadol (Ultram, Ultracet).[8] Degenhardt et al. describe the Drug Monitoring System (DRUMS) run by the Australian Government and the Australian Illicit Drug Reporting System (IDRS) which were analyzed (2001-2004).[27]

The Xyrem Success Program (Xyrem Risk Management Program) is described by Fuller and Hornfeldt in 2003.[61] This program control distribution of sodium oxybate (Xyrem), a drug for the treatment of narcolepsy, which has a potential for being a substance of abuse. All prescriptions must be written through a web site operated by Express Scripts. Details of the program are also discussed by them in a 2004 article.[61] The development of opioid formulations with limited diversion and abuse potential are discussed by Fudala and Johnsoni 2006.[62] The Food and Drug Administration (FDA) required Othto-McNeil Pharmaceutical to monitor abuse and of their tramadol drugs.[63]. The Researched Abuse, Diversion and Addiction-related Surveillance (RADARS) system was developed to assess the abuse and diversion of OxyContin along with other opioids.[64] In 2007, the FDA was petitioned by citizens to require pharmaceutical companies manufacturing controlled substances to demonstrate and certify in their application materials for FDA approval of new drugs that they have made every effort to formulate the drug in such a way that avoids or at least minimizes the drug's potential for both intentional and unintentional abuse

without compromising its therapeutic effectiveness and (2) Requiring pharmaceutical companies to include proactive risk management plans in all new applications for controlled drugs, demonstrating strong evidence of a prescription drug's safety, as well as concrete steps that will be taken to prevent the abuse of the drug while maintaining its maximum therapeutic effectiveness.[65]

A few articles have discussed the use of lab tests to determine if diversion has occurred, especially with unused portions returned to the pharmacy. In 1995 Kingsbury et al. describe a method for quantitative analysis of fentanyl[66]; a drug also focused on by Holth et al. in 2002 who propose methodology to detect drugs in discarded syringes. In 2002, Cone and Preston focus on lab tests for methodone[67]; as do Gonzalez et al.[68] In 2004 Kurashima et al. describe the determination of origin of ephedrine used as precursor for illicit methamphetamine.[69] In 2005, Wolf and Pilakis describe a rapid high-performance liquid chromatographic (HPLC) procedure for analysis of analgesic pharmaceutical mixtures for quality assurance and drug diversion testing.[70] They note the method “has been applied to detect not only errors in the preparation of solutions of scheduled drugs, but also to uncover illegal diversion of drugs of abuse by medical personnel.”

A general problem of control systems was suggested by Hellawell in 1995. “Despite increasing collaboration between law enforcement authorities in different countries, illicit drug problems appear likely to increase in the future because of the vast profits available, continuing (and increasing) demand and more permissive attitudes concerning drugs among young people.” He suggest greater emphasis must be placed on diversion schemes involving close links between police and drug treatment services.[71]. Another problem is related by Coleman et al. in 2005. “Control strategies typically focus on reducing the diversion of prescription drugs from legitimate sources. The proliferation of unregulated Internet sources, however, has rendered control strategies less effective. [9]

A general solution is proposed by Griffiths et al. in 2003. They describe initial abuse liability testing of a new compound; the classic acute dose-effect comparison study in volunteers with histories of drug abuse. This trial is most appropriate for predicting the likelihood of use by abusers and for predicting the extent of drug diversion and illicit street sales of the novel compound.[72] An additional solution is the use of combinations. In 2006, Robinson reported on a

sublingual formulation combining naloxone with Buprenorphine that is effective in both maintenance therapy and detoxification of individuals addicted to opioids.[73] The introduction of a sublingual formulation combining naloxone with buprenorphine further reduces the risk of diversion to illicit intravenous use. A similar advance in formulations is the extended-release treatment for ADHD (Vyvance) that tends to reduce euphoric qualities of immediate-release drugs.[74]

Success of control systems has also been reported. In 1996, four men – one an associate hospital pharmacy director—were indicted on charges relating to the theft and resale of more than \$3 million in prescription cancer drugs from two Syracuse hospitals over an eight-year period.[43]

### **Double Edge**

There is a double-edged problem with controlling drug diversion. On one hand, the drugs may be needed for legitimate treatment. On the other hand, availability of the drugs may lead to illegal activities. In 1989, discussing anabolic steroids, Phillips reports the Arkansas Department of Health seeks cooperation and assistance in helping combat the illegal diversion by physicians and pharmacies of these hazardous drugs and to ensure that these drugs are available to patients only through legitimate channels.[38]. In 1992, Schwartz commented on the affect to prescribing practices; ‘Several reports indicate a significant increase in the prescribing of benzodiazepine substitutes that are less safe and effective, along with increased overdoses of some substitute drugs. Changes in physicians' legitimate prescribing practices may reflect their fears of the damage to career and peace of mind that follows investigations by regulatory agencies.’[75] In 1994, Shapiro wrote “Governments throughout the world have struggled for decades to ensure the availability of narcotic analgesics for legitimate medical and scientific purposes while controlling the abuse and illegal diversion of such substances. While the international drug-control system has effectively limited illicit trafficking of opioids, concerns remain about its effectiveness in ensuring the availability of these drugs for legitimate purposes.”[76] In a discussion of substitution treatment for heroin addiction in 2002, Bell et al. noted “The first key issue concerns the balance between making treatment accessible and attractive, and minimizing the diversion to the black market.’[77] Regarding pain treatment, Manchikanti et al. put it this way: “In the United States, physicians are faced with two opposing dilemmas in the treatment of pain – the potential for drug abuse and

diversion, and the possible under treatment of pain'[78] Similar thoughts were written by Smith and Woody[5], Hertz and Knight[79], and in 2006 Passik et al. wrote "Physicians and patients have been singled out as the main players in the societal problem of diversion of prescription drugs. In fact, the problem can only be overcome when not only physicians and patients but also healthcare practitioners, third-party payers, law enforcement agencies and regulators, the pharmaceutical industry, and the media finally work together to prevent it, instead of fingering any one party for the blame."[80]

## **Specific Drugs**

Another way to look at diversion literature is to focus on specific drug classes. One topic is drugs used to treat addiction. One treatment method is maintenance with a less potent form of an addictive drug. The longest use of this technique is with methadone (Dolophine, Methadose, Physeptone) which is an opiate agonist. In addition to being an opiate detoxification adjunct, methadone is also an analgesic. This drug has been available since at least 1973. The first illicit use was reported in 1978.[3] Two studies of fatal use were reported in 1999.[21, 81] The risk-benefit of a drug that is both effective and dangerous has been studied as well as pharmacology and other matters related to the methadone and other replacement drugs.[1, 3, 8, 21, 24, 25, 27, 33, 67, 77, 81-92]

Nonmedical use and diversion of specific drugs are mentioned in:

- ADHD treatments [11, 19, 29, 31, 32, 48, 49, 74, 93-96]
- Anesthetics [23, 36, 40-42, 46, 54, 56, 70, 97-101]
- Antipsychotics [17]
- Benzodiazepines [35, 47, 50, 75, 79, 84, 85, 88, 102-104]
- fentanyl [8, 42, 46, 56, 66, 70, 97, 105, 106]
- ketamine [23, 46, 66, 84]
- Methadone [1, 3, 8, 21, 24, 25, 27, 33, 67, 77, 81-92]
- Opioids [1, 5, 16, 18, 30, 33, 35, 44, 46, 47, 50, 52, 64, 73, 76, 79, 80, 84, 87, 88, 92, 99, 107, 108]
- Tramadol [63, 109], steroids[38, 39, 110]
- Xyrem [61, 111]

## **Legal aspects of diversion**



Diversion is the topic of many articles related to the laws, regulation, and recommended practice of drug manufacture, transportation, prescribing and use of drugs that may be misused/abused, In 1983 Bayer mentions the Single Convention on Narcotic Drugs, 1961, and discusses the provision of the 1971 Convention on Psychotropic Substances.[112] In 1983, Murdoch mentions the same meetings.[113] Phillips discusses the Anabolic Steroid Legislation Act 249 of 1989 [Arkansas].[38] In 1990 the Maryland Committee on Drugs addressed specific issues including diversion.[114] In 1994, Shapiro discusses the legal bases for the control of analgesic drugs.[76] An article by Hill in 1996 focuses on government regulatory influences on opioid prescribing.[107] The Implementation of the Comprehensive methamphetamine Control Act of 1996; final rule of the Drug Enforcement Agency (DEA), was published in 2002. [115] DEA regulations concerning methadone were discussed by Jaffe and O'Keefe in 2003.[87]. The Drug Addiction Treatment Act of 2000 used by the DEA as authority for practitioners to dispense or prescribe approved narcotic controlled substances for maintenance or detoxification treatment was published in 2005. [116]

### **Full abstracts of all literature found, whether cited above or not**

The first mention of diversion in medical literature was found in 1973 in the Proceedings. National Conference on Methadone Treatment by T M Wochok, The title was Drugs, Diversion and Crime. [83] Neither the full text nor abstract could be located. We present below summaries of articles found in the search, in chronological order. We exclude only those citations that do not include an abstract.

1978: F. R. Goldman and C. I. Thistel published 'Diversion of methadone: illicit methadone use among applicants to two metropolitan drug abuse programs'. Interview of newly admitted patients from two comprehensive drug abuse programs in the Baltimore area were conducted concerning frequency of illicit methadone use and availability of illicit methadone for a 3-month period prior to their admission. **The results showed that a significant percentage of applicants had used illicit methadone prior to seeking treatment, and that for the most part they were using "program methadone" presumably diverted from take-home medication from patients active in treatment programs in the Maryland area.**[3]

1982 Poklis reports on a five year study (1977 to 1981) in St Louis, Missouri, on the intravenous use of a pentazocine/tripelennamine combination (T's and Blues) which has become a major drug abuse problem. There has been a continuous increase in the involvement of these drugs in (a) sudden and violent deaths (62 homicides, 7 fatal intoxications), (b) emergency room visits (137 in 1980), (c) admissions to drug treatment programs (7.7% in 1978 up to 64% in 1981), and (d) police laboratory cases (100 in 1977 - 78 up to 700 in 1981). Initial popularity of the drugs was related to

the decline in the quality of street heroin (2.5% in 1977 reduced to 0.5% by 1979) and the lack of strict legal controls. Serious adverse reactions include clonic-tonic seizures and pulmonary foreign body granulomatosis. Ethanol and diazepam were present in 53% and 10% of T's and Blues medical examiner's cases, respectively (n = 70). Addicts are usually black males, 20 - 30 years old, from impoverished areas of the city. **The drugs are available to the illicit trade through theft or diversion from legitimate sources.**[4]

1983 Bayer reports the establishment of international control of opiates has been an important achievement of the international community; this is substantiated by the fact that, at the beginning of this century, legally manufactured morphine and heroin were the principal sources of illicit supply, whereas at present the illicit traffic in these drugs is supplied from illicit sources. The poppy straw process has helped to promote measures to control opium poppy cultivation in a number of European countries; Turkey has been a successful example of such control. The present large-scale illicit traffic in cannabis resin and cocaine is the consequence of the lack of the implementation of provisions of the Single Convention on Narcotic Drugs, 1961, to control the cannabis plant and the coca bush at the national level. **The provisions of the 1971 Convention on Psychotropic Substances, being largely a result of international compromise, are not designed in the best possible way to prevent the diversion of psychotropic substances from legal sources to illicit channels.** There are no appropriate provisions for the control and monitoring of international transactions. There is a discrepancy between the rather limited scope of international control of substances listed in schedules III and IV of the 1971 Convention and the much larger scope of control of hypnotics, sedatives and tranquillizers at national levels. The provisions of the 1971 Convention, however, constitute a legal basis for bilateral and multilateral actions for the detection of suspected diversion cases, and offer possibilities of promoting the prevention of diversion of psychotropic substances. At present, the relationship between the control of psychotropic drugs, including the prevention of diversion and the organization of the national drug supply system, as well as the efficacy of national control over pharmaceutical products, has not been fully recognized by the international community.[112]

1983: Feldman et al. present results of a survey questionnaire concerning the procedures used to distribute controlled substances that was mailed to 100 randomly selected Massachusetts hospital pharmacies. The tabulated results were compared to a similar study surveying 285 short-term medical and surgical hospitals nationwide. Of the 58 responding hospitals, 47 (81%) reported controlling either all or some Schedule III Controlled Substances in a manner similar to that used for the distribution and accountability of Schedule II drugs. A total of 42 (72%) reported maintaining the same systems for Schedule IV agents. In contrast, only 24 (42%) of those respondents reported controlling Schedule V drugs in a manner similar to Schedule II Controlled Substances. Similar to the findings of a nationwide study, many of the responding Massachusetts hospitals reported **selective inclusion of those Schedule III, IV, and V drugs possessing an increased risk of illicit diversion into a more controlled distribution system.** Many Massachusetts hospitals distribute and account for controlled substances in a manner similar to that used nationwide.[22]

1983 Murdoch describes a computerized monitoring system which records the movements throughout Australia of selected legal drugs with abuse potential. **The Drugs of Dependence Monitoring System is designed to prevent diversion to the illicit market.** From the moment of import or manufacture, every movement of the selected drug is monitored until the drug reaches the final distributor, in most cases a pharmacy, a veterinarian or a hospital. Approximately 300,000 movements are checked each year. All drugs used in Australia, which are covered by the Single Convention on Narcotic Drugs, 1961, and the 1971 Convention on Psychotropic Substances are included in the system. Reports are generated on quantities imported, exported, locally produced, used in manufacture and distributed. The result is that the risk of diversion has been reduced to a minimum. Information obtained from the system has proved of considerable assistance in fulfilling Australia's international treaty obligations.[113]

1984 Aston reports on drug abuse in dental practice. In addition to use by dental practitioners, the article discusses precautionary practices for the dentist: (1) learn to detect those physical and behavioral signs in patients that are indicators of drug abuse; (2) **become familiar with tactics employed by drug abusers to obtain drugs for themselves or for further criminal diversion, and be prepared to defend against such tactics;** (3) understand and make clinical allowance for therapeutic complications that may arise in the treatment of drug-abuse patients. The dentist's social role as an informed, concerned, and empathic counselor in matters of drug abuse must be assumed as a personal imperative and not viewed as an intellectual abstraction. [35]

1984 . Smiledge and Davern report an anesthesia controlled substance dispensing system. **The problems associated with drug abuse or diversion by anesthesia personnel in the operating room (OR), causative factors, effective mechanisms of control of abusable drugs in this area of the hospital, and the need for these systems to be cost effective for the smaller hospital are discussed.** A system utilizing anesthesiologist/case specific drug kits that are dispensed by the pharmacy to the OR and then to individual anesthesiologists is presented. The system limits quantities of drugs available at one time to anesthesia personnel and provides for clear individual accounting for drugs and the rapid detection and reconciliation of discrepancies. The system demands modest increases in personnel expense and capital and consumable equipment costs. The authors conclude that the system described may provide for improved abusable drug control in the OR at costs reasonable for the smaller hospital.[36]

1985 Smith and Seymour discuss a clinical approach to the impaired health professional. They note; in recent years it has become abundantly clear that health professionals are at high risk for addiction to drugs and alcohol. Addiction is here defined as compulsion, loss of control, and continued use in spite of adverse consequences. Obviously health professionals with these symptoms are dangerous both to themselves and to their patients. De-stigmatization at the community level, identification of addicts, intervention, and diversion into treatment are important factors in dealing with the problem. **Programs for diversion and support are being developed in California for impaired physicians, nurses, and pharmacists.** These are replicable elsewhere for helping impaired health professionals.[37]

1988 A report of a Committee of the Institute for Behavior and Health, Inc. discusses abuse of benzodiazepines: the problems and the solutions. Benzodiazepines are medications used to treat many of the most frequent and disturbing symptoms seen in medical practice, including anxiety,

insomnia, muscle spasms, some forms of epilepsy, and other illnesses. The World Health Organization (WHO) has determined benzodiazepines to be "essential drugs" that should be available in all countries for medical purposes. As benzodiazepines were recognized as generally safe and effective drugs, their medical use increased but so did problems of abuse outside medical practice. This report focuses specifically on the nonmedical use, or abuse, of benzodiazepines for purposes, durations, or at dosage levels not intended by the prescribing physician or in ways outside medical guidelines. The principal contribution of this report to the resolution of the controversy about the use of benzodiazepines is to draw a sharp distinction between the medical use of these drugs and their nonmedical use, which this report labels "abuse." Problems which exist with the medical use of benzodiazepines, such as their use by patients who are better treated with other medications (or without medication) and the problems of withdrawal symptoms on discontinuation of medically prescribed benzodiazepines, are not addressed because these are problems of routine, legitimate medical practice. **On the other hand, aspects of medical practice which affect nonmedical use of benzodiazepines are extensively dealt with in this report including the diversion of legitimately prescribed benzodiazepines into the illicit drug market and the prescribing of benzodiazepines for drug abusers.** Extensive animal and human research has shown that benzodiazepines are "reinforcing" drugs in the sense that animals and humans will maintain behavior on which delivery of the drug is dependent. Animal studies of self-administration of potentially abused drugs show that benzodiazepines are less powerful reinforcers than intermediate half-life barbiturates (such as secobarbital) and psychomotor stimulants (such as amphetamine and cocaine). A substantial body of human research has shown that benzodiazepines are moderately "liked" for their reinforcing effects by drug abusers and alcoholic subjects but that both anxious people and normal (non-drug abusing, non-anxious) human subjects prefer placebo to benzodiazepines, demonstrating that these substances are usually not liked by people who are not drug abusers or alcoholics. Among drug abusers, benzodiazepines are preferred less than either intermediate half-life barbiturates or stimulants. This difference between the response of substance abusers and normal and anxious research subjects supports the fundamental distinction[102]

1988 Henderson studied designer drugs, their history and future. **Historically, drugs of abuse have come from two sources: plant products and diverted pharmaceuticals.** Today, new, totally synthetic drugs produced by clandestine laboratories have become an increasingly important source of abused substances. Of particular concern are the fentanyls, a family of very potent narcotic analgesics, which first appeared on the streets in California in 1979 under the name "China White". At least 10 different analogs have been identified to date and are thought to be responsible for over 100 overdose deaths. The fentanyls are not used by any particular ethnic or age group, but rather by the general heroin using population. Their use, however, does seem to be restricted to suburban, rather than urban areas, and almost exclusively to the state of California. The most potent analogs, the 3-methyl- and beta-hydroxy-fentanyls, may be up to 1000 times as potent as heroin, but are not chemically related to the opiates and therefore not detected by conventional narcotic screening tests. However, using a sensitive radioimmunoassay highly specific for the fentanyls they can be measured at the very low concentrations observed in body fluids, generally less than 10 ng/mL. It is likely that, as efforts to restrict the importation of natural products and prevent diversion of pharmaceuticals become more effective, the fentanyls and other synthetics will become increasingly important drugs of abuse.[105]

1989 Phillips discusses the Anabolic steroid legislation Act 249 of 1989 [Arkansas] and that health care professionals are urged to be alert to the potential for adverse effects common to the use of anabolic steroids by athletes and others, including high school and college students active in varsity sports or body lifting. **The Department of Health, Division of Pharmacy Services and Drug Control asks for cooperation and assistance in helping combat the illegal diversion by physicians and pharmacies of these hazardous drugs and to ensure that these drugs are available to patients only through legitimate channels.** Act 249 of 1989 was enacted to prevent the distribution and use of illegal anabolic steroids and growth hormones and for purposes of defining and setting penalties for the illegal use.[38]

1990 The Council on Scientific Affairs (AMA) reported Medical and nonmedical uses of anabolic-androgenic steroids. **They discussed recent trends in the use, abuse, and diversion of steroids for nonmedical purposes illustrate a growing problem that not only imposes health risks but presents ethical dilemmas as well.** Concern over the known adverse effects, the limited research into the long-term effects, and the ethics of engineering body size and performance through anabolic-androgenic steroid use has led to legislative, legal, and education responses. Increased penalties for distribution to minors and stricter controls in prescribing practices have been enacted through state legislation and federal initiatives. Government, some health professional organizations, and some sports groups have denounced the nonmedical use of anabolic-androgenic steroids and have developed materials to educate their members, other professionals, athletes, educators, and the public at large.[39]

1990 Committee on Drugs (Maryland): Prescription drug control and dispensing was formulated to discuss the issues of prescription drug control and dispensing, particularly as it relates to the problem of drug abuse in general, which is the purview of the Committee on Drugs, The issues are several: 1. The large morbidity and mortality associated with the use of prescription and nonprescription drugs in this country. 2. The issue of recreational use of drugs, most important numerically being alcohol, and the many other drugs which are both licit and illicit, primarily illicit. 3. The issue of drug addiction and how to prevent and treat it. **4. The issue of law enforcement with regard to both illicit drugs and the diversion of licit drugs and the increasing mortality associated with the trafficking and law enforcement of drug abuse.** 5. The issue of restricting the rational use of medicines. The question of whether a governmental system which totally proscribes certain drugs and provides extreme restrictions on the prescription of others will reduce deaths and morbidity is an open one. There seems little doubt that our country has extremely prohibitive and restrictive laws and yet has a huge mortality associated with distribution networks of illicit drugs and also more than ten thousand deaths a year from drug overdose.[114]

1990 **Angarola discussed success of national and international regulation of opioid drugs in preventing diversion from legitimate producers of opioids to illicit channels.** This has contributed to a reduction of opioid abuse and related illegal activities. However, the systems have fostered concepts and attitudes that have limited access to opioid drugs, which the international treaties recognize are indispensable for the reduction of pain and the treatment of other conditions. Patients who have a legitimate need for the relief that these drugs can provide have become the unintended victims of the drug control systems.[52]

1991 Pelton and Ikeda discuss recovering anesthesiologists and the effectiveness of the rehabilitation of anesthesiologists who are addicted to alcohol or other drugs. There has been some concern and discussion about allowing anesthesiologists who are addicted to alcohol or other drugs to continue practicing in their specialty. This article analyzes success rates, relapse rates, and failure rates among the anesthesiologists and residents of anesthesiology in the **California Physicians Diversion Program for chemically dependent doctors**. Of the 255 physicians who have successfully completed the program during the ten years prior to March 1990, 35 were practicing anesthesiologists, including six resident anesthesiologists. Although doctors in this specialty are more at risk for manifesting addiction to alcohol and other drugs, California's experience demonstrates that they have an equal chance of recovery and contradicts the pessimism about recovery in anesthesiologists.[40]

1991 **Weissman and Johnson used data from the five-site Epidemiologic Catchment Area study (ECA), a probability sample of 18,571 adults, to describe the prevalence of drug abuse in the United States and to evaluate the hypothesis that multiple prescription regulations are effective in reducing drug abuse and drug diversion.** The five sites surveyed were New Haven, Connecticut; Baltimore, Maryland; St. Louis, Missouri; Durham, North Carolina; and Los Angeles, California. The California triplicate prescription law was established in 1939 and is the longest continuously running triplicate prescription program in the country (Schedule II drugs). None of the other ECA sites had multiple prescription regulations in effect at the time the study was conducted. In general, the rates of drug use, abuse, and dependence were significantly higher in Los Angeles as compared with the other sites, both before and after controlling for sociodemographic differences. The proportion of users who go on to become abusers was consistent across sites (about 20%). **The vast majority of those with a DSM-III diagnosis of abuse of prescription drugs reported that they obtained the drugs from a source other than their physician, suggesting that "diversion" of prescriptions from legal channels occurred at all sites.**[53]

1992 Klein et al. present the results of a survey on the use of surgical satellite pharmacies in hospitals with anesthesiology training programs. In June 1990 a questionnaire was mailed to 158 directors of anesthesiology training programs for physicians. The questionnaire solicited information on the presence of surgical satellite pharmacies in the training hospitals and the nature of the services provided, including accounting for controlled substances. Responses were received from 102 program directors and their designees, for a 65% response rate. Some respondents returned questionnaires completed by affiliated hospitals; a total of 137 responses were accumulated. Surgical satellite pharmacies were present in 46 (34%) of the 137 hospitals. Of those 46 satellite pharmacies, only 14 dispensed all controlled substances to anesthetic-administration areas. Most of the satellite pharmacies provided services at least eight hours per day. All 46 pharmacies dispensed controlled substances, 31 provided i.v. admixtures, and 12 dispensed all i.v. solutions. Accountability for controlled drugs was provided through a daily inventory count (45 satellite pharmacies), daily comparison of agents received and returned (36), review of the anesthesia record (31), random audits of individual providers (18), or quantitative or qualitative analysis of residual drugs (16). **Accountability was considerably better in hospitals with surgical satellite pharmacies than in hospitals without them. Surgical satellite pharmacies provided increased accountability for controlled substances in institutions with anesthesiology training programs but did not use all the available methods for preventing drug diversion.**

1992 Schwartz reports specifically on benzodiazepines. In 1989 New York became the first state to add benzodiazepines to the list of controlled substances requiring a triplicate prescription, allowing the state to track prescribing patterns and target providers, pharmacies, and patients for investigation when misuse is suspected. **Studies by the state reporting that regulation has significantly reduced inappropriate prescribing and illicit diversion of benzodiazepines without affecting legitimate prescribing practices are being challenged by other studies showing that patients with legitimate needs for benzodiazepines are being denied them, often after abrupt discontinuation.** Several reports indicate a significant increase in the prescribing of benzodiazepine substitutes that are less safe and effective, along with increased overdoses of some substitute drugs. Changes in physicians' legitimate prescribing practices may reflect their fears of the damage to career and peace of mind that follows investigations by regulatory agencies.

1993 Dodd describes OSTAR-Oklahoma Schedule II abuse reduction: An electronic point of sale diversion control system. In its short history, **OSTAR has proven to be a fast, accurate tracking system for Schedule II prescriptions within Oklahoma.** Information is available immediately in many cases and, having been entered into the system by the pharmacist, is very accurate. Approximately 50 percent of the information is being transmitted through electronic means at this time, and that percentage is increasing daily due to software companies making modifications to their pharmacy programs. System deficiencies have proven to be minimal, even less than anticipated. Efforts are still underway to ensure that data is received in a uniform manner; i.e., some data systems include zeroes at the end of the patient number, which causes investigators to have to query in more than one form. These pharmacies and companies are currently being notified and are making the necessary changes. The technical problems usually encountered with a new system have been limited, and data has been useful from the first month of the program. Feedback from impaired physicians has indicated they would not have been so free to divert Schedule II substances through prescriptions if this system had been in place. OBN has active cases involving a large number of physician scammers that are a direct result of OSTAR and it has enhanced cases on at least one physician and provided valuable information for search warrants. Agents are able to make better cases for prosecutors while completing investigations in much shorter periods of time. Local law enforcement personnel who have accessed OSTAR have become convinced that it is a most effective tool, and use of the system has complemented their investigations.

1993 Mirro et al. describe a state program that tracks Schedule II drugs. By implementing the multiple copy prescription program, Indiana demonstrates its concern with the problems of doctor shoppers and physicians involved with abuse. **By trying to track illegal diversion of Schedule II drugs, states that have implemented tracking programs are trying to rid the streets of illicit drug use.** When it is time to renew the law, the state should consider using modern computer technology. Indiana's program could be even more effective if it incorporated electronic data transfer.

1993 Schmidt and Schlesinger describe a reliable accounting system for controlled substances in the operating room. Drug abuse is a leading occupational hazard for operating room personnel. Easy access to controlled substances allows drug dependence to develop and flourish. **A system that accurately audits the distribution of controlled substances used in the operating room**

**may decrease the onset of drug abuse and make it easier to identify drug addicts.** This system involves participation by anesthesiologists, operating room nurses, and pharmacists to accurately record amount and type of drugs dispensed, used, wasted, and returned. Periodic, random, qualitative, and quantitative analyses of drugs returned for wastage are performed. In the first 6 months in which the system was used, 6,336 patients were treated and 7,182 ampules of controlled substances were dispensed. Thirty-seven incident reports describing deviations from the protocol occurred. In each case an explanation for the discrepancy was determined and compliance with the protocol was subsequently improved. **No cases of drug diversion were discovered or suspected.** [41]

1994 Maltby et al. describe simple narcotic kits containing fentanyl-morphine-midazolam, alfentanil-midazolam and sufentanil-midazolam, for general operating rooms, and two kits with larger quantities of fentanyl and sufentanil for cardiac operating rooms to be used for controlled-substance dispensing and accountability. Operating rooms require a storage, dispensing and accounting system for restricted drugs which satisfies narcotics control authorities and is compatible with efficient care of patients. Sealed kits are delivered each morning from pharmacy to the locked narcotics cupboard in the recovery room. On request, the recovery room nurse unlocks the cupboard and the anesthetist signs out the required kit(s) for the day. A drug utilization form is enclosed with each kit, on which the anesthetist records the amount of drug administered to each patient, and before returning the kit to the locked narcotics cupboard, the total amount of each drug used, discarded, and returned. Used kits are collected the following morning by a pharmacy technician who reconciles the contents and drug form of each kit. More than 40 staff anesthetists and a similar number of residents have used the system for seven years, during which time 130,000 patients have passed through the operating rooms. **Detection of one case of drug diversion by a staff anesthetist was made partly by the control system, but mainly by behavioral changes.** [56]

1994 McNutt et al. report on an effort to reduce diversion of benzodiazepines for illicit use and reduce inappropriate prescribing, a regulation was implemented requiring the reporting of all benzodiazepine prescriptions to the New York State Department of Health. To assess the impact of the regulation on prescribing practices to the elderly, we followed the number of benzodiazepines and other central nervous system medications prescribed to a cohort of participants in an elderly pharmaceutical insurance program. Statistically significant ( $p < 0.05$ ) decreases were seen in all sex, age, race and marital status groups. Increases in number of prescriptions for miscellaneous anxiolytics, meprobamate, buspirone, chloral hydrate, antidepressants, barbiturates, and tranquilizers, some of which may be more toxic or less effective, were noted. New York State's reporting regulation was effective in reducing both the number of patients being prescribed benzodiazepines and the number of prescriptions given to those who remain on benzodiazepines in the elderly population studies.[103]

1994 Shapiro discusses the legal bases for the control of analgesic drugs. **Governments throughout the world have struggled for decades to ensure the availability of narcotic analgesics for legitimate medical and scientific purposes while controlling the abuse and illegal diversion of such substances. While the international drug-control system has effectively limited illicit trafficking of opioids, concerns remain about its effectiveness in ensuring the availability of these drugs for legitimate purposes.** In the United States, federal



legislation accommodates the use of controlled substances for medical and scientific purposes more effectively than state law. **Many states' controlled substance laws hinder appropriate opioid prescribing through (a) the use of ill-defined terms, (b) restriction of pain prescriptions to a specific number of dosage units; and/or (c) utilization of multiple-copy prescription programs. A more efficient state approach to monitoring inappropriate schedule II prescribing and dispensing may be through an electronic, computer-based pharmacy point-of-sale system, through which pharmacists can be alerted instantaneously to patients receiving the same drug from multiple pharmacies.** In addition, states should consider modifying their approaches to drug abuse by adopting the revised Uniform Controlled Substances Act and/or establishing state pain initiatives.

1995 Hellawell reports that illicit drugs have become a major global problem in recent decades following considerable recent political change, including the collapse of communism and the formation of international super-states to increase trade. Despite increasing collaboration between law enforcement authorities in different countries, illicit drug problems appear likely to increase in the future because of the vast profits available, continuing (and increasing) demand and more permissive attitudes concerning drugs among young people. While rejecting legalization or decriminalization, the search for more effective responses by law enforcement authorities and the community generally must be stepped up. Police services continue to play an important role restricting the availability of illicit drugs but increasing emphasis needs to be given to reducing demand, including more available and more effective preventive drug education in schools. Police also need to work with harm reduction approaches devised to reduce the negative consequences of drug use for those who continue to use illicit drugs. New measures proposed in Britain are outlined. These stress the importance of a multi-sectoral approach operating at both national and local levels with the objective of reducing drug-related crime, reducing the acceptability and availability of illicit drugs and reducing the harmful consequences of illicit drug use. Harm reduction requires a commitment for close collaboration between police and drug treatment services to maximize the effectiveness of needle-exchange schemes and other harm reduction approaches. Cautioning, now commonly used in Britain for selected minor drug offences, has a number of benefits including reducing criminal justice costs. **Greater emphasis must be placed on diversion schemes involving close links between police and drug treatment services.** Future progress requires firm commitments to providing adequate and effective drug treatment services, conducting research to develop and evaluate more effective diversion schemes, improving collaboration between sectors and effective leadership. In addition to the major costs of illicit drug use to the community, the huge cost to individuals must remain a major focus driving the search for more effective responses to the problems resulting from illicit drugs.

1995 Kingsbury et al provide a method for quantitative analysis of fentanyl in pharmaceutical preparations by gas chromatography-mass spectrometry. Reports of abuse of this highly addictive drug among health care personnel have prompted the need to verify the concentration in the unused portion of single-dose ampoules returned to the pharmacy. They describe a simple quantitative method for the analysis of fentanyl citrate (Sublimaze) in syringes returned to the pharmacy following surgery. This assay is useful in verifying that any unused fentanyl is discarded according to narcotic regulations, thereby avoiding the possibility of diversion for illicit consumption.[66]

1995 Poklis describe fentanyl. Fentanyl is a highly potent, short acting synthetic analgesic indicated as a pre-anesthetic medication. It is available for intravenous injection, as a transdermal patch and a lozenge dosage form. Fentanyl displays a large apparent volume of distribution, short plasma half life and extensive biotransformation. It is a popular drug of abuse among health care professionals. **Diversion of pharmaceutical fentanyl preparations, as well as the availability of illicitly synthesized potent and highly toxic fentanyl analogs have resulted in numerous overdose deaths.** Analysis of fentanyl and fentanyl analogs requires highly selective and sensitive methodologies. This review is intended as a quick reference source for clinical and analytical toxicologists.[42]

1995 Wolters reports that coercing drug users into treatment might seem contrary to the philosophy of drug addiction care, which sets great store by the user's own motivation. Nevertheless, legal pressure and even force are increasingly being brought to bear in the Netherlands to persuade users to attend drug care programs. The criminal justice system and the addiction care services have various means at their disposal to motivate addicts to come off drugs. This article discusses the relationship between addiction and crime. It begins with a brief description of how the addiction problem has evolved in the Netherlands over the years. This is followed by an explanation of how crime has developed during the same period and the effect this has had on social services for addicts. **The article concludes with some recent policy proposals concerning diversion, coercion and pressurization strategies.**[117]

1996 Special report. Drug theft from hospital pharmacies: lessons from the 'Syracuse scam'. **Theft and drug diversion by employees from hospital pharmacies pose increasing security concerns for institutions as evidenced by the indictment in May 1996 by an Onondaga County, Syracuse, NY, grand jury** of four men--one an associate hospital pharmacy director--on charges relating to the theft and resale of more than \$3 million in prescription drugs from two Syracuse hospitals over an eight-year period. The drugs were used to treat cancer patients. This report provides in-depth details of what was stolen and how it was stolen. It presents some advice from experts on how to prevent your hospital from becoming vulnerable to such large-scale losses. And gives insight into a vast black market that may indicate that what took place at the two Syracuse hospitals may not be an isolated occurrence.[43]

1996 Balevi et al. report on the dentist and prescription drug abuse. Because dentists are authorized to prescribe narcotic drugs to their patients, they may be sought out by "drug seeking individuals" (DSI), disguised as patients, who are engaged in the illegal diversion of pharmaceutical-quality drugs to the street market. **Two common methods of gaining illegal access to pharmaceutical-quality narcotics for resale on the street are: forgery and verbal misrepresentation, and multiple doctoring. The diversion of such drugs can produce a very high rate of return for DSIs, with only a minimal risk of arrest and conviction.** This paper discusses the problem of DSIs, and how dentists can reduce the risk of becoming involved in the illegal diversion of narcotics. Prudent judgment and responsible prescribing by the dentist will increase the effectiveness of his or her practice, and help to abate a growing social problem.

1996 Dalgarno and Shewan studied illicit use of ketamine in Scotland. Semi structured interviews were carried out with 20 illicit users of ketamine in Scotland. Participants had used a wide range of illegal drugs. Scottish drug agencies reported limited contact with ketamine users; however,

subjects were knowledgeable regarding the licit purpose of ketamine, its effects, and its legal status. **Ketamine was usually obtained through diversion from legitimate sources.** Three participants reported extensive use, indicating the potential for psychological dependence. A standard dose of ketamine was typically 1/8 g, usually taken intranasal. Participants reported the ketamine experience as being extremely intense and dissociative, usually lasting for approximately one hour. All participants reported using ketamine in a carefully preplanned setting, emphasizing comfort, security, and familiarity. Participants identified potential problems arising from using ketamine in a public place, or in unfamiliar surroundings, and also suggested that novice users may encounter problems through lack of knowledge concerning the intense nature of the experience. Accurate information concerning the effects and nature of ketamine as well as the importance of set and setting should be made available. However, publicizing the drug should be avoided as widespread interest could cause greater problems than currently exist.

1996 Hill reports on government regulatory influences on opioid prescribing and their impact on the treatment of pain of nonmalignant origin. Interpretation of regulations establishing standards for prescribing opioids by government regulatory boards and drug-enforcement agencies is more restrictive for treatment of nonmalignant pain than for malignant pain. Authority to regulate opioids is provided by health practice acts enacted by state governments and controlled substances acts, enacted by both state and federal governments. The methods used by boards/agencies to determine standards of practice for opioid use result in interpreting the language in these regulations based on myths, prejudices, and misinformation about opioids, and the unexamined belief that mere exposure of patients to these drugs causes psychological dependence (addiction) on them to all patients in all instances. **Interpretation is also strongly influenced by a failure of regulatory and enforcement bodies to recognize their coequal obligation of making opioids readily available to those who need them for legitimate medical purposes, while simultaneously policing their diversion to illegitimate uses. Emphasis on the police function of preventing diversion is paramount.** Disciplining practitioners using standards based on myths, prejudices, etc., reinforces physicians' fears of prescribing opioids for nonmalignant pain. Patients with nonmalignant pain who are not relieved if opioids are not provided will continue to suffer until regulatory boards/drug enforcement agencies define the standards of practice for opioid use for nonmalignant pain in clear and unequivocal terms. It is unlikely these standards will be developed until there is a consensus among pain specialists about opioid use for nonmalignant pain because boards/agencies have no consistent, reliable source of expert information. Pain specialists should initiate efforts to develop this consensus.

1998 Kobs discuss Joint Commission methods to avoid diversion in "Counting, checking, and locking". Medication use stimulates many questions: Is the JCAHO driving your actions; is it a sacred cow; is it "we've always done it this way"; do the state, local or federal laws and rules mandate that you do these things? The JCAHO requirements differ from other agency mandates-counting ensures an adequate supply of drugs and prevents diversion; checking maintains readiness; and locking controls and secures drugs.[59]

1998 Valdez et al. report on the legal importation of prescription drugs from Mexico. **The nature and magnitude of the problem of the diversion of prescription drugs from legal to illegal markets have been identified as a high priority by the federal government.** This study was

based on a random sample (2,005) of declaration forms of persons declaring Mexican prescription drugs at the US Customs office in Laredo, Texas. Of the 75 different types of drugs, the most frequently declared drugs were Valium (71%), Rohypnol (46%), and Tafil (25%), drugs highly associated with non-medicinal use among United States teenagers and young adults. These data reinforce a documented need for more transnational cooperative efforts between the United States and Mexico.[118]

1999 Cooper et al. report on a study of methadone in fatalities in the Strathclyde Region, 1991-1996. There was a substantial increase in the percent of drug screens testing positive for methadone between 1991 and 1996 in the Strathclyde region of Scotland. Seventy-nine per cent (n = 136) of these deaths were drug-related, involving methadone either alone or in combination with other drugs such as diazepam, temazepam, alcohol and morphine. **The involvement of methadone in the majority of these fatalities was due to diversion of legitimate supply.** This paper highlights the dangers of resuming methadone consumption following a period of abstinence or when taken in combination with other drugs.[81]

1999 Schwartz et al. describe a 12-year follow-up of a methadone medical maintenance program. Methadone Medical Maintenance (MDM) is an alternative for treatment of stable methadone maintained individuals. It involves a monthly physician's visit, at which methadone take-home doses are dispensed to last until the next appointment. The safety and efficacy of this treatment modality is currently under investigation. The purpose of this study was to evaluate the long-term safety and efficacy of MDM in a methadone program in Baltimore. A sample of 21 patients was enrolled in the study and followed for 12 years. They were evaluated once a month by a primary care physician affiliated with a methadone clinic that collected urine toxicology samples and dispensed the monthly methadone dose. The results showed that only 6 (28.6%) patients dropped out during the 12 years of the study. Twelve (0.5%) of 2,290 urine samples collected were positive for drugs. **No methadone overdose or diversion was observed.** Participants reported significant improvement in their quality of life. The results of this study support the safety and efficacy of medical maintenance of stable methadone maintained individuals.[21]

2000 Bell and Zador perform a risk-benefit analysis of methadone maintenance treatment. Methadone maintenance treatment for heroin (diamorphine) addiction has been extensively researched. There is consistent evidence that while in treatment, heroin addicts are at a lower risk of death, are less involved in crime, and feel and function better than while using heroin. Despite the research evidence supporting methadone treatment, there remains widespread public skepticism about this form of treatment. This skepticism is frequently expressed in terms of the perceived risks of methadone treatment. The perceived risk that methadone treatment may maintain people in an addicted lifestyle is not supported by research literature. **The risks of treatment include an increased risk of death during induction into treatment, and risks of diversion of drugs to the black market.** For some patients, adverse effects of methadone pose a problem and the availability of new pharmacotherapies may provide useful options for these patients. Risks can be reduced and benefits increased by directing greater attention to the quality of treatment.[82]

2000 Bouley et al. report that the drugs most diverted for toxicomanic use from their therapeutic indication are principally the opioids or related substances, with codeine still high in importance, in spite of the wide prescription of substitution treatments. The psychotropic

drugs, essentially the benzodiazepines and the stimulant antidepressants such as amineptine, are also frequently used. The market withdrawal of amineptine should diminish its misuse. The abuse of amphetamines-anorectics and barbiturates seems to be regressing. Nevertheless, substances such as nitrous oxide and ketamine are the subject of selective, recent misuse. Moreover high-dose buprenorphine misuse, as a concomitant buprenorphine-benzodiazepine combination and/or an intravenous injection of high doses of buprenorphine, can be implicated in severe adverse effects. Twenty-one lethal intoxications linked to such drug misuse have already been reported. However, the addictive drug potential is not the only explanation for drugs diverted for toxicomanic use. It is also associated with a polytoxicomania, a symptom of pre-existing difficulties, particularly familial, social and environmental in origin. Therefore, the therapeutic regime should be adapted to the drug addict's personality. We report a few cases of polydrug abusers, treated with methadone in a specialist unit. The misuse and the practical therapeutic response, adapted to each case, are compared and discussed in respect of the data published in the literature.[84]

2000 Fountain et al. discuss diversion of prescribed drugs by drug users in treatment: analysis of the UK market and new data from London. An analysis of the literature and new data in terms of the extent and nature of the market, the practicalities of trade, motives for selling, reasons for demand and the influence of variations in prescribing practice on diversion. Prices of diverted prescription drugs and details of their availability in London are presented. **The size of the market is substantial and appears to involve a large number of individuals, each diverting small amounts of their own prescribed drugs.** Major motives for selling prescribed drugs are to raise funds to buy other, preferred, drugs and/or to pay for a private prescription. Buyers in treatment appear to be motivated by a desire to supplement their own prescriptions because they are dissatisfied with the particular drug prescribed, dosage and formulation. Drug users in treatment can exploit the variations in prescribing practice--such as how much 'take-home' medication they are allowed and whether tests are conducted to ascertain if they are using it themselves--and divert their prescribed drugs. Prices of prescription drugs on the illicit market can fluctuate on a daily basis according to supply and demand. **The results suggest that, to be effective, diversion control must simultaneously involve deterrents from prescribers, drug treatment services, law enforcement agencies and dispensing pharmacists.**[85]

2000 Green et al. report that a retrospective review was undertaken of all autopsies in which methadone was detected at the Forensic Science Centre, South Australia, during a 3-year period from July 1996 to June 1999. Thirty-five cases were found in which methadone had either caused or contributed to death (age range = 14-54 years; average = 31 years; M:F = 3.4:1). Ten victims were participating in a methadone maintenance program, of whom four died within a week of enrollment. Eight victims (23%) not enrolled in a methadone maintenance program were found who had died after the use of "diverted" methadone (i.e., prescribed for someone else) (age range = 14-34 years; average = 25 years; M:F = 6:2). Deaths were directly attributable to methadone toxicity in seven of the eight cases, with additional drugs or alcohol being found in seven cases. **Prevention of ongoing deaths caused by methadone diversion could be achieved by allowing only daily releases of methadone, with the addict having to consume the drug under close supervision.**[24]

2000 Parran and Grey discuss the role of disabled physicians in the diversion of controlled drugs.

To test the assertion that disabled physicians are loose prescribers and clinically meaningful contributors to the diversion of controlled prescriptions, an anonymous survey of physicians in a confidential treatment program in Ohio was conducted to compare pre- and post-recovery: (1) self-reported number of controlled drug prescriptions written, and (2) self-rated appropriateness of prescribing practices. Forty (50%) of the surveyed physicians responded. Opioids alone showed a post recovery reduction in the number of prescriptions (-4.5; 95% CI: -9.5 to -0.5). The volume of prescribing in all controlled drug categories was small from both a law enforcement and clinical perspective. Respondent's self-assessment of prescribing practices indicated conservative pre-, and more conservative post-recovery prescribing, increasing from 2.0 in stimulants (CI: 1.0-4.0), to 3.5 in sedatives (CI: 1.0-6.0). **Despite limitations, this initial data provides evidence to refute the assertion that disabled physicians are loose prescribers and meaningful contributors to the diversion of controlled prescriptions.**[44]

2001 Forgiione et al. describe what states are doing to curb diversion of prescription drugs. **The diversion of legitimate controlled substances to the black market is a major cause of medical emergencies, fatalities, and drug-related dependencies.** The effects harm not only the illegal user, but also the legitimate patient who may be getting shorted on treatments and innocent medical providers who may be charged with false claim offenses or other professional failures because of diversions that take place during their watch. The dollar magnitude of this crime is estimated to rival the black markets for both crack cocaine and heroine combined. **This article addresses the various ways prescription drugs are diverted to the black market, some monitoring programs employed by the states, and guidelines that doctors, pharmacists, and other providers can use to protect themselves against possible liabilities arising from the diversion of prescription drugs.** We will also address some of the oppositions to monitoring programs that have been asserted and replies to these oppositions.[55]

2001 Rajagopal et al. discuss medical use, misuse, and diversion of opioids in India. **In less-developed countries, opioids such as morphine are often not available for pain relief because of excessive regulations imposed to prevent their misuse and diversion.** They describe the effect that these draconian measures have had on the availability of drugs for medical use in Kerala, India, and present results of a study, which was done to ascertain whether or not the misuse and diversion of opioids is as prevalent as the government reaction would suggest. They followed 1723 patients in Calicut, India, who were being treated for pain with oral morphine on an outpatient home-care basis. **Over 2 years, we did not identify any instances of misuse or diversion.** These results suggest that, in the context of India as a less-developed country, oral morphine can be dispensed safely to patients for use at home. They recommend that palliative care programs talk to concerned governmental authorities, to make them aware of the medical need for opioids, and communicate with local news media to increase awareness of palliative care and the use of these analgesics.[35]

2001 Robles et al. describe implementation of a clinic policy of client-regulated methadone dosing. A six-month interval (baseline) during which methadone doses above 99 mg required individual approval by the clinic's physician was compared with the subsequent 16-month period in which a policy of patient-regulated methadone dosing with no preset upper limit was implemented. During the later phase, all patients were required to remain at each selected dose for a minimum of four days, and standard compliance-based take-home dosing procedures were followed. For patients in the study sample (n=57), the daily maximum methadone dose increased from 165 mg

during baseline to 300 mg during the self-regulation period, while their average daily methadone dose increased from 76.84 mg to 80.04 mg (W=473, n=57, p=0.01). Monthly percent of opiate-positive urine specimens decreased significantly from 5.26% during baseline to 1.64% during the self-regulated dose period (W=169, n=57, p<0.01), and use of other drugs remained unchanged. **No patient failed to show possession of recalled take-home doses, and no instances of liquid methadone diversion were reported by law enforcement agencies in the area.**[25]

2001 Simoni-Wastila and Tompkins look at the effectiveness of some drug control programs. Narcotics and other prescription drugs play a significant and legitimate role in medical practice. The illicit use of prescribed medicines, however, remains a major problem. **This paper examines the effectiveness of two drug diversion control programs, multiple copy prescriptions programs (MCP) and electronic data transfer (EDT) systems, and their impact on medical practice.** Current evidence demonstrates that these programs decrease prescription drug use, with much of the decrease due to declines in inappropriate use. MCPs appear more effective than EDT in preventing diversion.[60]

2001 Sussman et al. present a study that provides a detailed, multiple-choice, self-report analysis of home, work, and other public locations where drug offenders report using drugs. In addition, these settings were examined as a function of gender, ethnicity, type of drug used, and drug abuse/dependence status. **The participants for the present study were 462 individuals attending drug diversion programs in southern California.** The single most frequently reported location of use was the subjects' living room with a small group of friends. However, heavier users used different drugs across a greater variety of locations. Not surprisingly, drugs were used least at work (though a surprising 47% had used at work). Popular situations of drug use among drug offenders are similar to that of high-risk youth.

2002 Implementation of the Comprehensive Methamphetamine Control Act of 1996; regulation of pseudoephedrine, phenylpropanolamine, and combination ephedrine drug products and reports of certain transactions to non-regulated persons. Final rule: DEA is amending its regulations to implement the requirements of the Comprehensive Methamphetamine Control Act of 1996 (MCA) with respect to the regulation of pseudoephedrine, phenylpropanolamine, and combination ephedrine drug products as List I chemicals, and the reporting of certain transactions involving pseudoephedrine, phenylpropanolamine, and combination ephedrine drug products. The MCA removed the previous exemption from regulation as List I chemicals which had applied to pseudoephedrine, phenylpropanolamine, and combination ephedrine drug products. This action makes persons who distribute the products subject to the registration requirement. **Also, distributions, importations, and exportations of the products became subject to the existing chemical controls relating to regulated transactions, except in certain circumstances specified in the MCA. The MCA also requires that reports be submitted for certain distributions involving pseudoephedrine, phenylpropanolamine, and ephedrine (including drug products containing those chemicals) by Postal Service or private or commercial carrier to non-regulated persons.** This final rule amends the regulations to make them consistent with the language of the MCA and to establish specific procedures to be followed to satisfy the new reporting requirement. **DEA has, where possible, taken action to limit the public impact of these new requirements while remaining consistent with the intent of the MCA to attack the**

## **diversion of regulated drug products to the clandestine manufacture of methamphetamine.[115]**

2002 Bell et al. describe substitution treatment for heroin addiction, defined here as maintenance prescribing of opioid agonist drugs to opioid dependent subjects, and has increased in the last decade. The recent history of substitution treatment in five countries--Canada, the U.K., Australia, Israel, and France--is reviewed. In all five countries, the critical issues around substitution treatment are similar. **The first key issue concerns the balance between making treatment accessible and attractive, and minimizing diversion to the black market.** The second issue concerns the role of primary health care in delivering MMT. In general, there has been increasing involvement of primary health care, with training and support for practitioners. However, there remains uncertainty and official ambivalence over whether treatment should be restricted to specialist clinics and practitioners, or available through primary care. Most importantly, underlying these issues is the problem of stigma being associated with both addiction, and with substitution treatment. The underlying problem that treatment is often at odds with community values places enormous strains on substitution treatment, and makes the treatment system vulnerable to shifting community support and abrupt, politically-driven changes in policy.[77]

2002 Cone and Preston present toxicological aspects of heroin substitution treatment. Heroin abuse is an international problem with which all countries must continually cope. Many countries have implemented heroin substitution therapy as an effective means of decreasing illicit heroin use, crime, HIV risk, and death, and in improving employment and social adjustment. Although methadone is the most commonly used medication for heroin substitution, other agonists in current use include levomethadyl acetate (LAAM), buprenorphine, and pharmaceutical-grade heroin. This report reviews toxicological issues that arise in these programs. A broad array of testing methodologies are available that allow selection of on-site testing or laboratory-based methodology. Urine specimens may be monitored for non-prescribed drugs on a qualitative or semiquantitative basis. Methods for differentiating opiate sources by urinalysis have been proposed to distinguish poppy seed consumption from heroin abuse and for distinguishing pharmaceutical-grade heroin from illicit heroin. **Therapeutic drug monitoring for methadone in plasma continues to be evaluated for use in establishing adequate dosing and detecting diversion,** and new methods have been devised for measurement of the optical isomers of methadone in plasma. Biologic specimens, in addition to plasma and urine, have been evaluated for use in drug monitoring, including sweat, hair, and oral fluid, with promising results. Overall, the many recent developments in testing methodology provide more effective means to assess patients in heroin substitution programs and should contribute to improvements in public health.[67]

2002 Gonzalez et al. report that new pharmacological treatments for heroin (diamorphine) addiction include drugs that reduce opiate withdrawal symptoms and agents that are given during the maintenance phase of treatment. A variety of different types of pharmacological agents (opioid agonists, partial opioid agonists, opioid antagonists and alpha(2)-adrenoreceptor agonists) are reviewed and the evidence of their use during managed withdrawal and maintenance are presented. Experimental approaches attempting to reduce the time of opiate withdrawal and to accelerate the transition to abstinence are being developed. The combination tablet of buprenorphine and naloxone that is to be introduced for office-based maintenance is currently undergoing intense



evaluation in the US. **This new approach may facilitate the expansion of treatment while reducing the potential for medication diversion and intravenous use.** [68]

2002 Holth et al. describe a simple method for quantifying fentanyl, sufentanil, or morphine in discarded syringes from anesthesia procedures. These drugs are commonly used in the conduct of anesthesia. Medical staff working with these drugs is at high risk of addiction. **To detect and prevent diversion, a method was developed to quantify these drugs in discard syringes using the BioRad REMEDi HS Drug Profiling System.** For fentanyl, the lowest concentration detected is 0.1 microg/mL, and the assay is linear to 5.0 microg/mL; the within-run coefficient of variation (CV) is 0.9% (n = 5), and between-run CV is 2.5% (n = 20). For sufentanil, the lowest concentration detected is 0.5 microg/mL, and the assay is linear to 11.0 microg/mL; the within-run CV is 2.0% (n = 5), and the between-run CV is 2.4% (n = 20). For morphine, the lowest concentration detected is 0.5 microg/mL, and the assay is linear to 10.0 microg/mL; the within-run CV is 11.6% (n = 5), and between-run CV is 11.3% (n = 20). Other drugs commonly used in the operating room were checked for cross-reactivity on the REMEDi HS; none cross-reacted. The REMEDi HS can be used for rapid, accurate quantification of fentanyl, sufentanil, and morphine in discard syringes from anesthesia procedures or related medical applications.[97]

2002 King et al. discuss methadone medical maintenance (MMM) as a rational, cost-effective method to match treatment intensity to level of needed services. In the present study, 73 highly stable methadone maintenance patients were randomly assigned to either a routine methadone treatment, MMM--a once monthly reporting schedule--at the methadone maintenance program or MMM at a physician office. A 'stepped care' intensified treatment approach was used for patients who had drug-positive urine specimens or failed the medication recall procedure. Patients left two urine specimens for analysis each month (at least one on a random basis) and responded to one medication recall each month. Results are presented for the first 6 months of the 1-year trial. **Only 1% of urine specimens were positive for illicit drugs, there was no evidence of methadone diversion and there were very low rates of medication misuse, with no between group differences. MMM patients initiated more new employment or family/social activities than the routine care patients.** MMM patients were more satisfied with their treatment than the routine treatment patients, but all patients rated themselves satisfied or very satisfied with their treatment. Stepped care was well-tolerated and helped match patients to an appropriate intensity of service. The good outcomes observed with the present sample suggest that MMM can be implemented effectively as part of a continuum of care in clinic and office-based sites.[42]

2002 Manchikant and Singh discuss the National All Schedules Prescription Electronic Reporting Act, or NASPER, a bill proposed by the American Society of Interventional Pain Physicians to provide and improve patient access with quality care, and protect patients and physicians from deleterious effects of controlled substance misuse, abuse and trafficking. Controlled prescription drugs, including narcotic analgesics, anxiolytics, anti-depressants, stimulants, and sedative-hypnotics play a significant and legitimate role in interventional pain management practices in managing chronic pain and related disorders. Based on the 1997 household survey on drug abuse it is estimated that 76.9 million Americans had used an illicit drug at least once in their life. In 1997, 4.2 million people used analgesics, 2.1 million used tranquilizers, and an additional 2.3 million people used various other drugs, including sedatives, tranquilizers, etc. The non-medical use of prescription drugs exceeds that of all illicit substances except for marijuana and hashish. The report

on epidemiology trends in drug abuse, based on community epidemiology work group analysis showed continued increase of abuse of prescription drugs in urban, suburban, and rural areas. The most commonly abused drugs include oxycodone, hydrocodone, hydromorphone, morphine, codeine, clonazepam, alprazolam, lorazepam, diazepam and carisoprodol. **The diversion of prescription controlled substances to illicit channels is a public health and safety issue.** This review describes the role of controlled substances in chronic pain management, prevalence and economic impact of controlled substance abuse, prescription accountability, effectiveness of prescription monitoring programs, and rationale for national controlled substance electronic reporting system.[119]

2002 Reilly et al. present a description and preliminary findings of a 12-month trial of a Local Court diversion program, called MERIT for Magistrates' Early Referral into Treatment. The aim of MERIT is to divert eligible drug offenders to treatment and rehabilitation services. A total of 172 offenders were assessed and 131 entered the program. The sources of referral were court (58%), police (17%) and self (10%). Main problem drugs were heroin (57%), cannabis (21%) and amphetamines (11%). The majority (85%) had previous convictions and 50% had been in jail. At the end of the trial period one-third (33%) completed the program and one-third (33%) remained in treatment. Main treatment interventions were case management and out-patient counseling, detoxification, residential rehabilitation and methadone maintenance. Police records showed that of the original 43 (33%) graduates only six had come to police notice, mainly for relatively minor offences. Early acceptance and preliminary results has led to an expansion of the MERIT program across New South Wales. **With the rapid expansion of drug courts and diversion programs across Australia, descriptive studies are useful to provide beneficial data to assist policy makers and service providers to develop programs.**[120].

2003 Fuller and Hornfeldt provide the history of a new drug. Narcolepsy, a rare disease with a prevalence of 0.05% in the general population, affects an estimated 140,000 patients in the United States. Patients have been able to lead fuller personal and professional lives since the Food and Drug Administration approved sodium oxybate (Xyrem) in 2002 for treatment of cataplexy in patients with narcolepsy. Previously, gamma-hydroxybutyrate (GHB), the active ingredient of sodium oxybate, had been a substance of abuse, most notoriously as a date-rape drug. Public Law 106-172, the date-rape prohibition act enacted in 2000, was modified to allow the drug to be legally administered for medical purposes. **Because of the apprehension regarding the risk of possible drug diversion after the approval of sodium oxybate and concerns about safety, the Xyrem Risk Management Program was created. This program has been successful in satisfying the needs of patients and physicians while ensuring responsible distribution of the drug.** [111] this article is followed-up in 2004.

2003 Griffiths et al., describe the rationale and procedures for conducting what is considered by many to be the current "gold standard" for initial abuse liability testing of a novel compound: the classic acute dose-effect comparison study in volunteers with histories of drug abuse. **Such a trial is most appropriate for predicting the likelihood of abuse by drug abusers and, in turn, the extent of drug diversion and illicit street sales if the novel compound became available in the community.** The dose-effect abuse liability trial typically involves a double-blind complete crossover design in 10-14 subjects with histories of polydrug abuse in a controlled clinical pharmacology laboratory setting. Drug conditions usually involve placebo, three doses of the novel

compound and three doses of an appropriate reference compound of known abuse liability. In each session, the time-course of effects of a single drug dose are evaluated. Intervals between experimental sessions are typically 1 to several days. The importance of testing high supra-therapeutic doses of the novel drug for the validity of the trial is emphasized, and the use of a dose run-up pilot study for selecting maximal doses and matching doses between the novel and comparison compound is explained. The rationale and description of outcome measures is discussed, including measures that reflect likelihood of abuse (e.g. drug vs. money choice and subject ratings of liking, good effects, estimated monetary street value), secondary measures that should be considered in interpreting likelihood of abuse (e.g. drug identification, subject-rated side effects and mood changes), and additional concurrent measures to establish equivalence of the novel and comparison compound (e.g. behavioral performance, observer-rated assessments, physiological measures)[72].

2003 Jaffe and O’Keeffe discuss the practice of prescribing opioid drugs for opioid dependent patients in the U.S. that has been subjected to special government scrutiny for almost 100 years. From 1920 until 1964, doctors who used opioids to treat addicts risked federal and/or state criminal prosecution. **Although that period ended when oral methadone maintenance was established as legitimate medical practice, public concern about methadone diversion and accidental overdose fatalities, combined with political pressure from both hostile bureaucracies and groups committed to drug-free treatments, led to the development of unprecedented and detailed Food and Drug Administration (FDA) regulations that specified the manner in which methadone (and later, levo-alpha-acetyl methadol, or levomethadyl acetate, (LAAM)) could be provided.** In 1974, Congress gave the Drug Enforcement Administration (DEA) additional oversight of methadone treatment programs. Efforts to liberalize the FDA regulations over the past 30 years have been resisted by both the DEA and existing treatment providers. Additional flexibility for clinicians may evolve from the most recent effort to create an accreditation system to replace some of the FDA regulations. The development of buprenorphine, a partial opioid agonist, as an effective treatment for opioid addiction reopened the possibility for having a less burdensome oversight process, especially because of its reduced toxicity if ingested by non-tolerant individuals. New legislation, the Drug Addiction Treatment Act (DATA) of 2000, created an opportunity for clinicians with special training to be exempted from both federal methadone regulations and the requirement to obtain a special DEA license when using buprenorphine to treat addicts. Some details of how the DATA was developed, moved through Congress, and signed into law are described.[87]

2004 Baker et al. present an investigation of systems to prevent diversion of opiate drugs in general practice in the UK. Statutory regulations govern the procedures that must be followed by general practitioners (GPs) in the UK to minimize the risk of diversion of prescribed opiate drugs for illicit use. However, evidence presented at the trial of Harold Shipman, a GP convicted of murdering patients with diamorphine, suggests that the regulations and monitoring of GPs' prescribing are failing. Aim: To assess the policies followed by general practices in Leicestershire and Rutland with regard to the controlled drugs regulations. A semi-structured interview was administered to a purposeful sample of lead GPs to explore how their practices applied the regulations. The controlled drugs registers and drug storage facilities in these practices were inspected. A questionnaire was sent to all the remaining practices to seek information about their application of the regulations, any concerns they had about the regulations, and any suggestions for

improving them. Of the 142 general practices in Leicestershire, the lead GP in 14 took part in the interviews. Respondents expressed dissatisfaction with current policies including the design of controlled drug registers, and generally supported the reintroduction of an inspection scheme. Ninety (70.9%) of the 127 practices to whom the questionnaire was sent responded and, of these, 31 (34.4%) no longer held a supply of controlled drugs. Those that did hold controlled drugs indicated concern about the regulations, confusion about some aspects including the return and disposal of unused drugs, and a desire for advice and support in the implementation of the regulations. Forty two of the 59 respondents who held a supply of controlled drugs (71.2%) would welcome regular inspection. **CONCLUSION: GPs are confused about the controlled drugs regulations and have little support in implementing them. The suspension of inspection schemes has reduced the amount of advice and support available to them and, in consequence, the regulations are interpreted differently in different practices. These findings are cause for concern about the risk of diversion of controlled drugs, and illustrate how patient safety systems can decay when they are not maintained.**[45]

2004 Brushwood and Kimberlin report a study to determine the frequency of media reports of controlled substance diversion. Quantitative search of news articles from LexisNexis Academic, using search strings related to four different types of controlled substance diversion. The measure is the number of media reports about diversion of controlled substances at the prescriber or dispenser levels, through pharmacy robberies or thefts, and through hijackings or robberies of shipments. They found media reports of controlled substance diversion indicate that theft and loss are important problems and that inappropriate prescribing and dispensing are substantial problems as well. **Leaks of controlled substances from the closed system of distribution seem to be increasing as rapidly through theft and loss as through inappropriate prescribing and dispensing. During the five biennia between 1993 and 2002, these percentage increases in media reports were observed for the different types of diversion: 200% for prescribers; 350% for dispensers; 133% for pharmacy robberies and thefts; and 1,800% for thefts from shipping channels.** [6]

2004 Fuller et al. discuss the Xyrem risk management program. Sodium oxybate, also known as gamma-hydroxybutyric acid (GHB), was discovered in 1960 and has been described both as a therapeutic agent with high medical value and, more recently, a substance of abuse. The naturally occurring form of this drug is found in various body tissues but has been studied most extensively in the CNS where its possible function as a neurotransmitter continues to be studied. Sodium oxybate has been approved in different countries for such varied uses as general anesthesia, the treatment of alcohol withdrawal and addiction, and, most recently, cataplexy associated with narcolepsy. During the 1980s, easy access to GHB-containing products led to various unapproved uses, including weight loss, bodybuilding and the treatment of sleeplessness, sometimes with serious long-term effects. The availability of these unapproved and unregulated forms of the drug led to GHB and its analogues being popularized as substances of abuse and subsequent notoriety as agents used in drug-facilitated sexual assault, or 'date rape', eventually leading to the prohibition of GHB sales in the US. Legal efforts to control the sale and distribution of GHB and its analogues nearly prevented the clinical development of sodium oxybate for narcolepsy in the US. However, following extensive discussions with a variety of interested parties, a satisfactory solution was devised, including legislative action and the development of the Xyrem Risk Management Program. Amendments to the US Controlled Substances Act made GHB a schedule I drug, but also

contained provisions that allow US FDA-approved products to be placed under schedule III. This unique, bifurcated schedule for sodium oxybate/GHB allowed the clinical development of sodium oxybate to proceed and, in July 2002, it was approved by the FDA as an orphan drug for the treatment of cataplexy in patients with narcolepsy as Xyrem(sodium oxybate) oral solution. **To promote the safe use of sodium oxybate, as well as alleviate concerns over possible diversion and abuse following product approval, a proprietary restricted drug distribution system was created, called the Xyrem Success Program. Components of the program include a centralized distribution and dispensing system, a physician and patient registry, compulsory educational materials for patients and physicians, a specially trained pharmacy staff, a method for tracking prescription shipments, and an initial post-marketing surveillance program.** The system has created a unique opportunity to provide both physician and patient education and ongoing patient counseling, promoting greater drug safety and enhanced patient compliance.

2004 Kurashima et al. describe the determination of origin of ephedrine used as precursor for illicit methamphetamine by carbon and nitrogen stable isotope ratio analysis. The sale of ephedrine, one of the precursors of methamphetamine, is strictly controlled and monitored in various countries to prevent the production of illicit methamphetamine. There are three kinds of production scheme for ephedrine manufacture, and it is very useful for precursor control to investigate the origin of ephedrine used for the synthesis of illicit methamphetamine. By means of stable isotope ratio mass spectrometry (IR-MS), we investigated the origin of ephedrine based on the delta(13)C and delta(15)N values. The various origins of ephedrine (biosynthetic, semi synthetic, or synthetic) could be discriminated clearly by using these values. The delta(15)N values of synthetic ephedrine were more negative than those of ephedrine from other sources. By the repeated distillation of methylamine in our laboratory, we confirmed that this could be due to isotope separation during distillation for the purification of methylamine used for ephedrine synthesis. The values for ephedrine used as the precursor were well-correlated with those for methamphetamine synthesized from it. **This drug characterization analysis should be useful to illuminate the origin of the precursors used for clandestine methamphetamine and to trace the diversion of medicinal ephedrine for illicit manufacture of methamphetamine.**[69]

2004 McCabe et al. discuss the use, misuse and diversion of prescription stimulants among middle and high school students. This present study investigated the prevalence and the factors associated with the use, misuse, and diversion of prescribed stimulant medication for attention-deficit hyperactivity disorder (ADHD) in a sample of middle and high school students. As part of a school-based, self-administered web survey in May 2002, students from a Midwestern public school district in the United States in grades six through eleven (n = 1536) reported on three aspects of prescription stimulants; they reported on their use, misuse, and diversion (e.g. trading, selling, offering) of stimulant medication for ADHD. The total student sample was 57% White, 40% African American, and 3% other racial and ethnic groups. Gender and school level were approximately equally distributed in the student sample, and 81% of students had plans to attend college. **The illicit use of stimulant medication was reported by 4.5% of the overall sample. Of the students who reported prescription stimulant use, 23.3% reported being approached to sell, give, or trade their prescription drugs.** After adjusting for socio-demographic factors, the odds for illicit use of stimulant medication was lower among African American students and higher

among those students with no plans for attending college. When compared with students who did not use stimulants or who did not misuse stimulant medications also reported significantly higher rates of alcohol and other drug use. High schools students had the highest rates of alcohol and other drug use. High schools students had the highest odds for being approached to divert their stimulant medications. Our findings suggest that community-based approaches are needed to reduce the illicit use and diversion of stimulant medications within middle and high school student populations.[29]

2004 Miller discusses reduced rates of addictive use of prescriptions of Schedule II medications in Michigan. Reduced rates of addictive patterns of prescribing of Schedule II medications. Improved the prescribing of Schedule II medication for pain disorders. Improved the prescribing of Schedule II medications in addictive disorders. Establish the need and direction for development of curriculum for Schedule II drugs for undergraduate medical education and continuing medical education. Establish the need and direction for development of curriculum for use of Schedule II medications in patients with addictive and pain disorders. Explore the need and direction for development of the monitoring system medical curriculum for Schedule III, IV, and V drugs. Demonstrate link between diversion and adverse effects on health caused by an addictive pattern of use and prescribing of Schedule II drugs. [121]

2004 Parry et al. examined the drug-crime nexus by investigating the prevalence of recent drug use among persons arrested by the police. Data were gathered during August/September 2000 from 1050 adult arrestees in eight police stations in Cape Town, Durban, and Johannesburg (South Africa). Measures included urinalysis results for cannabis, methaqualone (Mandrax), opiates, cocaine, amphetamines, and benzodiazepines, and a questionnaire designed to assess socioeconomic and demographic backgrounds of arrestees, history of prior arrests and imprisonment, current arrest information, profile of substance use, etc. Results of the study show high levels of drug use among arrestees, with 45% testing positive for at least one drug (mainly cannabis and Mandrax). A greater proportion of arrestees in Cape Town tested positive for drugs than in the other sites. Data were also analyzed in terms of gender, age, race, location (site and police station), and offense category. Persons arrested on charges of housebreaking or for drugs/alcohol offenses were particularly likely to test positive for drugs. Drug positive arrestees were more likely to have had a prior arrest. Among the conclusions of the study are that 1) strategies to reduce drug use and drug related crime must be area specific, 2) particular attention needs to focus on young offenders, 3) police need to be trained to recognize particular symptoms and to establish protocols on handling arrestees under the influence of drugs, and 4) **diversion to treatment of drug using offenders deserves more consideration.**[122]

2004 Woolf and Hashmi discuss use and abuse of opioid analgesics: potential methods to prevent and deter non-medical consumption of prescription opioids. Medicinal opiates can produce both analgesia and euphoria. The mood altering action of this class of drugs has led to their abuse (non-medical use), a problem compounded by their physical dependence and addictive qualities. The legitimate expansion of clinical opioid analgesic use for severe chronic non-malignant pain, together with the introduction of high-dose extended-release (modified-release) oral tablet formulations of opioids with good bioavailability, has created increased opportunities for the illicit use of these prescribed drugs. Such use is now a major societal problem, with an incidence that appears to exceed the use of street narcotics such as heroin in the US. **This review highlights the extent of the illicit use of prescribed opiate analgesics and some of the steps, legal, educational**

**and pharmaceutical, that can be taken to potentially reduce the risk of their misuse or diversion for abuse.[99]**

2005 Authority for practitioners to dispense or prescribe approved narcotic controlled substances for maintenance or detoxification treatment. Final rule: DEA is amending its regulations to allow qualified practitioners not otherwise registered as a narcotic treatment program to dispense and prescribe to narcotic dependent persons Schedule III, IV, and V narcotic controlled drugs approved by the Food and Drug Administration specifically for use in maintenance or detoxification treatment. This Final Rule is in response to amendments to the Controlled Substances Act by the Drug Addiction Treatment Act of 2000 (DATA) that are designed to expand and improve treatment of narcotic addiction. **This Final Rule is intended to accomplish the goals of DATA while preventing the diversion of Schedule III, IV, and V narcotic controlled drugs approved by the Food and Drug Administration specifically for maintenance / detoxification treatment.[116]**

2005 Barrett et al. describe characteristics of methylphenidate misuse in a university student sample. Methylphenidate (MPH) is a prescription stimulant drug with known abuse potential; however, little is known about its patterns of misuse or the characteristics of its abusers. A sample of 50 university students reporting MPH misuse and 50 control subjects matched for age, sex, and ethnicity completed structured face-to-face interviews about their MPH and other drug use. For each substance ever used, they provided information regarding routes of administration and other substances ever coadministered, as well as details about the most recent administration. MPH users provided additional information about their reasons for use and, in 36 cases, about how they obtained the drug. Relative to control subjects, those who misused MPH were more likely to have used various other prescription and nonprescription stimulant drugs over their lifetime, and most MPH users reported mixing the drug with other psychoactive substances. Of the MPH sample, 70% reported recreational use of the drug, while 30% reported that MPH was used exclusively for study purposes. Relative to those using it exclusively for study, recreational users were more likely to report using MPH intranasal, as well as co administering MPH with other substances. **Most of those who reported their source of MPH obtained it from an acquaintance with a prescription.** Those who misuse MPH are more likely than their peers to misuse various other substances, and MPH misuse frequently occurs in the context of simultaneous polydrug use. Because the primary supply of inappropriately used MPH appears to be prescribed users, efforts should be directed toward preventing its diversion.[7]

2005 Cicero et al. Rates of abuse of tramadol remain unchanged with the introduction of new branded and generic products: results of an abuse monitoring system, 1994-2004 Journal Article  
PURPOSE: The analgesic Tramadol HCl (Ultram) was approved in 1994 as a non-scheduled drug under the CSA provided that a novel risk-management program would be developed by an Independent Steering Committee (ISC). The risk-management program began in 1995 with the launch of Ultram, and has been modified over the past decade to accommodate Ultracet (Ultram and acetaminophen) in 2001 and generic tramadol in 2002. This provided a unique opportunity to study the potential changes in abuse as the generic and combination products became available. **To proactively detect cases of abuse and diversion, the ISC developed a comprehensive questionnaire which was completed quarterly by an extensive network of drug abuse experts (n = 309) and police agencies (n = 100) who were asked to indicate how many diversion cases involving Ultram, Ultracet, and generic tramadol were identified during the preceding 3**

**months and what were the ten most commonly diverted drugs in their catchment area during that period.** The data generated demonstrate that the abuse of tramadol remained very low despite new branded and generic formulations. **Contrary to the hypothesis that cheaper generic drugs would lead to higher rates of abuse, we found no increase in abuse with the introduction of generic tramadol.** Ultracet abuse rates, unlike those found with other widely used hydrocodone and oxycodone combination products, have been even lower than that observed for tramadol. **Since the FDA has now mandated that proactive risk-management plans be implemented for new drugs, the tramadol risk-management plan may be useful as a prototypic model which can be modified to accommodate other drugs with abuse potential.**[109]

2005 Cicero et al. Trends in abuse of Oxycontin and other opioid analgesics in the United States: 2002-2004. OxyContin (Purdue Pharma L.P., Stamford, Conn) was approved by the Food and Drug Administration (FDA) in 1995 as a sustained-release preparation of oxycodone hydrochloride and was thought to have much lower abuse potential than immediate-release oxycodone because of its slow-release properties. However, beginning in 2000, widespread reports of OxyContin abuse surfaced. In response, Purdue Pharma L.P. sponsored the **development of a proactive abuse surveillance program, named the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) system.** In this paper, we describe results obtained from one aspect of RADARS--the use of drug abuse experts (i.e., key informants)--as a source of data on the prevalence and magnitude of abuse of prescription drugs. The results indicate that prescription drug abuse has become prevalent, with cases reported in 60% of the zip codes surveyed. The prevalence of abuse was rank ordered as follows: OxyContin  $\geq$  hydrocodone  $>$  other oxycodone  $>$  methadone  $>$  morphine  $>$  hydromorphone  $>$  fentanyl  $>$  buprenorphine. In terms of the magnitude of abuse ( $\geq 5$  cases/100,000 persons in a 3-digit zip code), modest growth was seen with all analgesics over the 10 calendar quarters we monitored, but was most pronounced with OxyContin and hydrocodone. These results indicate that OxyContin abuse is a pervasive problem in this country, but that it needs to be considered in the context of a general pattern of increasing prescription drug abuse. **Over the past 5 years, there have been reports, frequently anecdotal, that opioid analgesic abuse has evolved into a national epidemic. In this study, we report systematic data to indicate that opioid analgesic abuse has in fact increased among street and recreational drug users, with OxyContin and hydrocodone products the most frequently abused.** Steps need to be taken to reduce prescription drug abuse, but very great care needs to be exercised in the nature of these actions so the legitimate and appropriate use of these drugs in the treatment of pain is not compromised as a result.[8]

2005 Coleman et al, **A recent federal report indicates that prescription drug abuse is now the second leading category of illicit drug use, following marijuana use. Control strategies typically focus on reducing the diversion of prescription drugs from legitimate sources. The proliferation of unregulated Internet sources, however, has rendered control strategies less effective. This study examines a new approach that focuses on reducing a usability through the use of abuse-resistant drug designs.** Drugs with and without such designs are compared and abuse levels assessed using multiple sources. In every instance, drugs employing abuse-resistant designs were found to have significantly lower levels of abuse than comparator drugs without such designs.[9]



2005 Haydon et al. discuss prescription drug abuse in Canada and the diversion of prescription drugs into the illicit drug market. Prescription drug abuse has received considerable attention in media reports in recent years. The purpose of this article is to describe the Canadian situation and context with regards to prescription drug abuse and the diversion of psychotropic prescription drugs into the illicit drug market, with a focus on the need for more data and interventions. Canada ranks within the top 10% of countries in the use of benzodiazepines, opioid prescriptions and stimulants. **There are many ways that prescription drugs are diverted into the illicit market and varied reasons for use and abuse.** Prescription drug abuse is further related to a number of negative consequences, including overdose. While seniors and women have been the primary focus for research in Canada on prescription drug abuse, adolescents and young adults have received less attention. Systematic epidemiological data specifically on prescription drug abuse in the Canada context are lacking and are needed in order to more clearly understand the reasons for the phenomenon and to develop and implement appropriate interventions.[104]

2005 Jenkinson et al. discuss buprenorphine diversion and injection in Melbourne, Australia: an emerging issue? Melbourne arm of the 2002 Illicit Drug Reporting System (IDRS) cross-sectional study. SETTING: Five Needle and Syringe Programme sites in Melbourne, Australia. PARTICIPANTS: A total of 156 current injecting drug users (IDU). Study eligibility criteria were at least monthly injection during the previous 6 months, and Melbourne residence for at least the preceding 12 months. MEASUREMENTS: Structured questionnaire covering demographic characteristics, drug use history, the price, purity and availability of drugs, criminal activity, risk-taking behaviours, health-related issues and general drug use trends. FINDINGS: Over one-third (37%) of the study sample reported injecting buprenorphine in their life-time and 33% reported injecting the drug in the last 6 months. **Recent buprenorphine injection was associated with the injection of other drug types (i.e. polydrug injectors), opioid substitution treatment, injection-related health problems and involvement in crime. Almost half (47%) of those who reported recent buprenorphine injection reported obtaining the drug illicitly at least once during that time.** CONCLUSIONS: Given the significant health harms associated with intravenous buprenorphine use (e.g. vein damage, abscesses and infections, precipitated withdrawal, blood-borne virus transmission, hospitalization and death), routine monitoring of the misuse of buprenorphine in Melbourne is warranted. These results suggest the need for development of effective countermeasures to address diversion and injection of buprenorphine in this setting.[26]

2005 Kintz et al. report that chemical dependency is a disease that can affect all professions. Among the health care professionals, anesthesiologists represent a specific group. Numerous factors have been proposed to explain the high incidence of drug abuse among anesthesiologists. **These include: easy access to potent drugs, particularly narcotics, highly addictive potential of agents with which they are in contact, and easy diversion of these agents since only small doses will initially provide an effect desired by the abuser.** Opioids are the drugs of choice for anesthesiologists, and among them fentanyl and sufentanil are the most commonly used. Alcohol is mostly abused by older anesthesiologists. Propofol, ketamine, thiopental and midazolam are also abused. In fact, all but quaternary ammonium drugs can be observed. Signs and symptoms of addiction in the hospital workplace include: unusual changes in behavior, desire to work alone, refusal of lunch relief or breaks, volunteer for extra cases, call, come in early and leave late, frequent restroom breaks, weight loss and pale skin, malpractice, behind on charts .... Toxicological investigations are difficult, as the drugs of interest are difficult to test for. In most cases, half-lives

of the compounds are short, and the circulating concentrations weak. It is, therefore, necessary to develop tandem mass spectrometry procedures to satisfy the criteria of identification and quantization. In most cases, blood and/or urine analyses are not useful to document impairment, as these specimens are collected at inadequate moments. Hair analysis appears, therefore, as the unique choice to evidence chronic exposure. Depending on the length of the hair shaft, it is possible to establish an historical record, associated to the pattern of drug use, considering a growth rate of about 1cm/month. An original procedure was developed to test for fentanyl derivatives. After decontamination with methylene chloride, drugs are extracted from the hair by liquid/liquid extraction after incubation in pH 8.4 phosphate buffer. Fentanyl derivatives are analyzed by GC-MS/MS. The following cases are included in this paper: Case 1: 50-year-old anesthetist, positive for fentanyl (644 pg/mg); Case 2: 42-year-old anesthetist, positive for fentanyl (101 pg/mg) and sufentanil (2 pg/mg); Case 3: 40-year-old anesthetist, positive for codeine (210 pg/mg), alfentanil (30 pg/mg) and midazolam (160 pg/mg); Case 4: 46-year-old nurse, found dead, positive for alfentanil (2 pg/mg) and fentanyl (8 pg/mg). In these cases, the combination of an alternative specimen (hair) and hyphenated analytical techniques (tandem mass spectrometry) appears to be a pre-requisite.[46]

2005 Manchikanti et al. describe the evolution of the National All Schedules Prescription Electronic Reporting Act (NASPER): a public law for balancing treatment of pain and drug abuse and diversion **In the United States, physicians are faced with two opposing dilemmas in the treatment of pain - the potential for drug abuse and diversion, and the possible under treatment of pain.** While controlled prescription drugs such as narcotic analgesics, anxiolytics, antidepressants, stimulants, and sedative-hypnotics, play a legitimate role in managing chronic pain and other conditions, the illicit use of prescribed medicines is increasing at epidemic proportions. Diversion and abuse of prescription drugs is costly in terms of addiction, overdose, death, and related criminal activities, but chronic pain carries significant economic, social, and health impact as well. The American Society of Interventional Pain Physicians (ASIPP), as the introducing organization, was joined by several physician and nurse practitioner organizations in support of the National All Schedules Prescription Electronic Reporting (NASPER) Act of 2005, legislation that not only will give physicians an information tool to aid in prescribing controlled substances but also will help identify illicit use and abuse. NASPER is the law that provides for the establishment of a controlled substances monitoring program in each state. The concept for NASPER originated with ASIPP and was modeled after the highly successful Kentucky All Schedules Prescription Electronic Reporting Program (KASPER).[78]

2005 McCabe and Boyd describe sources of prescription drugs for illicit use. This exploratory study investigated the sources of four classes of abusable prescription medications (sleeping, sedative/anxiety, stimulant, and pain medications) that were used illicitly by undergraduate students in the past year. The relationship between these sources and other substance use was examined. METHODS: In the spring of 2003, a random sample of 9,161 undergraduate students attending a large public Midwestern research university was selected to self-administer a Web-based survey. **The respondents identified 18 sources of prescription drugs that were classified into three broad categories: peer, family, and other sources. The majority of respondents who were illicit users obtained their prescription drugs from peer sources. Undergraduate students who obtained prescription medication from peer sources reported significantly higher rates of**

**alcohol and other drug use than students who did not use prescription drugs illicitly or students who obtained prescription medication from family sources.[10]**

2005 Sander and Hays studied prescription opioid dependence and treatment with methadone in pregnancy. **Prescription opioids are used medically to treat pain, but their diversion and abuse continues to escalate in the United States. Abuse of OxyContin (Purdue Pharma LP, Stamford, CT), a timed-release form of oxycodone, is a major focus of public health and law enforcement agencies. The rise in opioid abuse may lead to an increase in opioid dependence in pregnancy, which was a focus of this study.** Our retrospective chart review examined the demographics and patterns of opioid addiction of pregnant women admitted to an inpatient psychiatric unit in an academic medical center in central Kentucky. Charts of 94 women admitted from January 2001 to May 2004 were reviewed. Information obtained included demographics and details of their opioid use, including the specific opioid(s) used, route of administration, and duration of use. Treatment information included length of hospital stay, stabilizing dose of methadone, comorbid drug use, and concomitant Axis I diagnoses. Most women were in their mid-twenties and in the second trimester of pregnancy when they sought treatment. Benzodiazepines were the most common comorbid drugs of abuse and the most frequent medical complication of their drug use was hepatitis C, newly diagnosed in 11 patients. This study demonstrates the need for further research in prescription opioid dependency in pregnancy, methadone maintenance therapy, the safety of detoxification, and neonatal outcomes.[88]

2005 Smith and Woody report on nonmedical use and abuse of scheduled medications prescribed for pain, pain-related symptoms, and psychiatric disorders: patterns, user characteristics, and management options. **The nonmedical use of scheduled medications commonly prescribed for pain, pain-related symptoms, and psychiatric disorders began rising in the mid-1990s. Physicians are confronted with the dilemma of how to minimize the abuse and diversion potential of these products without compromising access for patients with a legitimate medical need.** Using data from the National Survey on Drug Use and Health, we describe the scope of nonmedical use of opioids, stimulants, and tranquilizers; characteristics of nonmedical users; and options available to reduce abuse liability. In 2003, lifetime prevalence estimates of nonmedical use were 31.2 million for opioids, 20.7 million for stimulants, and 20.2 million for tranquilizers. Nonmedical users of psychotherapeutics were more likely to be Caucasian; use alcohol, cocaine, or heroin; and to use needles to inject drugs than those who reported using illicit drugs only. Sources of diversion are enumerated, and options for minimizing the abuse liability associated with these medications are described.[5]

2005 Strang et al. report a national survey of GPs in England and Wales. GPs occupy a pivotal position in relation to providing services to opiate misusers in the UK, and this is now cited to support initiatives in other countries. AIMS: To investigate GP involvement in the management of opiate misusers; and to examine the nature of this prescribing of methadone and other opioids. DESIGN: GP data collected via self-completion postal questionnaire from a 10% random sample of the 30 000 GPs across England and Wales. Patient prescription data obtained on opiate misusers treated during the preceding 4 weeks. SETTING: Primary healthcare practice in England and Wales in mid-2001. METHOD: A questionnaire was mailed to a random 10% sample of GPs stratified by number of partners in the practice, with three follow-up mailshots. Data on drugs prescribed by these practitioners were also studied, including drug prescribed, form, dose and dispensing

arrangements. RESULTS: The response rate was 66%. Opiate misusers had been seen by 51% of GPs in the preceding 4 weeks (mean of 4.1 such patients), of whom 50% had prescribed opiate-substitution drugs. This provided a study sample of 1482 opiate misusers to whom GPs were prescribing methadone (86.7%), dihydrocodeine (8.5%) or buprenorphine (4.4%). Of 1292 methadone prescriptions, mean daily dose was 36.9 mg - 47.9% being for 30 mg or less. Daily interval dispensing was stipulated by 44.6%, while 42.9% permitted weekly take-away supply. CONCLUSIONS: **In 2001 nearly three times as many GPs were seeing opiate misusers than was the case in 1985. Half were prescribing substitute-opiate drugs such as methadone (to an estimated 30 000 patients). However, there are grounds for concern about the quality of this prescribing. Most doses were too low to constitute optimal methadone maintenance; widespread disregard of the availability of supervised or interval dispensing increases the risks of diversion to the blackmarket and deaths from methadone overdose. Increased quantity of care has been achieved. Increased quality is now required.** [33]

2005 Upadhyaya et al. Attention-deficit/hyperactivity disorder, medication treatment, and substance use patterns among adolescents and young adults Journal Article

OBJECTIVE: The aim of this study was to examine the relationship between current active attention-deficit/hyperactivity disorder (ADHD) symptoms, medication treatment, and substance use patterns among college students. METHOD: Three hundred and thirty-four students at a local college were surveyed for current ADHD symptoms and psychopharmacological treatment. The survey was conducted in conjunction with an annual national survey that probes students about their substance use patterns and attitudes. RESULTS: Participants with ADHD as ascertained by medication treatment of ADHD had greater past-year tobacco and marijuana use. Among those with ADHD, participants with active ADHD symptoms were more likely to have past-year tobacco and other drug (besides tobacco, alcohol, and marijuana) use as compared to those without active ADHD symptoms. In addition, participants with active ADHD symptoms were more likely to have past-month "other" drug use as compared to those without active ADHD symptoms. **Among those prescribed medications for ADHD, 25% reported ever using their medication to "get high" and almost 29% reported ever giving or selling their medication to someone else.**

CONCLUSIONS: Results of our preliminary study indicated that ADHD symptom control may be important to protect against increased risk of substance use (particularly tobacco and drugs other than alcohol and marijuana) among college-age students with ADHD. **Further studies of misuse/diversion of prescription stimulant medication among college students are needed.**[93]

2005 Wolf and Poklis A rapid HPLC procedure for analysis of analgesic pharmaceutical mixtures for quality assurance and drug diversion testing. A simple high-performance liquid chromatographic (HPLC) method that allows for the rapid identification and quantification of analgesic and anesthetic solutions typically used in surgical procedures or patient controlled analgesia is presented. The separation of bupivacaine, clonidine, fentanyl, hydromorphone, midazolam, and morphine is complete in less than 20 min. The method allows test solutions to be either directly injected or diluted prior to injection into the HPLC system. The method is useful from the standpoint that pharmaceutical preparations are usually submitted with the known drug of interest and expected concentration. The method is also useful for initial screening of solutions submitted that are either unknown or of questionable identity. **The method has been successfully applied as part of hospital-based quality control and quality assurance programs to detect not**

**only errors in the preparation of solutions of scheduled drugs, but also to uncover illegal diversion of drugs of abuse by medical personnel.[70]**

2006 Carrieri et al. Buprenorphine use: the international experience. The confluence of the heroin injection epidemic and the human immunodeficiency virus (HIV) infection epidemic has increased the call for expanded access to effective treatments for both conditions. Buprenorphine and methadone are now listed on the World Health Organization's Model Essential Drugs List. **In France, which has the most extensive experience, buprenorphine has been associated with a dramatic decrease in deaths due to overdose, and buprenorphine diversion appears to be associated with inadequate dosage, social vulnerability, and prescriptions from multiple providers.** Other treatment models (in the United States, Australia, Germany, and Italy) and buprenorphine use in specific populations are also reviewed in the present article. In countries experiencing a dual epidemic of heroin use and HIV infection, such as former states of the Soviet Union and other eastern European and Asian countries, access to buprenorphine and methadone may be one potential tool for reducing the spread of HIV infection among injection drug users and for better engaging them in medical care.[89]

2006 Compton and Volkow Abuse of prescription drugs and the risk of addiction. Abuse of several categories of prescription drugs has increased markedly in the United States in the past decade and is now at alarming levels for certain agents, especially opioid analgesics and stimulants. Prescription drugs of abuse fit into the same pharmacological classes as their non-prescription counterparts. Thus, the potential factors associated with abuse or addiction versus safe therapeutic use of these agents relates to the expected variables: dose, route of administration, co-administration with other drugs, context of use, and expectations. Future scientific work on prescription drug abuse will include identification of clinical practices that minimize the risks of addiction, the development of guidelines for early detection and management of addiction, and the development of clinically effective agents that minimize the risks for abuse. **With the high rates of prescription drug abuse among teenagers in the United States, a particularly urgent priority is the investigation of best practices for effective prevention and treatment for adolescents, as well as the development of strategies to reduce diversion and abuse of medications intended for medical use.[13]**

2006 Degenhardt et al. Trends in morphine prescriptions, illicit morphine use and associated harms among regular injecting drug users in Australia. This paper examines population trends in morphine prescriptions in Australia, and contrasts them with findings from annual surveys with regular injecting drug users (IDU). Data on morphine prescriptions from 1995 to 2003 were obtained from the Drug Monitoring System (DRUMS) run by the Australian Government Department of Health and Ageing. Data collected from regular IDU as part of the Australian Illicit Drug Reporting System (IDRS) were analyzed (2001 - 2004). The rate of morphine prescription per person aged 15 - 54 years increased by 89% across Australia between 1995 and 2003 (from 46.3 to 85.9 mg per person). Almost half (46%) of IDU surveyed in 2004 reported illicit morphine use, with the highest rates in jurisdictions where heroin was less available. Recent morphine injectors were significantly more likely to be male, unemployed, out of treatment and homeless in comparison to IDU who had not injected morphine. They were also more likely to have injected other pharmaceutical drugs and to report injection related problems. Among those who had injected morphine recently, the most commonly reported injecting harms were morphine dependence

(38%), difficulty finding veins into which to inject (36%) and scarring or bruising (27%). Morphine use and injection is a common practice among regular IDU in Australia. In some cases, morphine may be a substitute for illicit heroin; in others, it may be being used to treat heroin dependence where other pharmacotherapies, such as methadone and buprenorphine, are perceived as being unavailable or undesirable by IDU. **Morphine injection appears to be associated with polydrug use, and with it, a range of problems related to drug injection. Further research is required to monitor and reduce morphine diversion and related harms by such polydrug injectors.**[27]

2006 Fudala and Johnson Development of opioid formulations with limited diversion and abuse potential. **Non-medical abuse of prescription opioid medications is not a new phenomenon, but such use has been increasing in recent years. Various methods have been used and continue to be developed in an effort to limit diversion and abuse of opioid medications. A number of these methods will be described for opioid analgesic and addiction treatment formulations using relevant historical examples (e.g. propoxyphene, pentazocine, buprenorphine) as well as examples of formulations currently being considered or under development (e.g. oxycodone plus naltrexone, sustained-release buprenorphine).** The focus, though not exclusively, will be on those formulations that represent a combination of an opioid agonist with an antagonist. These methods must take into consideration the pharmacokinetic profile of the agonist and antagonist, the expected primary route of abuse of the medication and the medication combination, the dose of medication that is likely to be abused, the availability of alternative drugs of abuse, and the population of potential abusers that is being targeted with the revised formulation.[62]

2006 Hertz and Knight Prescription drug misuse: a growing national problem. Misuse of prescription drugs has been a growing problem in the United States affecting all age groups, including adolescents. Recent years have produced many advances in medical management of chronic pain, depression and anxiety, and attention-deficit/hyperactivity disorder. Many of the medications used to treat these disorders, such as the opioids, benzodiazepines, and psychostimulants, also have potential for abuse and dependence. **The challenge for the clinician today is to maximize safe and effective treatment with available medication, while preventing the diversion of prescribed medication or the development of substance-related disorders in patients receiving these medications.**[79]

2006 Inciardi et al. The Diversion of Ultram, Ultracet, and generic tramadol HCL. Ultram (tramadol HCL) was approved by the Food and Drug Administration in 1994 as a non-scheduled drug under the Controlled Substance Act. The non-scheduled status was contingent on the development and implementation of a comprehensive post-marketing surveillance program by an Independent Steering Committee external to Ortho-McNeil Pharmaceutical charged with monitoring abuse and recommending scheduling if unexpectedly high abuse occurred. The program developed by this committee was composed of a variety of studies, and the results of the first three years of the surveillance efforts revealed that the rate of Ultram abuse was low. At a meeting of the FDA in 1998 to reexamine the scheduling status of Ultram, it was recommended that the scope of the post-marketing surveillance program be broadened to include data on diversion. After a 1-year pilot study, by January 2002, a nationwide diversion survey was fully operational. **This brief communication describes the experiences of this diversion study, and compares the findings on the diversion of Ultram and other tramadol HCL products with that of more widely abused drugs.** Survey data suggest that the diversion of Ultram and other tramadol products is low,

and overall, diversion investigators did not consider tramadol to be a problem in their respective jurisdictions.[63]

2006 Inciardi et al. The diversion of prescription drugs by health care workers in Cincinnati, Ohio. **Data are reported from drug diversion cases involving health care workers who were investigated by the Cincinnati Police Division Pharmaceutical Diversion Squad over an 11-year period. This type of information is rarely available because few U.S. police jurisdictions dedicate resources to prescription drug diversion surveillance.** Data from 1992 through 2002 show that opioids were the drugs most commonly diverted by health care workers, followed by benzodiazepines. Nurses, nursing assistants, and medical assistants were involved in almost three quarters of all cases. Hospitals were the most common sources of complaint to police, followed by pharmacies. Health care professional associations are advised to promote greater awareness of drug misuse and dependence concerns among their memberships, and health care facilities that stock pharmaceuticals liable for misuse and diversion are advised to increase the security of their supplies.[47]

2006 Kroutil et al. Nonmedical use of prescription stimulants in the United States. This study estimated prevalence and correlates of stimulant diversion in the United States and examined relationships between diversion and measures of abuse or dependence. **METHODS:** We conducted descriptive and multivariate analysis of data from the National Survey on Drug Use and Health. Key measures were nonmedical use (misuse) of any prescription stimulant, any stimulant other than methamphetamine, and stimulants indicated for attention-deficit/hyperactivity disorder (ADHD). **RESULTS: Lifetime stimulant misuse included some misuse of longer-acting ADHD drugs. The majority of past-year misuse involved drugs other than methamphetamine, particularly for youth aged 12-17.** Past year misuse was more prevalent among persons aged 12-25, compared with older adults, and among Whites, compared with other groups. Prevalence in large metropolitan areas was lower than or similar to those in less populated areas. About 13% of past-year stimulant misusers met the survey criteria for dependence or abuse, as did about 10% of persons aged 12-25 who misused only nonmethamphetamine stimulants. Most stimulant misuse in the United States (particularly among youth) involved prescription drugs other than methamphetamine. The problem is not limited to metropolitan areas.[94]

2006 Manchikanti studied prescription drug abuse: what is being done to address this new drug epidemic? Testimony before the Subcommittee on Criminal Justice, Drug Policy and Human Resources. This comprehensive health policy review of the prescription drug abuse epidemic is based on the written and oral testimony of witnesses at a July 26, 2006 Congressional Hearing, including that of Laxmaiah Manchikanti, MD, the chief executive officer of the American Society of Interventional Pain Physicians and additions from review of the literature. Honorable Mark E. Souder, chairman of the Subcommittee on Criminal Justice, Drug Policy, and Human Resources, introduced the issue as follows: "Prescription drug abuse today is second only to marijuana abuse. In the most recent household survey, initiates to drug abuse started with prescription drugs (especially pain medications) more often than with marijuana. The abuse of prescription drugs is facilitated by easy access (via physicians, the Internet, and the medicine cabinet) and a perception of safety (since the drugs are FDA approved). In addition to the personal toll of drug abuse using prescription drugs, indirect costs associated with prescription drug abuse and diversion include product theft, commission of other crimes to support addiction, law enforcement costs, and

encouraging the practice of defensive medicine." The Administration witnesses, Bertha Madras, Nora D. Volkow, MD, Sandra Kweder, MD, and Joe Rannazzisi reviewed the problem of drug abuse and discussed what is being done at the present time as well as future strategies to combat drug abuse, including prescription drug monitoring programs, reducing malprescriptions, public education, eliminating Internet drug pharmacies, and the development of future drugs which are not only tamper-resistant but also non-addictive. The second panel, consisting of consumers and advocates, included Misty Fetco, Linda Surks, and Barbara van Rooyan, all of whom lost their children to drugs, presented their stories and strategies to prevent drug abuse, focusing on education at all levels, development of resistant drugs, and non-opioid treatment of chronic pain. Mathea Falco, JD, and Stephen E. Johnson presented issues related to drug abuse and measures to curb drug abuse by various means. Stephen J. Pasierb presented startling statistics on teen drug abuse and various educational programs to deter abuse. Laxmaiah Manchikanti, MD presented an overview of prescription drug abuse, strategies to prevent drug abuse, including immediate funding and rapid implementation of NASPER, education at all levels and improving relations with the DEA and the provider community.

2006 McCabe et al. Medical use, illicit use and diversion of prescription stimulant medication. The objective of this study was to examine the prevalence and factors associated with the illicit use of prescription stimulants and to assess the relationship between the medical and illicit use of prescription stimulants among undergraduate college students. A Web survey was self-administered by a random sample of 9,161 undergraduate students attending a large public Midwestern university in the spring of 2003. **A total of 8.1% reported lifetime illicit use of prescription stimulants and 5.4% reported past year illicit use. The number of undergraduate students who reported illicit use of prescription stimulants exceeded the number of students who reported medical use of prescription stimulants for ADHD. The leading sources of prescription stimulants for illicit use were friends and peers.** Multivariate logistic regression analyses revealed several risk factors for illicit use of prescription stimulants such as being male, White, member of a social fraternity or sorority, Jewish religious affiliation, and lower grade point average. All of these characteristics were also related to medically prescribed use of prescription stimulants. Those who initiated medically prescribed use of prescription stimulants for ADHD in elementary school were generally not at increased risk for illicit use of prescription stimulants or other drugs during college as compared to those who were never prescribed stimulant medication. The present study provides evidence that the illicit use of prescription stimulants is a problem among undergraduate college students, and certain subgroups appear to be at heightened risk.[11]

2006 McCabe et al. Medical use, illicit use, and diversion of abusable prescription drugs. The authors investigated the medical use, illicit use, and diversion of 4 distinct classes of abusable prescription medication (sleeping medication, sedative or anxiety medication, stimulant medication, and pain medication) in a random sample of undergraduate students. In spring 2003, 9,161 undergraduate students attending a large, public, Midwestern research university in the United States self-administered a Web-based survey. **The prevalence rate for illicit use within the past year was highest for pain medication, followed by stimulant medication, sedative or anxiety medication, and sleeping medication.** Women generally reported higher past-year medical use rates. However, undergraduate men reported higher illicit use rates. The illicit use-medical use ratio



for stimulant medication was the highest among the 4 classes of prescription drugs. Medical users of stimulants for attention deficit hyperactivity disorder were the most likely to be approached to divert their medication. Multivariate results indicated that illicit users of prescription drugs were more likely to use other drugs than were students who did not use prescription drugs illicitly. The authors provide evidence that prescription drug abuse is a problem among college students.[12]

2006 McColl and Sellers Research design strategies to evaluate the impact of formulations on abuse liability. Scheduling of a chemical drug substance under the Controlled Substances Act (CSA) includes an evaluation of preclinical and clinical safety, and experimental abuse liability studies, **as well as information on diversion and overdose.** Formulations that mitigate abuse liability, dependence potential and public health risks (e.g., altered absorption rate and tamperability, long half-life, pro-drugs and combination products) are amenable to preclinical and clinical studies to compare their abuse potential to reference compounds. For new formulations (NF) as marketed agents, direct comparison to the immediate release (IR) formulation of the reference compound is typically needed across the full range of potential studies. While the public health advantage of formulation changes in the marketplace can be conceptualized in behavioral economic terms, generating persuasive data is challenging. Study complexity increases because of additional conditions (e.g., placebo, 2-3 doses of the IR formulation, 2-3 doses of the new formulation, and 2-3 doses of the unscheduled or negative control drug), larger sample sizes (study power driven by the comparison of the new formulation versus the IR or placebo), and associated increases in study duration. However, the use of single maximal doses of well-characterized controls can reduce the number of study arms, and using incomplete block designs can reduce study duration. Less typical experimental approaches may also be useful, such as human choice or discrimination procedures, or pre-marketing consumer studies among experienced drug tamperers. New formulations that demonstrate a substantial difference from marketed or reference products have a potential marketing advantage and should require less onerous risk management. Post-marketing epidemiological data demonstrating the lack of abuse will carry the most weight from a public health and physician perspective.[123]

2006 McCormick Regulatory challenges for new formulations of controlled substances in today's environment. The pharmaceutical industry has made substantial innovations in the area of targeted drug delivery and optimization of pharmacokinetics for existing drugs to try to maximize therapeutic effect while simultaneously minimizing adverse consequences of medication abuse. These innovations, however, have not come without a price. **Designer drugs and high content modified release formulations have been exploited both in casual recreational drug abuse as well as, on a much larger scale, by the criminal diversion of these products for profit.** In this paper we will consider the challenges before manufacturers and regulators as they approach the problem of abuse potential of these new drug products and some of the solutions specifically designed to counteract abuse.[14]

2006 Miller Failure of enforcement controlled substance laws in health policy for prescribing opiate medications: a painful assessment of morbidity and mortality. Controlled substances can be used for legitimate medical purposes to relieve pain and suffering, and allow management of medical and surgical conditions, whether acute or chronic in duration. **However, because these are attractive, addicting drugs, diversion from sources such as physicians and pharmacists can lead to serious health problems. Of importance is that addiction to opiate medications can**

**interfere with treatment of the original pain condition, and can lead to life threatening states because of poor judgment and depressed mood in the users.** Consequently, the public has a vested interest in protecting the medical uses of these medications on the one hand, although reducing the morbidity and mortality from their diversion and addictive use. The controlled substance laws contain 3 sources of policy framework that governs the medical use and diversion of controlled substances: (1) international treaties, (2) federal laws and regulations, and (3) state laws and regulations. These laws are aimed at balancing the need to controlling use with adverse consequences against the therapeutic benefits opiate medications provide the public.[15]

2006 Passik et al. Reality and responsibility: a commentary on the treatment of pain and suffering in a drug-using society. While opioids are a necessary part of the armamentarium of pain management, there has been a growing trend toward prescription drug abuse and diversion in our society. Meeting the goal of treating pain while not contributing to drug abuse and diversion requires vigilance and education. **Physicians and patients have been singled out as the main players in the societal problem of diversion of prescription drugs. In fact, the problem can only be overcome when not only physicians and patients but also healthcare practitioners, third-party payers, law enforcement agencies and regulators, the pharmaceutical industry, and the media finally work together to prevent it, instead of fingering any one party for the blame.**[80]

2006 Robinson Buprenorphine-containing treatments: place in the management of opioid addiction. Although the synthetic opioid buprenorphine has been available clinically for almost 30 years, its use has only recently become much more widespread for the treatment of opioid addiction. The pharmacodynamic and pharmacokinetic profiles of buprenorphine make it unique in the armamentarium of drugs for the treatment of opioid addiction. Buprenorphine has partial mu-opioid receptor agonist activity and is a kappa-opioid receptor antagonist; hence, it can substitute for other micro-opioid receptor agonists, yet is less apt to produce overdose reactions or dysphoria. On the other hand, buprenorphine can block the effects of opioids such as heroin (diamorphine) and morphine, and can even precipitate withdrawal in individuals physically dependent upon these drugs. Buprenorphine has significant sublingual bioavailability and a long half-life, making administration on a less than daily basis possible. Furthermore, its discontinuation is associated with only a mild withdrawal syndrome. Clinical trials have demonstrated that sublingual buprenorphine is effective in both maintenance therapy and detoxification of individuals addicted to opioids. **The introduction of a sublingual formulation combining naloxone with buprenorphine further reduces the risk of diversion to illicit intravenous use. Because of its relative safety and lower risk of illegal diversion, buprenorphine has been made available in several countries for treating opioid addiction in the private office setting, greatly enhancing treatment options for this condition.**[73]

2006 Surratt et al. Prescription opioid abuse among drug-involved street-based sex workers. National population surveys and individual studies over the past decade have documented the escalating abuse of a variety of prescription medications, particularly prescription opioids. Although surveillance data provide important information for estimating the prevalence of prescription opioid abuse in the general population, studies documenting the patterns of prescription drug abuse among chronic street-drug-using populations are extremely rare. This paper examines the abuse of prescription opioids among drug-involved street-based sex workers in

Miami, Florida. The data for this study were drawn from an ongoing HIV intervention trial initiated in 2001, designed to test the relative effectiveness of two alternative HIV prevention protocols for this population. Participants in the study were recruited through traditional targeted sampling strategies, and complete data are available on 588 street-based sex workers. In terms of prescription drug abuse, 12.2 percent of the sample reported using at least one opioid analgesic in the past 90 days without having a legitimate prescription. Logistic regression analyses were conducted to examine the associations between prescription opioid abuse and its predictors. In the multivariate model, factors positively associated with prescription opioid abuse included: Caucasian race (OR = 2.53; 95 percent CI 1.30 to 4.91), current powder cocaine use (OR = 2.28; 95 percent CI 1.28 to 4.08), current heroin use (OR = 2.08; 95 percent CI 1.10 to 3.92), 90-day physical abuse/victimization (OR = 2.07; 95percent CI 1.18 to 3.61), and shorter sex-work involvement (OR = 1.98; 95 percent CI 1.13 to 3.48). In contrast, daily crack smoking was negatively associated with prescription opioid abuse (OR = 0.61; 95 percent CI 0.33 to 1.10). **This study provides some of the first empirical evidence to indicate that prescription opioid abuse is emerging in a heretofore unstudied community of marginalized drug-using sex workers. In addition, data on this population's mechanisms of access to prescription opioids clearly suggest that there is an active black market for these drugs. These findings warrant intensive study to determine the relative contribution of each mechanism of diversion to the illicit market.**[16]

2006 Wilens et al. Characteristics of adolescents and young adults with ADHD who divert or misuse their prescribed medications. Little is known about the risks and characteristics of attention-deficit/hyperactivity disorder (ADHD) patients who misuse or divert their stimulant medications. As part of a 10-year longitudinal study of youths with ADHD, the authors evaluated medication diversion or misuse at the last follow-up period. **METHOD:** Structured psychiatric interviews for diagnosis and a self-report questionnaire regarding medication use in medicated subjects with ADHD compared with controls without ADHD receiving psychotropics for non-ADHD treatment were employed. **RESULTS:** Of 98 subjects receiving psychotropic medications (mean age of 20.8 +/- 5 years), 55 (56%) were ADHD subjects and 43 (44%) were controls receiving medications for other purposes. The authors found that 11% of the ADHD group reported selling their medications compared with no subjects in the control group ( $z = 0.00$ ,  $p < .05$ ). An additional 22% of the ADHD group reported misusing their medications compared with 5% of the control subjects ( $z = 1.7$   $p = .09$ ) and that those with conduct or substance use disorders accounted for the misuse and diversion. A minority of subjects reported escalating their doses and concomitant use with alcohol and drugs. **The data indicate that the majority of ADHD individuals, particularly those without conduct or substance use disorders, use their medications appropriately. The authors' findings also highlight the need to monitor medication use in ADHD individuals with conduct and/or substance use disorders and to carefully select agents with a low likelihood of diversion or misuse in this group.**[31]

2007 Boeuf and Lapeyre-Mestre Survey of forged prescriptions to investigate risk of psychoactive medications abuse in France: results of OSIAP survey. **OBJECTIVE:** To describe patterns of drug diversion from 2001 to 2004 in France and to define different profiles of forged prescriptions. **METHODS:** Data from a national cross sectional survey carried out each year since 2001 were analyzed. A national network of community pharmacies is requested to collect suspect prescriptions during two periods each year in May and November. Data included were date, age and sex of the patient, type of prescription form, drugs and criteria of suspicion. **RESULTS:**

Between 2001 and 2004, a sample of 1710 abnormal prescription forms were analyzed. These concerned women in 54% of cases. The average age of those sampled was 47 years. Sixty-one percent of the 597 varieties of medication belonged to the anatomic therapeutic chemical (ATC) nervous system class. The most frequently involved drugs were benzodiazepines and benzodiazepine analogues (flunitrazepam, zolpidem) or opioids (buprenorphine, morphine). Multiple correspondence analysis underlined two opposite profiles for suspicious prescriptions: (i) specific prescription forms for scheduled drugs presented by men aged <45 years involving drugs for the nervous system and presenting the criteria of stolen, falsified and abnormal prescriptions; and (ii) prescription forms presented by women aged >45 years involving cardiovascular and muscular-skeletal system drugs, presenting the criteria of alteration to the prescription.

**CONCLUSION: Analysis of data collected from community pharmacies in the OSIAP (Ordonnances Suspectes Indicateur d'Abus et de Pharmacodependance) survey gives information about patterns of diversion of medication in France. This system is able to evaluate the impact of measures implemented in order to decrease the misuse of drugs and able to identify new patterns of drug diversion.** Identification of profiles of suspicious 'prescription forms' could help pharmacists to better identify abnormal prescriptions. A European project has recently been implemented to extend this kind of survey to other countries in Europe.[50]

2007 Boyd et al. Prescription drug abuse and diversion among adolescents in a southeast Michigan school district. **OBJECTIVES:** To determine the prevalence of medical use of 4 classes of prescription medications relative to nonmedical use (illicit use), to examine the relative rates among the 4 drug classes, and to assess whether gender differences exist in the trading, selling, loaning, or giving away of medications. **DESIGN:** A Web-based survey was administered to 7th- to 12th-grade students residing in 1 ethnically diverse school district; a 68% response rate was achieved. **SETTING:** During a 3-week period in May 2005, teachers brought students to their schools' computing center where students took the survey using a unique personal identification number to sign on to the survey. **PARTICIPANTS:** There were 1086 secondary students, including 586 girls, 498 boys, 484 black students, and 565 white students. **MAIN OUTCOME MEASURES:** Students were asked about their medical and nonmedical use of sleeping, sedative or anxiety, stimulant, and pain medications. **Diversion of prescription medication was assessed by determining who asked the student to divert his or her prescription and who received it.** **RESULTS:** Thirty-six percent of students reported having a recent prescription for 1 of the 4 drug classes. A higher percentage of girls reported giving away their medications than boys (27.5% vs. 17.4%, respectively;  $\chi^2(1) = 6.7$ ;  $P = .01$ ); girls were significantly more likely than boys to divert to female friends (64.0% vs. 21.2%, respectively;  $\chi^2(1) = 17.5$ ;  $P < .001$ ) whereas boys were more likely than girls to divert to male friends (45.5% vs. 25.6%, respectively;  $\chi^2(1) = 4.4$ ;  $P = .04$ ). Ten percent diverted their drugs to parents. **CONCLUSION:** Physicians should discuss the proper use of prescription medications with their patients and their patients' families.[28]

2007 Cicero et al. The development of a comprehensive risk-management program for prescription opioid analgesics: researched abuse, diversion and addiction-related surveillance (RADARS). **OBJECTIVE.** Beginning in the late 1990's a marked increase in abuse of OxyContin emerged, which led to the development and establishment of a proactive surveillance program to monitor and characterize abuse, named the Researched Abuse, Diversion and Addiction Related

Surveillance (RADARS) System. The main goal of RADARS was to develop proactive, timely and geographically sensitive methods to assess the abuse and diversion of OxyContin, along with a number of other Schedule II and III opioids with the aim of using this information to guide risk reduction interventions. Thus, its major focus was the detection of abuse of OxyContin and other commonly prescribed opioid analgesics at the three-digit ZIP code level across the country utilizing a number of different detection systems. METHODS: The detection systems selected were: (1) Quarterly-surveys of drug abuse experts who are knowledgeable about cases of prescription drug abuse; (2) Surveys of law enforcement agencies that detect diversion of prescription drugs; and (3) Poison Control Center reports of intentional misuse or abuse of prescription opioids. Collectively, the three systems provide overlapping coverage of over 80% of the nation's 973 three-digit ZIP codes. RESULTS: **Preliminary results indicate that prescription drug abuse is prevalent nationwide, but it seems to be heavily localized in rural, suburban and small urban areas. Our results also indicate that hydrocodone and extended and immediate release oxycodone products are by far the most widely abused drugs in the country, but the abuse of all prescription opioids seems to have grown over the 14 quarters since the inception of RADARS.** CONCLUSION: The next step in these studies is to develop regionally specific, risk-minimization-strategies, which is the goal of all risk-management programs. If successful, RADARS will serve as a prototype of such programs for any new drug approved that has measurable abuse potential.[64]

2007 Dupont et al. School-based administration of ADHD drugs decline, along with diversion, theft, and misuse. Since 2000 researchers have reported a decline in the administration of attention-deficit/hyperactivity disorder (ADHD) medications given by school nurses, although no decline has been noted in the incidence of ADHD in school-age populations. Government data for the same period show reduced levels of methylphenidate abuse as measured by its involvement in hospital emergency department (ED) admissions. Offsetting this, however, is an increase in the involvement of amphetamine-dextroamphetamine in hospital ED admissions for the same period. **Because ADHD medications are often administered in the school setting, a survey of school nurses was undertaken to identify factors related to the administration as well as to the diversion, theft, and misuse of ADHD medications. Of 311 school nurses responding, 295 (95%) reported a significant or moderate decline between 2002 and 2004 in the need for school-based administration of ADHD medications. Respondents also reported reductions in diversion, theft, and misuse of ADHD drugs.**[32]

2007 Faraone and Upadhyaya The effect of stimulant treatment for ADHD on later substance abuse and the potential for medication misuse, abuse, and diversion. Attention-deficit/hyperactivity disorder (ADHD) is known to be a strong risk factor for substance use disorders (SUD) in adolescence and in adulthood. Research shows that stimulant treatment does not increase the risk of SUD in adolescents or adults with ADHD but rather that stimulant treatments may have a protective effect. **However, 2 in 10 youths with ADHD misuse their medication. Recent evidence suggests that slow uptake of medication in the brain allows for effective treatment without patients experiencing the euphoric qualities of immediate-release agents that lead to abuse or diversion. As a result, extended-release products and different formulations, such as lisdexamfetamine dimesylate (LDX), are less likely to be misused and diverted and may have lower abuse potential.**[74]

2007 Ghodse 'Uppers' keep going up. Amphetamine-type stimulants are the second most widely used drugs in the world. **Overprescription results in diversion for recreational use and the development of dependence.** The internet plays a significant role in global misuse of amphetamine-type stimulants, permitting uncontrolled dispensing by online pharmacies and providing information on techniques for illicit manufacture.[124]

2007 Hughes Evidence-based policy or policy-based evidence? The role of evidence in the development and implementation of the Illicit Drug Diversion Initiative. ISSUES: Evidence-based policy is promoted as the ideal in drug policy, yet public policy theorists suggest that policy-based evidence may be a more fitting analogy, where evidence is used selectively to support a predetermined policy direction. **The paper assesses the resonance of this notion to the development of the Illicit Drug Diversion Initiative (IDDI),** an apparently pragmatic reform adopted in Australia in 1999 through the Federal Coalition 'Tough on Drugs' strategy. It utilizes interviews with key informants from the Australian drug policy arena conducted in 2005 to assess the role of evidence in the design and implementation of the IDDI. KEY FINDINGS: The current paper shows that while policy-makers were generally supportive of the IDDI and viewed drug diversion as a more pragmatic response to drug users, they contend that implementation has suffered through a selective and variable emphasis upon evidence. Most notably, the IDDI is not premised upon best-practice objectives of reducing harm from drug use, but instead on 'Tough on Drugs' objectives of reducing drug use and crime. IMPLICATIONS: This paper contends that policy-based evidence may facilitate the adoption of pragmatic reforms, but reduce the capacity for effective reform. It therefore has both functional and dysfunctional elements. The paper concludes that greater attention is needed to understanding how to mesh political and pragmatic objectives, and hence to maximize the benefits from policy-based evidence.[125]

2007 Inciardi et al. Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. OBJECTIVE: **Prescription drug diversion involves the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace, and can occur along all points in the drug delivery process, from the original manufacturing site to the wholesale distributor, the physician's office, the retail pharmacy, or the patient. However, empirical data on diversion are limited.** METHOD: In an attempt to develop a better understanding of how specific drug-using populations are diverting prescription opioids and other medications, or obtaining controlled drugs that have already been diverted, qualitative interviews and focus group data were collected on four separate populations of prescription drug abusers in Miami, Florida--club drug users, street-based illicit drug users, methadone maintenance patients, and HIV positive individuals who abuse and/or divert drugs. RESULTS: **Sources of abused prescription drugs cited by focus group participants were extremely diverse, including their physicians and pharmacists; parents and relatives; "doctor shopping"; leftover supplies following an illness or injury; personal visits to Mexico, South America and the Caribbean; prescriptions intended for the treatment of mental illness; direct sales on the street and in nightclubs; pharmacy and hospital theft; through friends or acquaintances; under-the-door apartment flyers advertising telephone numbers to call; and "stealing from grandma's medicine cabinet."** CONCLUSION: While doctor shoppers, physicians and the Internet receive much of the attention regarding diversion, the data reported in this paper suggest that there are numerous active street markets involving patients, Medicaid recipients and pharmacies as well. In

addition, there are other data which suggest that the contributions of residential burglaries, pharmacy robberies and thefts, and "sneak thefts" to the diversion problem may be understated.[1]

2007 Knotkova and Pappagallo Adjuvant analgesics. Chronic pain, whether arising from viscera, bone, or any other tissue or structure, is, more often than commonly thought, the result of a mixture of pain mechanisms, and therefore there is no simple formula available to manage chronic complex pain states. Box 1 summarizes a pharmacological algorithm for difficult-to-treat chronic pain, which merely introduces the medication aspect of the treatment. In effect, any comprehensive algorithm should call for an interdisciplinary approach that would include rehabilitation, as well as psychosocial, and when indicated, interventional techniques. Box 1 Analgesic algorithm for difficult-to-treat pain syndromes. Pharmacological Interventions. Moderate to severe pain/functional impairment; pain with a score of >4 on the brief pain inventory. 1. Gabapentinoid (gabapentin, pregabalin)+/-Opioid/opioid rotation or 2. Antidepressant (TCA, duloxetine, venlafaxine)+/-Opioid/opioid rotation or 3. Gabapentinoid+antidepressant+Opioid/opioid rotation; in addition, may consider trials of one or more of the following adjuvants when clinically appropriate: Topical therapies for cutaneous allodynia/hyperalgesia. Anti-inflammatory drugs (corticosteroids for acute inflammatory neuropathic pain)IV bisphosphonates for cancer bone pain or CRPS/RSDNon-gabapentinoid AEDs such as carbamazepine or oxcarbazepine or lamotrigine+/- baclofen for intermittent lancinating pain due to cranial neuralgiasNMDA antagonists Mexiletine On a compassionate basis, according to the patient's clinical condition and pain mechanism, the physician may want to consider an empirical trial of one or more of the emergent topical, oral or parenteral/intrathecal therapies as discussed in the text. If SMP, consider topical clonidine and sympatholytic interventions; if clinically feasible, trials of topical therapies, eg, lidocaine 5% patch, may be considered for a variety of pain states and features. The major rationale for introducing adjuvants is to better balance efficacy and adverse effects. The following scenarios should prompt the use of adjuvants in clinical practice: The toxic limit of a primary analgesic has been reached. The therapeutic benefit of a primary analgesic has plateaued, eg, treatment has reached its true efficacy limit or pharmacodynamic tolerance has developed. The primary analgesic is contraindicated, eg, substance abuse, aberrant behavior, organ failure, allergy, and so forth. Subjective and qualitative symptoms demand broader coverage. Patients often convey that different medications will impart distinct analgesic benefits. Presence of disabling non-painful complaints and need to manage symptoms such as insomnia, depression, anxiety, and fatigue that all cause worsening of the patient's quality of life and function. Physicians have also been drawn to the adjuvants secondary to new realities of clinical practice. **Moreover, aversion to addiction and diversion remains a potent force that shapes prescribing profiles.**[110]

2007 McCabe et al. Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. METHOD: A self-administered, cross-sectional Web survey was conducted in 2005 at a large public Midwestern 4-year university in the U.S. using a probability-based sampling approach. The final sample included 4580 full-time undergraduate students. RESULTS: **The three most common motives associated with the nonmedical use of prescription opioids were to relieve pain, get high, and experiment. The leading sources of prescription opioids were friends and parents although there were gender differences in reports of primary sources. More than 1 in every 10 nonmedical users reported intranasal administration.** Multivariate analyses indicated nonmedical users of prescription opioids who used for motives other than to relieve pain, obtained these drugs from non-parental sources, or used

these drugs via non-oral routes of administration were significantly more likely to experience substance use related problems. CONCLUSIONS: These results indicate that nonmedical use of prescription opioids represents a considerable problem for particular subgroups of college students. While additional research is needed, the present study offers important new directions for policy and research regarding prescription opioid misuse.[18]

2007 McCabe ET AL. Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. The present study examined the associations between early onset of non-medical use of prescription drugs (NMUPD) (i.e. sedatives, tranquilizers, opioids, stimulants) and the development of prescription drug abuse and dependence in the United States. DESIGN: Data were collected from structured diagnostic interviews using the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Alcohol Use Disorder and Associated Disabilities Interview Schedule: Diagnostic and Statistical Manual version IV (DSM-IV). SETTING: National prevalence estimates were derived from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, n = 43,093). PARTICIPANTS: A nationally representative cross-sectional sample of civilian non-institutionalized adults aged 18 years or older in the United States, of whom 52% were women, 71% white, 12% Hispanic, 11% African American, 4% Asian and 2% Native American or of other racial background. FINDINGS: **A higher percentage of individuals who began using prescription drugs non-medically at or before 13 years of age were found to have developed prescription drug abuse and dependence versus those individuals who began using at or after 21 years of age.** Multivariate logistic regression analyses indicated that the odds of developing any life-time prescription drug abuse among non-medical users was reduced by approximately 5% with each year non-medical use was delayed [adjusted odds ratio (AOR) = 0.95, 95% CI = 0.94, 0.97], and that the odds of developing any life-time prescription drug dependence were reduced by about 2% with each year onset was delayed (AOR = 0.98, 95% CI = 0.96, 1.00) when controlling for relevant covariates. CONCLUSIONS: The results of this study indicate that early onset of NMUPD was a significant predictor of prescription drug abuse and dependence. These findings reinforce the importance of developing prevention efforts to reduce NMUPD and diversion of prescription drugs among children and adolescents. [30].

2007 Morin Possible intranasal quetiapine misuse Journal Article

PURPOSE: A possible case of intranasal quetiapine misuse in a patient with schizoaffective disorder and substance abuse is presented SUMMARY: A 28-year-old Caucasian female with schizoaffective disorder (bipolar type), comorbid polysubstance abuse, tobacco dependence, and personality disorder was admitted to an inpatient psychiatric facility following a hit-and-run conviction. Medications on admission included quetiapine, benztropine, haloperidol, lorazepam, diphenhydramine, and trazodone. As-needed medication orders included benztropine and lorazepam. The patient was hospitalized in order to undergo rehabilitation and psychiatric stabilization. During the first four weeks of the patient's hospital stay, the nursing staff suspected her of "cheeking" or "palming" her quetiapine dose on several occasions. During this time she was also suspected of using cocaine and alcohol while away from the hospital. The patient demonstrated symptoms that are consistent with cocaine withdrawal, but the patient denied the use of cocaine. Aspirin tablets, quetiapine tablets, and white powder were found in her room. The patient stated that the white powder was aspirin. It was suspected that it also contained quetiapine, which the patient later admitted to crushing and snorting for its "calming" effects. Quetiapine was



discontinued. There have been reports in the literature of oral and intranasal quetiapine abuse among prison inmates. **CONCLUSION: Possible intranasal quetiapine misuse was detected in a patient with schizoaffective disorder and a history of substance abuse. While antipsychotic medications are not typically thought of as drugs with an abuse potential, reports of the use and diversion of intranasal quetiapine among prison inmates, i.v. quetiapine abuse, and this case report indicate otherwise.[17]**

2007 Novak et al. The nonmedical use of prescription ADHD medications: results from a national Internet panel . Emerging evidence suggests that nonmedical use (NMU) of prescription attention deficit/hyperactivity disorder (ADHD) medications is rising, but many previous investigations have used clinical or regionally based samples or limited their investigations to stimulants rather than to medications specifically used to treat ADHD. Using an Internet-based epidemiological survey, this paper advances understanding of the prevalence and correlates of NMU of medications used to treat ADHD, sources of diverted medications, motivations for use, and consumption patterns. **METHODS:** The study used a self-administered Internet survey of civilian, noninstitutionalized adults (N = 4,297) aged 18 to 49 in the United States. National-level estimates were created using propensity scoring methods and weighting procedures using data from three nationally representative probability surveys: a random-digit dialed telephone survey, the current U.S. Census, and the National Survey on Drug Use and Health (NSDUH). **RESULTS:** Past-year prevalence of NMU of ADHD medications was approximately 2%, with 4.3% reported among those aged 18 to 25 and 1.3% among those aged 26 to 49. Most respondents reporting NMU used on multiple occasions. **Receipt of medications for ADHD was a significant correlate of past-year NMU, though most nonmedical users never had a prescription. Among persons who had never been prescribed medication to treat ADHD, friends or family members were the most common source. Productivity was the most frequently endorsed reason for NMU.** Alcohol was the substance most commonly used in combination with ADHD drugs. **CONCLUSION:** Because most prescription ADHD medications currently are highly regulated, policy options for supply-side reduction of nonmedical use may include identifying those medications with lower abuse liability for inclusion on insurance formularies. Patient and physician education programs also may be useful tools to heighten awareness of intentional and unintentional diversion of ADHD medications for nonmedical purposes.[49]

2007 Vlahov et al. Risk factors for methadone outside treatment programs: implications for HIV treatment among injection drug users. **Diversion of methadone outside treatment programs occurs, yet reasons for use of 'street methadone' are characterized poorly. Self-medication for withdrawal symptoms is one plausible hypothesis. Among HIV-infected drug users, some antiretroviral medications can reduce potency of methadone, yet any association between such effects and the use of supplemental methadone sources remains undetermined.** **OBJECTIVE:** To estimate the frequency and risk factors for use of street methadone. **METHODS:** Injection drug users (IDUs) recruited through extensive community outreach in 1988-89 and 1994 were followed semi-annually with questionnaires about health history, use of licit and illicit drugs including methadone and HIV-related assays. Analyses were performed using generalized estimating equation logistic regression. **RESULTS:** Of 2811 IDUs enrolled and eligible for analysis, 493 people reported use of street methadone over 12 316 person-years of follow-up (4.0/100 person-years). In multivariate analyses, street methadone use was more common among women, whites, those 40-59 years old, those who reported withdrawal symptoms, past methadone

program attendance (6-12 months before visit), recent heroin injection with or without cocaine (but not cocaine alone), smoking or sniffing heroin and reported trading sex. Street methadone was not associated with HIV infection or treatment. CONCLUSION: The results suggest that older IDUs still using heroin may be using street methadone to treat signs of withdrawal. The absence of a higher rate of street methadone use in HIV seropositive IDUs reveals that antiretroviral/methadone interactions are not a primary determinant of use outside of treatment settings.[91]

2007 Weisler Emerging drugs for attention-deficit/hyperactivity disorder. Symptoms of attention-deficit/hyperactivity disorder (ADHD) are heterogeneous and often accompanied by comorbid psychiatric disorders. Although symptoms tend to lessen with age, many patients continue to be affected by the disorder into adulthood. Although many medications are available to treat ADHD, it is unlikely that a single medication will ever be developed to work for all patients. **Recent advances, such as long-acting, extended-release formulations and transdermal delivery systems, have lengthened the duration of effectiveness, which has increased compliance and eliminated the need for additional medication dosing during the school or work day. Additional safe, well-tolerated, long-acting medications with further reduced potential for diversion and abuse are needed.** Catecholamine pathways and their effect on executive functions and ADHD symptom control have been productive areas of research. Potential therapies such as adrenergic receptor agonists, glutamatergic agents, GABA receptor antagonists and nicotine receptor agonists are being explored as future pharmacotherapies for ADHD.[95]

2008 Arria et al. Nonmedical use of prescription stimulants among college students: associations with attention-deficit-hyperactivity disorder and polydrug use. OBJECTIVE: To define, among a sample of college students, the nature and extent of nonmedical use of prescription stimulants (NPS), including both overuse and use of someone else's drug, for attention-deficit-hyperactivity disorder (ADHD); to characterize NPS among individuals not medically using a prescription stimulant for ADHD; and to determine whether NPS and overuse of a medically prescribed stimulant for ADHD were independently associated with an increased risk of other illicit drug use and dependence on alcohol and marijuana. DESIGN: Cross-sectional analysis of personal interview data. SETTING: Large public university in the mid-Atlantic region. Participants. A cohort of 1253 first-year college students aged 17-20 years. MEASUREMENTS AND MAIN RESULTS: All students completed a 2-hour personal interview to ascertain medical use and overuse of prescription stimulants, NPS, nonmedical use of other prescription drugs and illicit drug use, and dependence on alcohol and marijuana. Comparisons were made among nonusers, nonmedical users, and medical users of prescription stimulants for ADHD (ADHD+), some of whom overused their drug. **Of 1208 students who were not using prescription stimulants medically for ADHD (ADHD-), 218 (18.0%) engaged in NPS. Of 45 ADHD+ students, 12 (26.7%) overused their ADHD drug at least once in their lifetime, and seven (15.6%) non-medically used someone else's prescription stimulants at least once in their lifetime. Among 225 nonmedical users, NPS was infrequent and mainly associated with studying, although 35 (15.6%) used prescription stimulants to party or to get high.** Lifetime NPS was associated with past-year other drug use. Both NPS and overuse of prescribed stimulants for ADHD were independently associated with past-year use of five drugs, holding constant sociodemographic characteristics; NPS was also associated with alcohol and marijuana dependence. CONCLUSIONS: Physicians should be vigilant for possible overuse and/or diversion of prescription stimulants for ADHD among college students who are medical users of these drugs, as well as the occurrence of illicit drug use with NPS. Initiation of

comprehensive drug prevention activities that involve parents as well as college personnel is encouraged to raise awareness of NPS and its association with illicit drug use.[19]

2008 Davis and Johnson Prescription opioid use, misuse, and diversion among street drug users in New York City. OBJECTIVE: The use of heroin, cocaine, and other drugs is well researched in New York City, but prescription opioids (POs) have been overlooked. This study documents patterns of PO use, misuse, and diversion among street drug users, and begins to indicate how drug culture practices interact with the legitimate therapeutic goals of PO prescriptions (e.g. pain management). METHODS: Staff completed interviews inquiring about the reasons for use of POs and illicit drugs with 586 street drug users. Ethnographers wrote extensive field notes about subjects' complex patterns of PO use. RESULTS: **Methadone was used (71.9%) and sold (64.7%) at a higher level than OxyContin, Vicodin, and Percocet, used by between 34% and 38% of the users and sold by between 28% and 41% of the sellers. Recent PO use is associated with the recency of using heroin and cocaine (p<.001). Half of the heroin/cocaine sellers sold POs, and one quarter of the PO sellers only sold POs. Subjects were classified into four groups by whether they diverted POs or used POs to relieve pain or withdrawal rather than for euphoria. This classification was associated with frequency of PO use, whether POs were obtained from doctors/pharmacies or from drug dealers and family members, and those mostly likely to use POs for pain and withdrawal.** CONCLUSIONS: POs are an important component of street drug users' drug-taking regimes, especially those who are Physically Ill Chemical Abusers (PICA). Future research is needed to model PO use, misuse, and diversion among this population.[92]

2008 Riggs Non-medical use and abuse of commonly prescribed medications. The steep escalation in non-medical use and abuse of prescription medications in recent years has begun to seriously affect public health, calling for increased clinician awareness. Effective action and collaborative efforts are required to reduce prescription drug abuse while ensuring that availability of needed prescription medications for the majority of patients who use them appropriately is not inadvertently diminished. OBJECTIVE: To educate physicians, clinicians, and other healthcare providers about the scope of non-medical prescription drug abuse and effective clinical management strategies to reduce abuse and diversion of prescription medications. RESEARCH DESIGN AND METHODS: Articles were identified through PubMed and PsycINFO searches (January 2000 to November 2007). Search terms included combinations of 'prescription drug abuse', 'substance abuse', and 'non-medical use of prescription drugs'. Government agency Web sites were searched for additional references. RESULTS: Data from recent national surveys and other published reports indicate that the lifetime prevalence of non-medical prescription drug use/abuse in the United States is approximately 20% (48 million persons aged  $\geq$  12 years). Public health concern is further heightened by a significant increase in past-month use among adolescents (3.3% of 12-17 year olds) and young adults (6.4% of 18-25 year olds) and the vulnerability of a growing elderly population. CONCLUSIONS: **Increased clinician awareness of the scope, demographics, and current trends in prescription medication abuse can be used to enhance screening and effective clinical management skills and strategies to reduce abuse and diversion of prescription drugs without compromising access to needed medications for the majority of patients who use them appropriately.**[2]

2008 Schoedel and Sellers Assessing abuse liability during drug development: changing standards and expectations. **As public health concerns have changed, regulatory expectations for assessing abuse liability of new central nervous system (CNS) drugs have increased. All CNS-active drugs with any properties indicating stimulant, depressant, hallucinogenic, or mood-elevating effects will require an evaluation of abuse liability. Abuse liability assessment involves the collection, analysis, and interpretation of data on chemistry and tampering, animal behavioral pharmacology, clinical trial adverse events (AEs), diversion and overdose, and potentially reinforcing (subjective) effects in recreational drug users.**[126]

2008. Wilens et al. Misuse and diversion of stimulants prescribed for ADHD: a systematic review of the literature/. **OBJECTIVE:** Recent studies have provided variable information on the frequency and context of diversion and the use of nonprescribed and prescribed stimulant medications in adolescent and young adult populations. The purpose of this systematic review of the literature is to evaluate the extent and characteristics of stimulant misuse and diversion in attention-deficit/hyperactivity disorder (ADHD) and non-ADHD individuals. **METHOD:** We conducted a systematic review of the literature of available studies looking at misuse and diversion of prescription ADHD medications using misuse, diversion, stimulants, illicit use, and ADHD medications as key words for the search. **RESULTS:** We identified 21 studies representing 113,104 subjects. The studies reported rates of past year nonprescribed stimulant use to range from 5% to 9% in grade school- and high school-age children and 5% to 35% in college-age individuals. Lifetime rates of diversion ranged from 16% to 29% of students with stimulant prescriptions asked to give, sell, or trade their medications. Recent work suggests that whites, members of fraternities and sororities, individuals with lower grade point averages, use of immediate-release compared to extended-release preparations, and individuals who report ADHD symptoms are at highest risk for misusing and diverting stimulants. Reported reasons for use, misuse, and diversion of stimulants include to concentrate, improve alertness, "get high," or to experiment. **CONCLUSIONS: The literature suggests that individuals both with and without ADHD misuse stimulant medications. Recent work has begun to document the context, motivation, and demographic profile of those most at risk for using, misusing, and diverting stimulants.** The literature highlights the need to carefully monitor high-risk individuals for the use of nonprescribed stimulants and educate individuals with ADHD as to the pitfalls of the misuse and diversion of the stimulants.[48]

2008. **OBJECTIVES:** We sought to document the frequency, circumstances, and consequences of prescription medication-sharing behaviors and to use a medication-sharing impact framework to organize the resulting data regarding medication-loaning and -borrowing practices. **METHODS:** One-on-one interviews were conducted in 2006, and participants indicated **(1) prescription medicine taken in the past year, (2) whether they had previously loaned or borrowed prescription medicine, (3) scenarios in which they would consider loaning or borrowing prescription medicine, and (4) the types of prescription medicines they had loaned or borrowed.** **RESULTS:** Of the 700 participants, **22.9% reported having loaned their medications to someone else and 26.9% reported having borrowed someone else's prescription.** An even greater proportion of participants reported situations in which medication sharing was acceptable to them. **CONCLUSIONS:** Sharing prescription medication places individuals at risk for diverse consequences, and further research regarding medication loaning and borrowing behaviors and their associated consequences is merited.

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