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Health Policy Review

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

Laxmaiah Manchikanti, MD

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

Key words: Prescription drug abuse epidemic, opioid abuse, NASPER, chronic pain, intractable pain, drug diversion, Internet, DEA, NIDA, ONDCP, prescription accountability, prescription drug monitoring, federal drug control

The misuse and abuse of controlled substances, especially those containing opiates, by the general public and in patients suffering with chronic pain is a problem attracting nationwide attention. This fact is reinforced by multiple congressional committees with jurisdiction over the epidemic, numerous hearings conducted by various committees, and the focus the administration. The United States and all of the world have entered into an era where we have to look at a new problem – prescription drug abuse; the byproduct of compassion coupled with a lack of understanding of the complex puzzle of pain and its management. The United States is facing an epidemic of prescription drug abuse and addiction. Abuse of prescription drugs has been steadily, but sharply, rising.

This review is based on the testimony of Manchikanti and others before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources, Committee On Government Reform, the United States House of Representatives, on Wednesday, July 26, 2006, at 10:00 a.m. in Room 2154 of the Rayburn House Office Building. The Subcommittee held a hearing titled "Prescription Drug Abuse: What is Being Done to Address this New Drug Epidemic?" The hearing was called so that the subcommittee could make informed recommendations concerning potential legislation. The purpose of the hearing was to explore the extent to which federal efforts are aimed at reducing the incidence of prescription drug abuse and the success of such efforts. Of particular interest, the Subcommittee was focused on exploring the extent to which the Federal Drug Administration (FDA) and the Drug Enforcement Administration (DEA) are working on minimizing the abuse and diversion of controlled substances. Table 1 illustrates the membership of the Subcommittee, whereas Table 2 provides a list of witnesses.

This comprehensive health policy review will present the causes of the prescription drug abuse epidemic, what is being done at the present time, and a description of a strategic approach for the future.

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1.0 Chronic Pain

1.1 Definitions

Because chronic pain is difficult to define. Hence, a combination of definitions will be utilized (1-3):

- Pain that persists beyond the usual course of an acute disease or a reasonable time for any injury to heal that is associated with chronic pathologic processes that cause continuous pain or pain at intervals for months or years
- Persistent pain that is not amenable to routine pain control methods.
- Pain where healing may never occur.

1.2 Prevalence

The prevalence of chronic pain in the adult population ranges from 2% to 40%, with a median point prevalence of 15% (1-4). Persistent pain has been reported with an overall prevalence of 20% of primary care patients, with approximately 48% reporting back pain (4). The literature also has consistently described the high prevalence of chronic pain in children and the elderly (1-3, 5-10). Historically, even though back pain research has primarily focused on younger, working adults, there is clear evidence that back pain is one of the most frequent complaints in older persons (8-10), and is an independent correlate of functional limitations (5, 11), perceived difficulty in performing daily life activities (12), and a risk factor for future disability. In addition, chronic pain with the involvement of multiple regions is a common occurrence in more than 60% of patients (13).

1.3 Chronicity

It is conventionallky believed that most episodes of low back pain will be short-lived, with 80% to 90% of attacks resolving in about 6 weeks irrespective of the administration or type of treatment, and with only 5% to 10% of patients developing persistent back pain. However, this concept is flawed as the condition tends to relapse and most patients will experience recurrent episodes. Modern evidence has shown that chronic persistent low back pain and neck pain are seen in up to 60% of patients, 5 years or longer after the initial episode (1-3).

1.4 Health and Economic Impact

Chronic non-cancer pain is associated with significant economic, societal, and health impact (14-22). The cost of uncontrolled chronic pain is enormous, both to individuals and to society as it leads to a decline in the quality of life and disability (17, 19-22). Estimates and patterns of direct healthcare expenditures among individuals with back pain in the United States reached $90.7 billion for the year 1998 (17). On average, individuals with back pain generate healthcare expenditures about 60% higher than do individuals without back pain. It was estimated that the cost of healthcare for patients with chronic pain might exceed the combined cost of treating patients with coronary artery disease, cancer, and AIDS (1-3).

Table 1. *Membership of the Subcommittee on Criminal Justice, Drug Policy, and Human Resources, Committee on Government Reform, the US House of Representatives*

Mark E. Souder (R-IN), Chairman
Elijah E. Cummings (D-MD)
[Ranking Member]
Dan Burton (R-IN)
Bernard Sanders (I-VT)
John L. Mica (R-FL)
Danny Davis (D-IL)
Gil Gutknecht (R-MN)
Diane E. Watson (D-CA)
Steve C. LaTourette (R-OH)
Linda T. Sanchez (D-CA)
Christopher Cannon (R-UT)
C. A. (Dutch) Ruppersberger (D-MD)
Candice Miller (R-MI)
Major R. Owens (D-NY)
Virginia Foxx (R-NC)
Jean Schmidt (R-OH)
Eleanor Holmes Norton (D-DC)
Patrick McHenry (R-NC)

2.0 Prescription Drug Abuse

2.1 Substance Abuse and Mental Health Services Administration (SAMHSA) Survey

The 2004 National Survey on Drug Use and Health (NSDUH) (23) showed startling statistics (Fig. 1). An estimated 19.1 million Americans or 7.9% of the population aged 12 and older were cur-

Table 2. *The witness list of the hearing of the Subcommittee on Criminal Justice, Drug Policy, and Human Resources, Committee on Government Reform, the US House of Representatives on Prescription Drug Abuse.*

Panel I
Bertha Madras, MD Deputy Director for Demand Reduction White House Office of National Drug Control Policy
Nora D. Volkow, MD Director of the National Institute on Drug Abuse National Institutes of Health
Sandra Kweder, MD Deputy Director, Office of New Drugs Center for Drug Evaluation and Review Food and Drug Administration
Joe Rannazzisi Deputy Assistant Administrator Office of Diversion Control Drug Enforcement Administration
Panel II
Misty Fetco
Linda Surks
Barbara van Rooyan
Mathea Falco, JD President, Drug Strategies
Stephen E. Johnson Executive Director, Commercial Planning Pain Therapeutics Inc.
Laxmaiah Manchikanti, MD Chief Executive Officer, American Society of Interventional Pain Physicians
Stephen J. Pasierb President and CEO, the Partnership for a Drug-Free America

rent users of illicit drugs in 2004. Approximately 2.4 million persons used pain relievers non-medically for the first time within the past 12 months (Table 3). Almost half of all Americans have tried an illicit drug at least once in their lifetime. The rate of illicit drug use among youth was 10.6%. Approximately 2.1 million persons had used marijuana for the first time within the past 12 months, and 1 in 6 youths is approached by someone selling drugs.

While the true extent of prescription drug abuse and diversion is unknown, estimates from a national survey indicate that the principle drug of abuse for nearly 10% of U.S. patients in treatment is a prescription drug (24). The most commonly abused drugs include oxycodone (Percodan, Percocet, Roxicet, Tylox, OxyContin), hydrocodone (Vicodin, Vicoprofen, Lorcet, Lortab), hydromorphone, methadone, morphine (Astramorph, Duramorph, MS Contin, Roxanol), codeine, clonazepam (Klonopin), alprazolam (Xanax), lorazepam (Ativan), diazepam (Valium), methylphenidate (Ritalin) and carisoprodol (Soma) (23, 25-31).

Non-medical use of prescription drugs is the second most prevalent category of drug abuse, after marijuana as shown in Table 4 (23). In fact, 56% more Americans abuse prescription drugs than abuse cocaine, heroin, hallucinogens, and inhalants – combined (27). Among teenagers, the problem of prescription drug abuse is even more worrisome. According to recent data published by the Partnership for a Drug-Free America, 19% of children ages 12 to 17 report having abused prescription

Table 3. *Past year initiates for illicit drugs from 1995 to 2004 (numbers in thousands)*

	1995	1996	1997	1998	1999	2000	2001	2002[1]	2003[2]	2004
Pain Relievers	917	1,100	1,316	1,548	1,810	2,268	2,400	2,699	2,581	2,422
Tranquilizers	580	659	668	860	916	1,298	1,212	1,253	1,322	1,180
Stimulants	533	577	553	648	706	808	853	775	764	793
Sedatives	117	115	120	147	164	191	225	267	245	240
Marijuana	2,635	2,483	2,603	2,498	2,640	2,746	2,793	2,686	2,463	2,142
Cocaine	744	825	861	868	917	1,002	1,140	1,073	1,094	998
Heroin	111	140	114	140	121	114	154	147	96	118

Source: http://www.samhsa.gov/
1 Estimated using 2003-2004 NSDHUs data only.
2 Estimated using 2004 NSDHUs data only

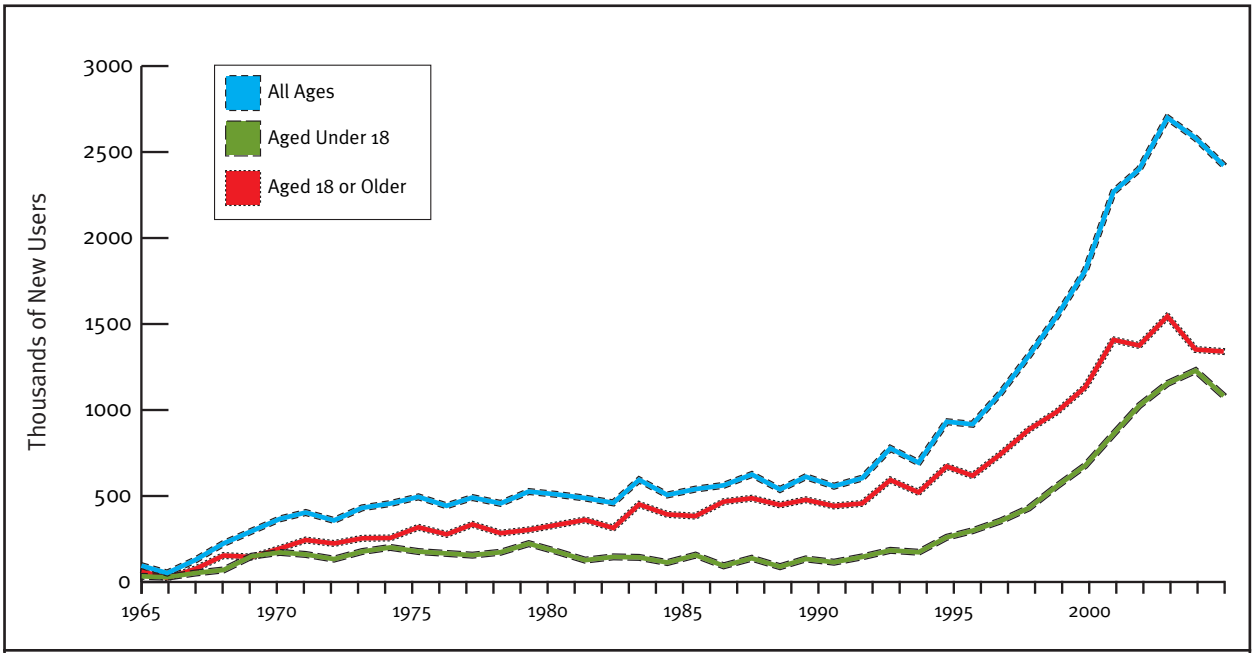

Fig. 1. *Annual numbers of new non-medical users of pain relievers: 1965-2004 (23)*

Table 4. *Types of illicit drug use in past year among persons aged 12 or older from 1995 to 2004 (numbers in thousands)*

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
Non-medical use of Psychotherapeutic drugs	6,166 (2.9%)	6,652 (3.1%)	6,111 (2.8%)	5,759 (2.6%)	9,220 (4.2%)	8,761 (3.9%)	11,102 (4.9%)	14,680 (6.2%)	14,986 (6.3%)	14,643 (6.1%)
Marijuana	17,755 (8.4%)	18,398 (8.6%)	19,446 (9.0%)	18,710 (8.6%)	19,102 (8.6%)	18,589 (8.3%)	21,086 (9.3%)	25,755 (11.0%)	25,231 (10.6%)	25,451 (10.6%)
Cocaine	3,664 (1.7%)	4,033 (1.9%)	4,169 (1.9%)	3,811 (1.7%)	3,742 (1.7%)	3,328 (1.5%)	4,186 (1.9%)	5,902 (2.5%)	5,908 (2.5%)	5,658 (2.4)
Total or Any Illicit Drug usage	22,662 (10.7%)	23,182 (10.8%)	24,189 (11.2%)	23,115 (10.6%)	25,402 (11.5%)	24,535 (11.0%)	28,409 (12.6%)	35,132 (14.9%)	34,993 (14.7%)	34,807 (14.5%)

Source: http://www.samhsa.gov

drugs, of which the largest category is pain relievers. The largest group of prescription drug abusers is comprised of individuals who abuse opioids.

The 2004 NSDUH survey (23) showed lifetime non-medical use of psychotherapeutics has increased to 20% of the population or 48 million adults in America. This survey showed current past year and lifetime use of pain relievers in the US population of 4.4 million, 11.3 million, and 31.8 million respectively. Current OxyContin use was 330,000 persons, past year use was 1.2 million persons, and lifetime use was 3.1 million persons. Total psychotherapeutic drug usage was 6 million or 2.5% of the US population, past year use was 14.6 million or 6.1% of the population, and lifetime use was 48 million or 20% of the US population (Table 4).

2.2 Center on Addiction and Substance Abuse (CASA) Survey

Joseph A. Califano, Jr., chairman and president of the National Center on Addiction and Substance Abuse at Columbia University (CASA), in a July 2005 editorial on the Diversion and Abuse of Controlled Prescription Drugs in the United States (25) noted the following:

> "While America has been congratulating itself in recent years on curbing increases in alcohol and illicit drug abuse and in the decline in teen smoking, abuse and addiction of controlled prescription drugs - opioids, central nervous system depressants and stimulants - have been stealthily, but sharply, rising. Between 1992 and 2003, while the US population increased 14%, the number of people abusing controlled prescription drugs jumped 94% - twice the increase in the number of people abusing marijuana, five times in the number abusing cocaine and 60 times the increase in the number abusing heroin. Controlled prescription drugs like OxyContin, Ritalin, and Valium are now the fourth most abused substances in America behind only marijuana, alcohol, and tobacco."

The CASA report (25) presented alarming statistics including a 212% increase from 1992 to 2003 in the number of 12- to 17-year-olds abusing controlled prescription drugs, and the increasing number of teens trying these drugs for the first time (Fig. 2). The report also illustrated that new abuse of prescription opioids among teens is up an astounding 542%, more than four times the rate of increase among adults. Furthermore, disturbing statistics also show that teens who abuse opioids are likely to use other drugs including alcohol, marijuana, heroin, ecstasy, and cocaine at rates respectively of 2, 5, 12, 15, and 21 times that of teens who do not abuse such drugs.

As per the CASA report (25), the United States is in the throes of an epidemic of controlled prescription drug abuse and addiction with 15.1 million people admitting to abusing prescription drugs - more than the combined number of those who admit abusing cocaine (5.9 million), hallucinogens (4 million), inhalants (2.1 million), and heroin (0.3 million).

2.3 Non-Medical Use of Psychotherapeutic Drugs

Psychotherapeutic drugs used for non-medical purposes include pain relievers, tranquilizers, stimulants and sedatives. Pain relievers are the most commonly abused prescription drugs, representing 75% of non-medical use for the past year as shown in Table 4 (23, 29). Lifetime use of pain relievers increased 22.1% to 24.3%, similar to increases in the use of pain relievers during the past month, 4.1% to 4.7%.

The type of drug for new initiatives was also predominantly with pain relievers with 2.4 million (85%) of the total 2.8 million past year initiatives into non-medical use of prescription drugs

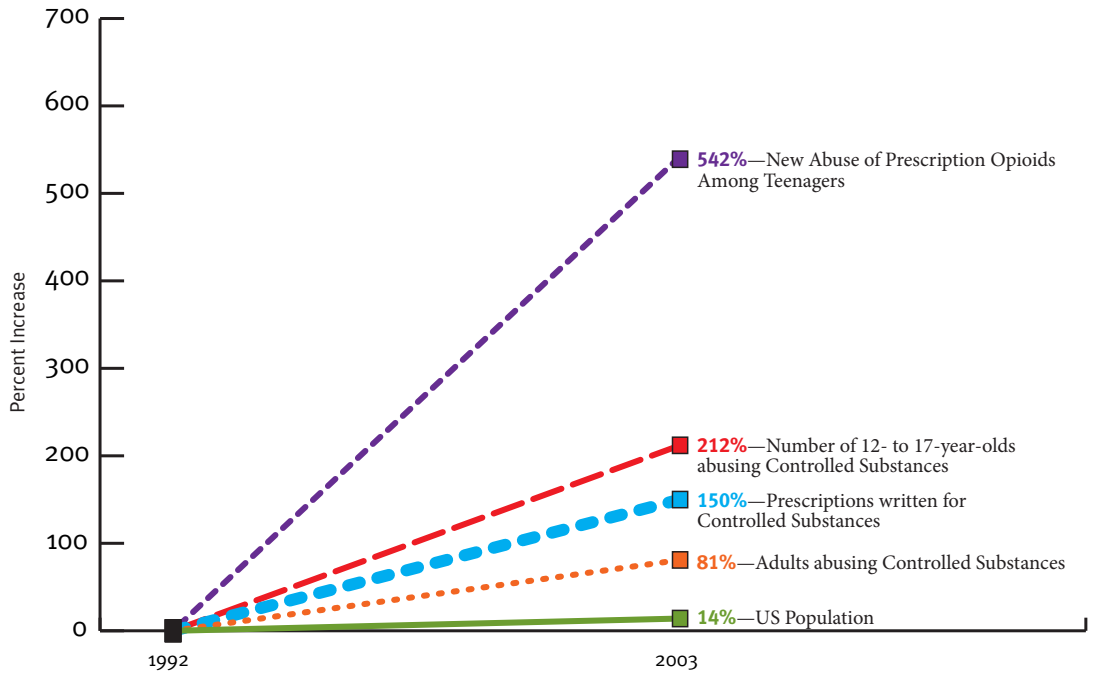

Fig. 2. *Increase of controlled substance abuse from 1992 to 2003, in comparison to US population and prescriptions written for controlled substances (25)*

(Table 3). Another major concern is that new users represented 21.5% of past year pain reliever users (24, 30). Specifically, 1.2 million Americans used OxyContin non-medically in the past year, and of these, 50.7% were new users (29). Figure 3 illustrates the OxyContin initiates since its release. Similarly, Monitoring the Future (MTF) data reported that past year use of OxyContin among 12th graders increased 39.2% over 3 years – from 4% in 2002 (the first year for which data on OxyContin were collected) to 5.5% in 2005. Past year use of Vicodin remained stable, averaging 10% among 12th graders (29, 32). Figure 4 illustrates the percentage of 12th graders reporting non-medical use of OxyContin and Vicodin in the past year from years 2002 to 2005.

Characteristics of recent initiatives for non-medical use of pain relievers in 2004 are as follows (23):

- Among persons aged 12 or older, 2.4 million initiated non-medical use of prescription pain relievers within the past year.
- There were 615,000 new non-medical users of OxyContin in 2004.
- Three-fourths (73.8%) of past year initiates of non-medical pain reliever use had used another illicit drug prior to using pain relievers non-medically.
- Nearly all (99.1%) past-year initiates of non-medical OxyContin use had used another illicit drug prior to using OxyContin non-medically.
- Non-medical use of OxyContin has been skyrocketing with 221,000 persons using it for non-medical purposes in 1997, increasing to 3,176,800 in 2004.
- A survey of USA Today published on July 20, 2006 stated that 1 in 5 adults have a close relative who is or was addicted to drugs or alcohol.

2.4 Special Populations

The growing problem of prescription drug abuse affects individuals at all stages in life and is alarming (33). In adolescents, the increase in prescription drug abuse reported over the past 5 years contrasts with the steady declines in overall illicit drug abuse that has been reported in this group over this same time period (33).

The elderly currently make up only 13% of the population, but receive approximately one-third of all medications prescribed. For practical reasons, older patients are sometimes prescribed long-term and multiple prescriptions, which could lead to abuse or unintentional misuse (33). These medications can interact with over-the-counter medicines and dietary supplements, which older adults tend to consume in significant quantities (33). Older adults also experience higher rates of other illnesses, changes in drug metabolism, and increased susceptibility to toxic effects, with cognitive impairment and other adverse effects. Thus, abuse or unintentional misuse of prescription drugs by elderly persons could lead to more severe health consequences.

Prescription drug abuse among women, because of their combined vulnerabilities, is crucial (33). First, women are more likely than men to suffer from depression, anxiety, trauma, and victim-

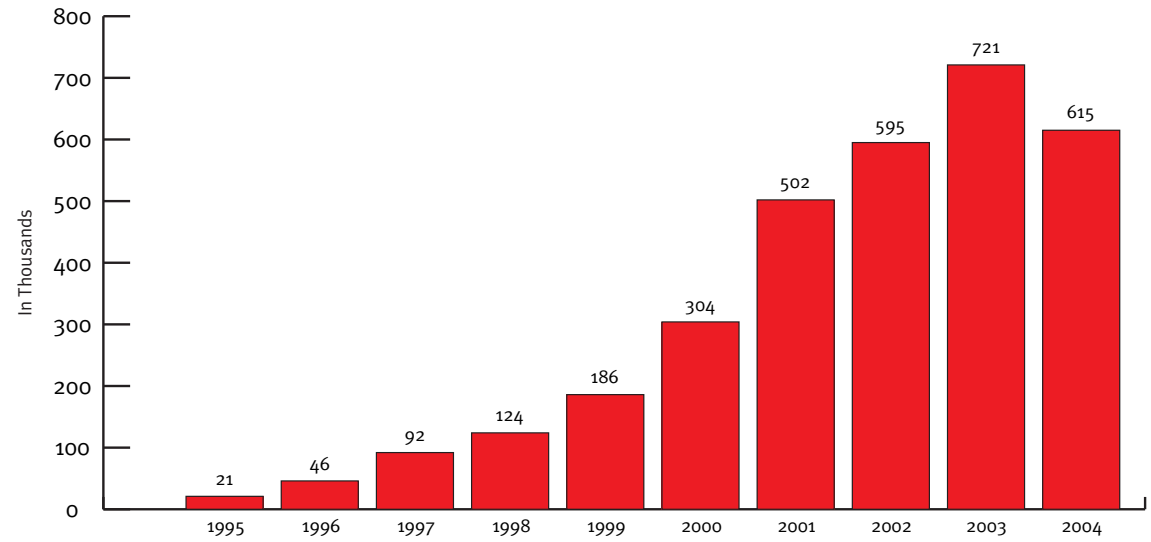

Fig. 3. *Annual number of new non-medical users of OxyContin from 1995 to 2004*
Source: http://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html

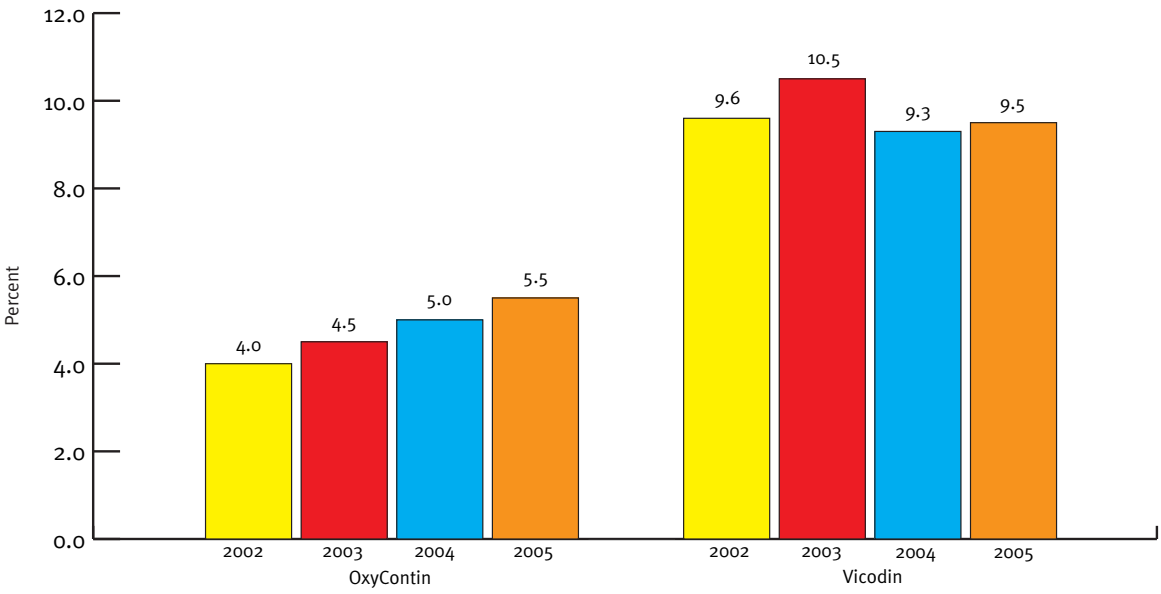

Fig. 4. *Percent of 12th graders reporting non-medical use of OxyContin and Vicodin in the past year remained high: between 2002 and 2005, the abuse of OxyContin by 12th graders increased significantly (32).*

ization, all of which frequently appear with substance abuse in the form of co-morbidities. Second, girls and women report using drugs to cope with stressful situations in their lives. Third, studies suggest that women are significantly more likely than men to be prescribed an abusable drug, particularly in the form of narcotics and anti-anxiety medications. These cumulative risks notwithstanding, adult men and women have roughly similar rates of non-medical use of prescription drugs; 12- to 17-year-old girls, however, are more likely than boys to abuse psychotherapeutic drugs, including stimulants. Survey data collected between 2002 and 2004 suggest that 109,000 pregnant women abused pain relievers in the past year (34). And past-year abuse of any stimulants (including methamphetamine) or sedatives/tranquilizers was reported by 32,000 and 56,000 pregnant women, respectively (33). However, there is overall less non-

medical abuse of prescription psychotherapeutics among pregnant women than among non-pregnant women (6% and 9.3%, respectively), although this is not the case in pregnant adolescent girls (15-17 years), in whom the rate of prescription drug abuse is higher than in those who are not pregnant.

2.5 Drug Abuse Warning Network (DAWN) Reports

The Drug Abuse Warning Network (DAWN) (34) examined the involvement of opiates and deaths related to drug misuse. Nearly 1.3 million emergency department (ED) visits in 2004 were associated with drug misuse/abuse. Non-medical use of pharmaceuticals was involved in nearly a half million of these ED visits with opioids constituting over 158,000 visits and benzodiazepines constituting over 144,000 visits. Two-thirds or more of ED visits associated with opiates/opioids, benzodiazepines, and muscle relaxants involved multiple drugs, and alcohol was one of the other drugs in about a quarter of such visits. The DAWN data (34) also showed that opioids account for more overdose deaths in the United States than either heroin or cocaine.

2.6 Healthcare and Social Costs

Prescription drug abuse inflicts enormous costs on our society. In 2002 alone, abuse of prescription drugs costs were nearly $181 billion (35). Direct costs related to non-medical use of prescription drugs are considerable – for example, 25% of visits to hospital emergency departments are associated with abuse of prescription drugs (27, 34). Indirect costs result from drug theft, the commission of crimes to support addiction, doctor shopping, loss of productivity and wages, and the administration of law enforcement. According to the United Nations Office of Drug Abuse and Crime, the value of the global illicit drug market for the year 2003 was estimated at $322 billion based on retail prices (36).

In a study of increasing deaths from opioid analgesics in the United States (37), unintentional drug poisoning mortality rates increased an average of 5.3% per year from 1979 to 1990 and 18.1% per year from 1990 to 2002. The rapid increase during the 1990s reflects the rising number of deaths attributed to narcotics and unspecified drugs. Between 1999 and 2002, the number of opioid analgesic poisonings on death certificates increased 91.2%, while heroin and cocaine poisonings increased 12.4% and 22.8%, respectively. By 2002, opioid analgesic poisoning was listed in 5,528 deaths – more than either heroin or cocaine. The study noted that the increase in deaths generally matched the increase in sales for each type of opioid. Figure 5 illustrates unintentional drug poisoning mortality rates by drug category from 1979 to 1998. Table 5 illustrates deaths from "narcotic and psy-

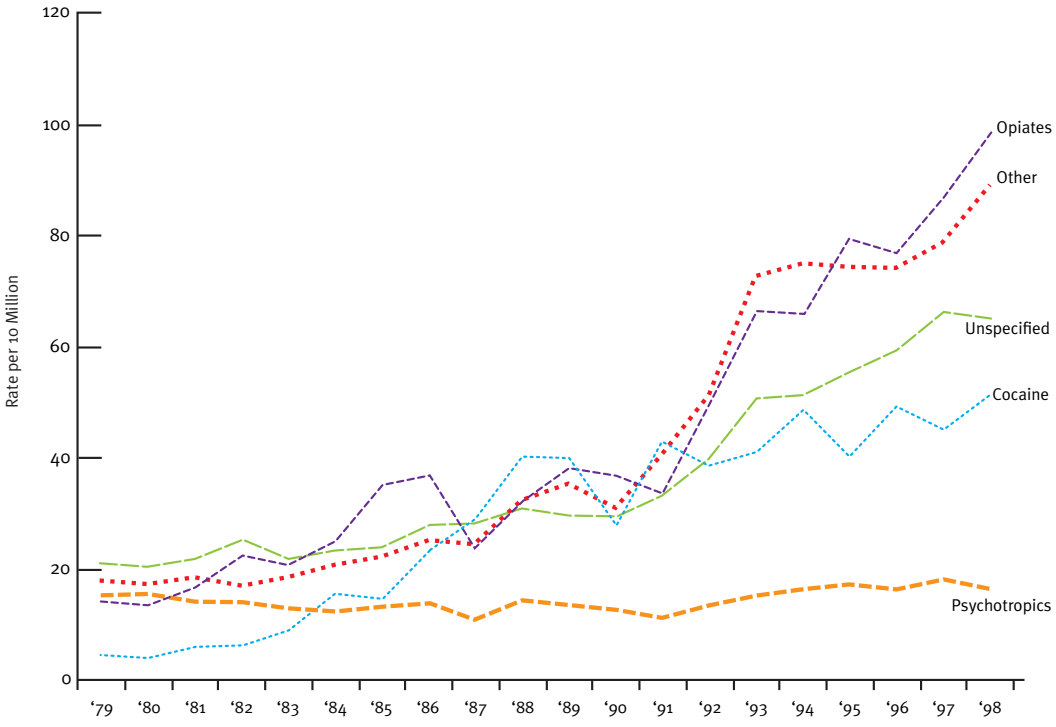

Fig. 5. *Unintentional drug poisoning mortality rates by drug category in the United States from 1979 to 1998.*

Source: Paulozzi et al. Increasing deaths from opioid analgesics in the United States (37)

Table 5. *Deaths from "narcotics and psychodysleptics" and "other and unspecified" drugs* by major type of drug poisoning, US, 1999-2002*

Drug Type†	1999	2000	2001	2002	Percentage change (1999-2002)
Opioid analgesic					
Without heroin or cocaine	1942	2368	3149	4451	+129.2
With heroin, without cocaine	367	260	228	260	-29.2
With cocaine, without heroin	469	418	519	724	+54.4
With heroin and cocaine	113	84	86	93	-17.7
Total‡	2891	3130	3982	5528	+91.2
Cocaine					
Without heroin or opioid‡	2215	2113	2197	2569	+16.0
Total	3182	3022	3197	3909	+22.8
Heroin					
Without heroin or opioid‡	858	942	928	1061	+23.7
Total	1723	1693	1637	1937	+12.4
Cocaine and heroin without opioid‡	385	407	395	523	+35.8
Other specified drugs‡	1666	1668	1636	1790	+7.4
Unspecified drugs‡	2255	2532	2885	3635	+61.2
No drugs listed‡	25	19	11	19	-24.0
Total number	10295	10811	12034	15125	+46.9

*Deaths from "narcotics and psychodysleptics" are those coded to ICD-10 cod X42. Deaths from "other and unspecified drugs" are those coded to X44.
†"Opioid analgesic" is defined as T40.2 ("other opioids"), T40.3 ("methadone"), or T40.4 ("other synthetic narcotics"). "Cocaine" is defined as T40.5. "Heroin" is defined as T40.1. "Other specified drugs" are all other codes from T36-T50.8 range. "Unspecified drugs" are defined as T50.9.
‡These rows are included in the column totals.

Source: Paulozzi et al. Increasing deaths from opioid analgesics in the United States (37)

Table 6. *Retail sales of opioid medications (grams of medication) 1997-2004*

	1997	2004	% of Change
Methadone	518,737	4,730,157	812%
Oxycodone	4,449,562	29,177,530	556%
Fentanyl Base	74,086	370,739	400%
Morphine	5,922,872	14,319,243	142%
Hydrocodone	8,669,311	24,081,900	178%
Hydromorphone	241,078	655,395	172%
Meperidine	5,765,954	4,856,644	-16%
Codeine	25,071,410	20,264,555	-19%

Source: http://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html

chodysleptics" and "other and unspecified drugs" by major type of drug poisoning in the United States from 1999 to 2002. Table 6 shows increasing retail sales of opioid medications in the United States from 1997 to 2004 with oxycodone increasing 556%, followed by methadone increasing 812%, followed by fentanyl base increasing 400%, with morphine, hydrocodone, and hydromorphone increasing less than 200%.

Drug spending is skyrocketing. Significant amounts of Medicaid funds ($110 billion in 2003) are spent on drugs (38). Drug spending in some states has increased by 65% in 2003. Further, the source of payment for specialty treatment or drug abuse and addiction treatment is highest for federal funds (Fig. 6). Federal drug control spending has been gradually increasing over the years (Fig. 7). The abuse and diversion of prescription drugs affect all Americans with higher medical care and law enforcement costs.

3.0 Therapeutic Use Of Controlled Substances

3.1 General Considerations

Considerable controversy sur-

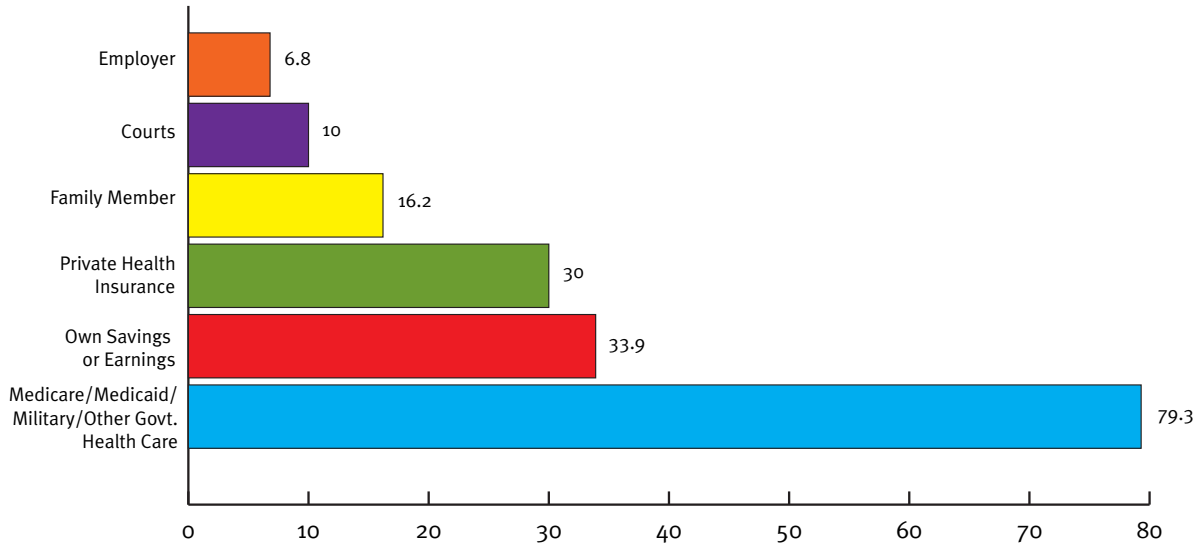

Fig. 6. *Percent source of payment for treatment*
(Note that the estimates of treatment by source of payment include persons reporting more than one source.)
Source: 2002 National Survey on Drug Use and Health (NSDUH). Results from the 2002 National Survey on Drug Use and Health: National Findings. Department of Health and Human Services (30, 31)

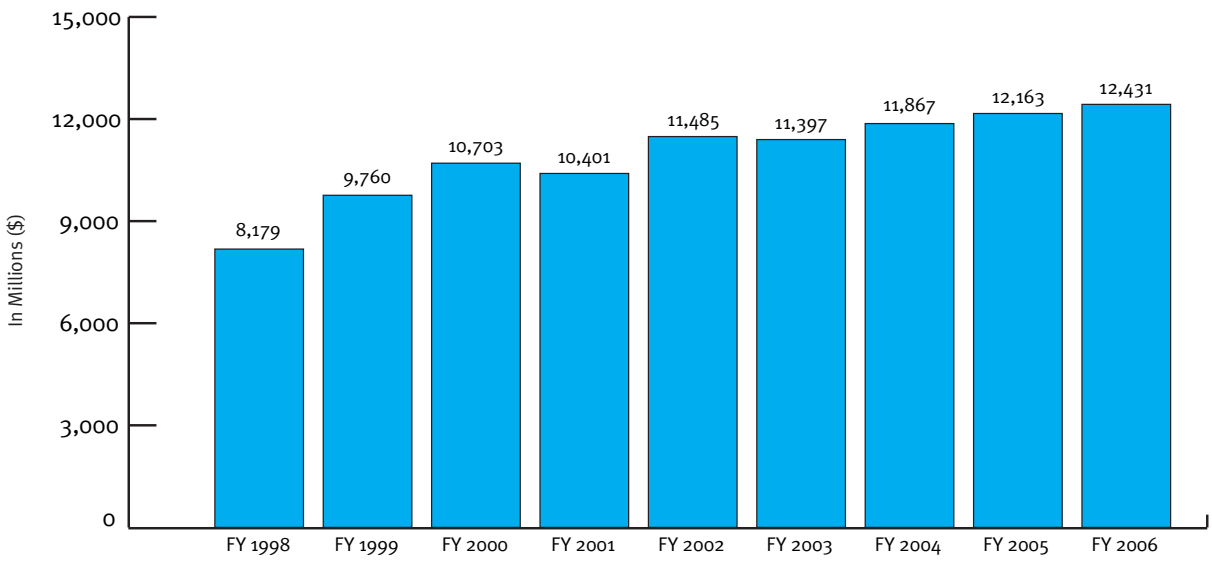

Fig. 7. *Federal drug control spending*

rounds the use of opioids for the treatment of chronic pain of non-cancer origin. Inadequate treatment of pain has been attributed to a lack of knowledge about pain management options, inadequate understanding of addiction, or to fears of investigation or sanction by federal, state, and local regulatory agencies (1-3, 38-40). Many authors contend that drug therapy with opioid analgesics plays an important role in pain management and should be available when needed for the treatment of all kinds of pain, including non-cancer pain (1-3, 37, 38-41). The DEA also took the position that clinicians should be knowledgeable about using opioids to treat pain, and should not hesitate to prescribe them when opioids are the best clinical choice of treatment (42).

3.2 Response to Alleged Undertreatment

The alleged undertreatment of pain as a major health problem in the United States has led to the development of initiatives to address the multiple alleged barriers responsible for the undertreatment of pain (38). Patient advocacy groups and professional organizations have been formed with a focus on improving the management of pain (38). Consequently, numerous clinical guidelines also have been developed, even though none of them have been developed using evidence-based medicine. These include model guidelines adapted by the Federation of State Medical Boards (FSMB) (43). In addition, based on the influence of advocacy groups, over one-third of the state legislatures have instituted intractable pain treatment acts that provide immunity from discipline for physicians who prescribe opioids within the requirements of the statute.

3.3 Opioid Use in Chronic Pain

In pain management settings, as many as 90% of patients have been reported to receive opioids for chronic pain management (44-71). A prospective evaluation (45) showed that 90% of the patients were on opioids and 42% were on benzodiazepines prior to presenting to an interventional pain management center. Many of the patients also received more than one type of opioid, most commonly one for sustained release and one for breakthrough pain. Multiple other reports (72-87) revealed widespread use of opioids in the management of chronic pain (Fig. 8). Finally, the increasing retail sale of opioid medications is proof that opioids are used much more frequently (Table 6). Sales of hydrocodone increased 178% from 1997 to 2004, compared to 556% for oxycodone.

The renewed interest and an unprecedented demand in managing chronic pain has led to an exponential growth in prescription of controlled substances. Factors responsible for this activity include:

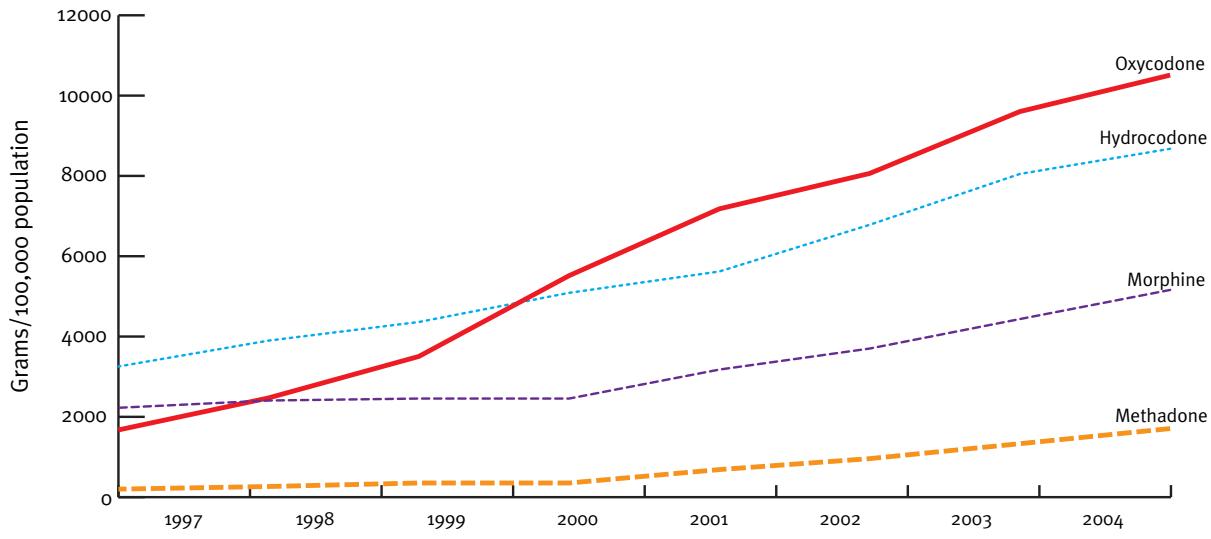

Fig. 8. The increase in therapeutic opioids use in the United States (grams/100,000 population) from 1997 to 2004.

Source: Based on data from US Drug Enforcement Administration. Automation of Reports and Consolidated Orders System (ARCOS); http://www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html

- Pharmaceutical companies providing marketing and gifts.
- Numerous organizations providing guidelines and standards.
- Patient advocacy groups demanding opioids for benign pain.
- Enactment of the Patient's Bill of Rights in many states.
- Unproven regulations from JCAHO and other organizations mandating monitoring and appropriate treatment of pain, which is misunderstood by the media and the public.
- Perceived patient's right to pain relief.
- Increasing and easy availability on Internet.
- Unscrupulous providers running "pill mills."
- High street value of prescription drugs with easy income.
- Perceived legitimacy provided by prescription drugs.
- Perceived safety and purity of prescription drugs.

3.4 Cost of Opioids for Chronic Pain

Frequent use of opioids in managing chronic non-cancer pain has been a major strain on US health care (37, 88, 89). With the majority of patients receiving opioids for chronic pain and increased production of opioids, costs for opioid users have been much higher even than when patients were not abusing. Evaluation of direct costs of opioid abuse in the insured population in the United States showed prescription drug claims for opioids of approximately 20%, whereas opioid abusers had drug claims of almost 60% (88). Mean annual direct healthcare costs for opioid abusers were more than 8 times higher than for non-abusers with $15,884 for abusers versus $1,830 for non-abusers.

It has been shown that Medicaid patients also received significant amounts of opioids in their management with a cost of $100 billion in 2003 (38). Workers compensation carriers in many states are taking measures to curtail opioid use in response to the explosive growth in opioid and other controlled substance use in persons following injuries.

3.5 Effectiveness of Opioids in Chronic Pain

An extensive review of the literature revealed that the effectiveness of prescription opioids for chronic non-malignant pain is limited. In a systematic review (61) evaluating comparative efficacy and safety of long-acting oral opioids for the treatment of chronic non-cancer pain, all of the trials were of relatively short duration, ranging from 5 days to 16 weeks. The results showed poor evidence that one or more long-acting opioids were superior to placebo or short-acting opioids in reducing pain and improving functional outcomes when used for treatment of adults with chronic non-cancer pain. In a second systematic review (62), the authors showed disappointing results with mean pain relief with opioids of about 30% and only 20% of patients experiencing no adverse events or side effects, leading to the conclusion that the short-term efficacy of opioids was good in chronic non-cancer pain, with only a minority of patients in these studies going on to long-term management with opioids.

A third review (60) concluded that a cautious approach must be used in dose escalation and recommended discontinuation of opioids if treatment goals were not met. While their evaluation showed significant pain relief for periods of one week to several months, the beneficial effects on functioning were observed less consistently. In a fourth review (59), it was shown that the average change in pain intensity from baseline was approximately 28% for patients receiving opioids versus 7% for patients receiving placebo. Over one-third of patients receiving a trial of opioids rejected the trial because of adverse effects.

Finally, in evidence synthesis for guidelines (2), the authors concluded that the evidence was limited due to lack of long-term studies, either comparative or placebo-controlled. They concluded that long-term opioid therapy was associated with multiple side effects including opioid-induced immunologic effects, hormonal changes, hyperalgesia, changes in psychomotor performance, addiction and abuse.

4.0 Substance Abuse In Chronic Pain

4.1 Abuse of Controlled Substances

It has been reported that the principle drug of abuse for nearly 10% of youths in drug treatment programs is a prescription drug (24). In a comprehensive review (51), between 3.2% and 18.9% of patients were found to have been diagnosed with a substance abuse disorder. In addition, it was also concluded that diagnoses of abuse, drug dependency, and drug addiction occur in a significant proportion of chronic pain patients.

While opioids are by far the most abused drugs, other controlled substances such as benzodiazepines, sedative hypnotics, and central nervous system stimulants, though described as having less potential for abuse, are also of major concern to interventional pain specialists as they appear to be widely used for non-medical purposes as well (23, 34, 44, 90). This is exemplified by the fact that benzodiazepine-related emergency department visits increased from 71,609 in 1995 to 100,784 in 2002 (90) and to 158,281 for opioids in 2004, whereas, it was 144,385 for benzodiazepines (34). Further, it has been reported that 77.3% of suicide attempts involved benzodiazepines (91). Multiple investigators (52-56, 58, 66-68, 70, 71, 92-94) have shown a prevalence of drug abuse in 18% to 41% in patients receiving opioids for chronic pain. A study evaluating the prevalence, comorbidities and utilization of opioid abuse in a cohort of managed care patients with matched controls showed that opioid abuse rose from 2000 to 2002 with opioid abuse prevalence of 6.7 per 10,000 patients in 2002 (81). Opioid abusers also presented with higher prevalence of opioid prescriptions and comorbidities as compared to controls.

In an evaluation of direct costs of opioid abuse in the insured population of the United States, 740 patients were identified as opioid abusers, a prevalence of 8 in 10,000 persons aged 12 to 64 years continuously enrolled in

healthcare plans for whom 12 months of data were available for calculating costs (88). Opioid abusers, compared with non-abusers, had significantly higher prevalence rates for a number of specific comorbidities including non-opioid poisoning, hepatitis, psychiatric illnesses, and pancreatitis, which were approximately 78, 36, 9, and 21 times higher, respectively, compared to non-abusers.

Increasing abuse and diversion of prescription drugs "on the street" are serious problems. A study evaluating severe dependence on oral opioids illustrated that the majority of patients with severe dependence (39%) obtained opioids by going to different physicians (93). Another frequent form of obtaining opioids included "street" purchase by 26% of the patients. This study also showed that many patients used more than one method of acquiring the drugs. In evaluating prescription opioid abuse in patients presenting for methadone maintenance treatment (94), at admission, most patients (83%) had been using prescription opioids with or without heroin. This study showed that 24% had used prescription opioids only, 24% used prescription opioids initially and heroin later, 35% used heroin first and prescription opioids subsequently, and 17% had used heroin only. Subjects reported regular use of prescription opioids at higher than therapeutic doses.

4.2 Illicit Drug Use in Chronic Pain

Illicit drug use is also a common phenomenon in chronic pain patients. Illicit drug use without controlled substance abuse was found in 14% to 16% of patients, and illicit drug use in patients with controlled substance abuse was present in 34% of the patients (57, 67-71). Illicit drug use was similar in patients using either long-acting or short-acting opioids (49).

4.3 Cost of Opioid Abuse in Chronic Pain

Between 1992 and 2002, the population of the United States increased by 13%. The number of prescriptions written for non-controlled drugs increased by 57%, and the number of prescriptions filled for controlled drugs increased by 154% (95-97). In addition, there was a 90% increase in the number of people who admitted abusing controlled prescription drugs (95-97). In two studies evaluating opioid abuse (87, 88), in the insured population of the United States, opioid abuse was determined to be present from 6.7 to 8 per 10,000 persons insured. Opioid abusers presented with numerous comorbidities and expenses of 8 times higher than for non-abusers ($15,884 versus $1,830). Figure 6 illustrates the percent of the source of payment for treatment of drug abuse (30, 31). Medicare, Medicaid, the military, and other government healthcare paid or supplemented payments for treatment in at least 80% of the population. Overall prescriptions for opioids increased from 222 million in 1994 to 354 million in 2003 (Fig. 9). Prescriptions for hydrocodone and oxycodone reached 120 million in 2005 (33). In addition, sales of ADHD medications alone reached $3.1 billion in 2004 (33). As shown in Figure 5 and Table 5, opioid-related deaths have increased substantially from 1979 to 2002. In 2002, opioid analgesic poisoning was listed in 5,528 deaths – more than either heroin or cocaine (37).

The White House Budget Office estimated drug abuse costs to the US government to be approximately $300

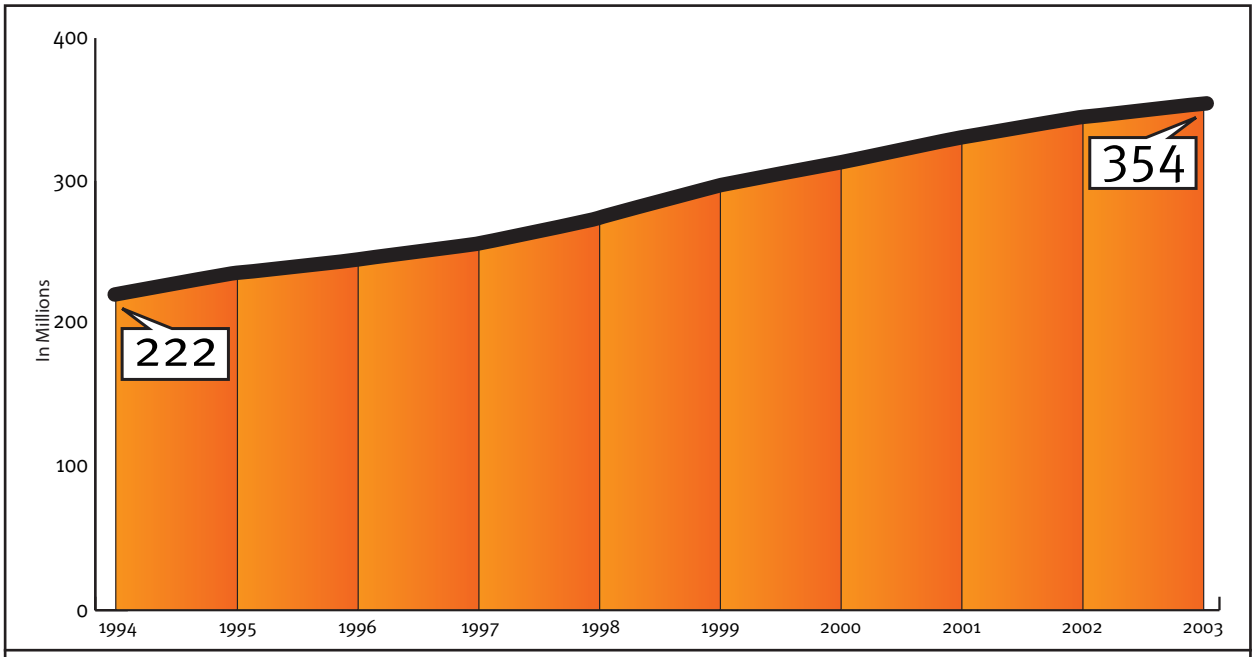

Fig. 9. *Estimated number of prescriptions filled for controlled substances (in millions)*

Source: National Association of Chain Drug Stores and Drug Enforcement Administration

billion a year. In Medicaid programs, the incidence of drug abuse varies from 9.4% to 16.4%, thereby increasing the cost of management (96). Federal government drug spending has been increasing as shown in Figure 7.

5.0 Drug Diversion

5.1 Modes of Diversion

Drugs can be diverted from their lawful purpose to illicit use at any point in the pharmaceutical manufacturing and distribution process. The diversion of prescription drugs among adults is typically described to occur through one or more of the following: doctor shopping, illegal Internet pharmacies, drug theft, prescription forgery, or illicit prescriptions by physicians. Youths typically acquire drugs by stealing them from relatives or buying them from classmates who are selling legitimate prescriptions.

5.2 Doctor Shopping

"Doctor shopping" is one of the most common methods of obtaining prescription drugs for legal and illegal use (2-6, 26, 38, 49, 50, 54, 55, 57, 58, 64-70, 97-99). The majority of physicians perceive "doctor shopping" as the major mechanism of diversion (25). Doctor shopping typically involves an individual going to several different doctors complaining of a wide array of symptoms in order to get prescriptions. This type of diversion can also involve individuals who use people with legitimate medical needs, like cancer patients, to go to various physicians in several cities to get prescription medications. Patients practicing doctor shopping may target physicians who readily dispense prescriptions without thorough examinations or screening. Some patients with a legitimate medical condition may get prescriptions from multiple physicians in various states or even in the same state (95). It has been reported that individuals may collect thousands of pills during a 1-year period and sell them on the street (95). Recently, some elderly have been supplementing their Social Security checks by selling part of their prescriptions (100). Street values of drugs are illustrated in Table 7 (38).

5.3 Internet Sale of Drugs

Since 1999, illegal Internet pharmacies have provided a convenient alternative for individuals wishing to fill their prescriptions (95, 101-103). In 2003, the Government Accountability Office (GAO) estimated the number of Internet pharmacies selling drugs illegally to be about 400, with approximately 50% of the pharmacies located outside the United States (101). Rogue sites, many under the guise of a legitimate pharmacy, provide controlled substances to people without prescriptions. This is particularly troubling with respect to the 30 million youth nationwide with Internet access (95). There are numerous concerns regarding rogue Internet pharmacies, such as the ability to evade state licensing requirements and standards, dispensing controlled substances without a prescription; and providing fake substandard or inappropriate medication (101). However, state and federal laws governing traditional pharmacy stores apply to Internet sales regardless of the method used by an Internet pharmacy to dispense the medication.

CASA (25) has reported the number of Internet pharmacies in operation at any one time has reached as high as 1,400. ComScore networks reported that 17.4 million people visited an online pharmacy in the fourth quarter of 2004, an increase of 14% from the previous quarter (104, 105). Sixty-three percent of these sites did not require a prescription to obtain controlled substances.

Thus, sales of psychoactive prescription drugs over the Internet is not only becoming a major enterprise, but also is presenting new challenges to drug abuse prevention and treatment (106). The global reach of the Internet makes it as easy for an adolescent to buy drugs as it is to buy a book or CD with a credit card, PayPal or even cash. Some sites provide drugs free initially without immediate payment. With more than 200 million Internet users in the United States, the Web is a vital medium for communication, entertainment, and commerce. The Pew Internet and

Table 7. *Street values of "legal" drugs*

Generic Name	Brand Name	Brand Cost/100	Street Value Per 100
Acetaminophen w/Codeine 30 mg	Tylenol #3	$56.49	$800.00
Diazepam 10 mg	Valium 10 mg	$298.04	$1,000.00
Hydromorphone	Dilaudid 4 mg	$88.94	$10,000.00
Methylphenidate	Ritalin	$88.24	$1,500.00
Oxycodone	OxyContin 80 mg	$1,081.36	$8,000.00

Source: Kentucky All Schedule Prescription Electronic Reporting (KASPER). A Comprehensive Report on Kentucky's Prescription Monitoring Program Prepared by the Cabinet for Health and Family Services Office of the Inspector General, Version 1 – 3/29/2006

American Life Project (107) reported that 87% of 12- to 17-year-olds and 82% of 18- to 24-year-olds go online at least monthly. Similarly, 43% of the teens and two-thirds of adult Internet users go online to make purchases and a large number of adults, approximately 79% also use the Internet to look for health and medical information (107). About half of all adult Americans take a prescription medication regularly, and 1 in 4 have used the Internet to learn about prescription medications (107). Fortunately, the majority of Americans have greater confidence in their local pharmacies than Internet-based pharmacies, and only about 4% report having purchased medications online (108). No prescription websites (NPWs) are online pharmacies that supply consumers with controlled substances without a valid prescription (109). An evaluation of 27 Google searches using a wide variety of opioid search terms, specifically "no prescription Vicodin" and "no prescription Hydrocodone" yielded 80% to 90% NPWs, with no links to addiction health information websites.

5.4 Drug Theft

Prescription drug theft can occur at any point from manufacturer to the patient. Thefts are on the rise, largely due to drastic increases in prescription drug abuse and high street prices (37, 93-95, 104, 110-115). Several drugs ranging from OxyContin to Soma have been implicated. Prescription forgery is also fairly common, either by altering the prescription or stealing blank prescription pads in order to write fake prescriptions (25, 38, 95, 112, 116). Prescription forgery may also occur by calling in prescriptions with false identity. The legitimate prescriptions may be altered typically to increase the quantity of controlled substances. Similarly, pharmacists may get involved in prescription drug diversion, first by selling the controlled substances and then, using their database of physicians and patients to write and forge prescriptions to cover their illegal sales. However, the vast majority of prescription forgery is from non-healthcare professionals.

5.5 Improper Prescribing

Illicit prescriptions written by physicians, though rare, are a real phenomenon. Making the headlines are criminal cases involving physicians who become involved in diverting prescription drugs for huge profits (95, 117-120). However, malprescribing, either due to lack of knowledge or due to prescribing inappropriately through "pill mills," is more common (118-124). Malprescribing often represents a lack of knowledge rather than a deliberate attempt to profit from writing these transactions. Arrests by the DEA of physician prescribers have, in fact, decreased from 81 in 1999 to 63 in 2005 (123). However, actions by medical licensure boards have been increasing (122).

5.6 Sharing Among Family and Friends

The preliminary data suggest that the most common method in which controlled substance prescriptions are diverted may be through friends and family (110). This may be accomplished when a person with a lawful and genuine medical need for a controlled substance uses only a portion of the prescribed amount and shares the remaining with friends and family. Alternatively, if the home has someone addicted to controlled substance prescription drugs; the mere availability of unused controlled substance prescriptions in the house may prove to be an irresistible temptation to an inquisitive youngster (110).

5.7 Diversion and Abuse of Methadone

Methadone is emerging as a common drug of choice for the management of chronic non-cancer pain, both as a first line medication and as a replacement opioid, in addition to its long use in management of heroin addiction (93). Diversion of methadone falls into a separate category compared to other prescription opioids. Methadone has a long, successful history as a potent analgesic and is a highly effective medication for reducing the morbidity and mortality associated with opioid addiction. However, recent reports of methadone-associated deaths have stirred public concern. Diversion, abuse, and deaths associated with many opioid medications, including methadone, have been the subject of front-page news. Methadone has been described as a "killer drug" that is widely "abused and dangerous."

In 2001, SAMHSA assumed responsibility from the FDA for the regulation and oversight of the nation's opioid treatment programs, referred to as methadone clinics, or OTPs. Retail sales of methadone in grams increased 812% from 1997 to 2004, second only to oxycodone (Table 6). Figure 8 illustrates the change in prescription volume of methadone compared to other drugs. Although, use of all formulations of methadone has shown steady, incremental growth over the past several years, liquid formulation continues to be predominant (Fig. 10). In 2002, methadone clinics purchased 68% of methadone products, followed by pharmacies purchasing 29%, methadone clinics accounting for the largest amount of methadone products. In 2002, within opioid treatment programs nationwide, 65% of methadone was distributed as liquid, 26% as diskettes and less than 1% as tablets (93). Even then, SAMHSA's Center for Substance Abuse Treatment (CSAT) working with the Centers for Disease Control and Prevention, the DEA, the National Institute on Drug Abuse (NIDA), and the FDA, in a national assessment concluded that opioid treatment programs and the revised federal regulations are not significant contributors to methadone-associated mortality. In fact, they concluded that the greatest incremental growth in methadone distribution in recent years is associated with use of the drug as an analgesic and its distribution through pharmacies.

Medwatch, the FDA's safety information and adverse event reporting program reported 1,114 cases of

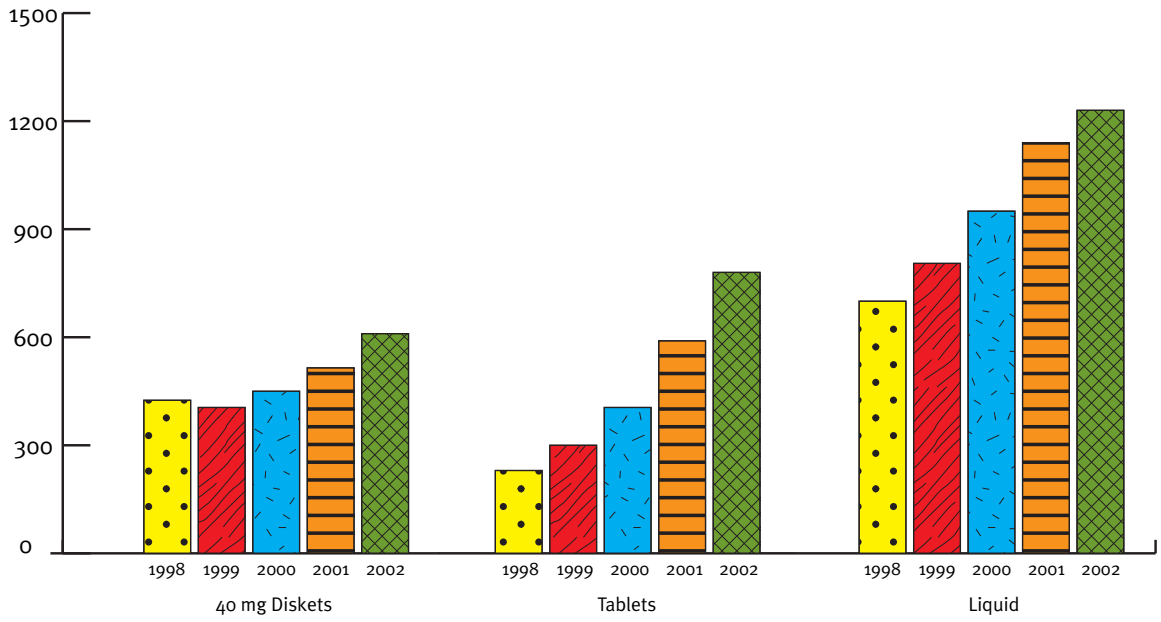

Fig. 10. *Methadone distribution, by formulation, 1998-2002 (grams per 100,000 population)*

Source: Adapted from DEA ARCOS-2 data provided by June E. Howard, Methadone-associated mortality from a report of a national assessment (93)

methadone-associated deaths in adults from 1970 through 2002 (93). Methadone tablet seizures increased 133% between 2001 and 2002; in contrast, seizures of liquid methadone increased only 11% during the same period (93). From 1994 to 2001, DAWN reported an increasing number of opioid analgesic mentions in drug-related emergency department visits, with the largest increases reported for oxycodone with 352%, methadone 230%, and hydrocodone 131% (90).

State-level data on methadone use and associated mortality shows grave concern (125-133). Even though methadone-associated deaths are largely blamed on its distribution for pain management, methadone clinics contribute to a substantial amount of diversion and a significant proportion of the deaths. Methadone clinics no longer only treat heroin addicts in the modern era, the clinics treat any patient meeting the criteria of opioid abuse (very loosely defined) as long as they can afford to stay in the system. In addition, methadone clinics, whether it is necessary or not, escalate the doses thus creating addiction. The report of the National Assessment on Methadone-Associated Mortality (93) cited that among patients in addiction treatment, the largest proportion of methadone-associated deaths have occurred during the drug's induction phase, usually when treatment personnel overestimate a patient's degree of tolerance to opioids, or a patient uses opioids or other central nervous system depressant drugs in addition to the prescribed methadone. The drugs in methadone clinics are dispensed by medical assistants, nurse's aids, etc., in addition to registered nurses with very little supervision. Thus, a significant proportion of patients attending these opioid treatment programs or methadone clinics do not fit the medical necessity criteria to be at these clinics. In fact, one published study (94) showed that 83% of the patients were on prescription opioids with or without heroin. In addition, this study showed that 24% had used only prescription opioids, whereas only 17% used heroin only.

5.8 Cost of Drug Diversion and Abuse to the Society

The diversion and abuse of prescription drugs are associated with incalculable costs to society in terms of addiction, overdose, death, and related criminal activities. The DEA has stated that the diversion and abuse of legitimately produced controlled pharmaceuticals constitute a multi-billion dollar illicit market nationwide (36, 104). As of February 2002, OxyContin has been involved in 464 deaths from prescription drug abuse, as reported by DEA on the basis of medical examiners' autopsy findings for 2000 and 2001 from 32 states. Similarly, there have been multiple deaths reported with methadone (93). Unintentional drug poisoning mortality rates increased substantially from 1992 to 2002 with opioid analgesic poisoning deaths increasing 91.2%, reaching 5,528 deaths by 2002 (37).

As previously indicated, from 1994 to 2001, DAWN recorded an increasing number of opioid analgesic mentions in drug-related emergency department visits, with the largest increases report-

ed for oxycodone of 352%, methadone of 230%, and hydrocodone of 131% (90). Further, in numerous committee hearings, many individuals have presented the data of deaths related to controlled substances (134-137).

The cost of drug abuse, diversion, prevention to society is enormous. Figure 7 illustrates federal spending on drug control programs.

6.0 Causes And Reasons Leading To Abuse

6.1 Increasing Supply and Demand

Among the factors postulated to fuel increased diversion of legitimate prescription drugs are:

- Significant increases in drug availability, number of prescriptions for opioids, and increased prescriptions for sleeping and attention deficit disorders, leading to exponential growth (86, 114, 129).
- Retail sales of opioids has shown exponential growth (Table 6).
- Substantial increase of therapeutic opioids (Figs. 8 and 9).
- In pain management settings, as many as 90% of patients have been reported to receive opioids (44-71).
- The renewed interest and an unprecedented demand for psychotherapeutic drugs.
- Between 1992 and 2002, opioid prescriptions increased by 154%, compared to a 57% increase of all prescriptions, and a 13% increase in the population (25, 95-97).
- Exponential growth in opioid and other psychotherapeutic drug prescriptions in Medicaid, Workers Compensation, and the managed care population (38, 87, 88, 95-97).
- The number of prescriptions for hydrocodone and oxycodone reached 120 million in 2005 (33).

6.1.1 Advertising and Advocacy

- Increased direct-to-consumer advertising, which fosters the view that prescription drugs are integral to our lives.
- Aggressive marketing techniques with pharmaceutical companies providing gifts and unproven information.
- Patient advocacy groups demanding opioids for benign pain and considering that it is their right to receive medication at any cost for any type of pain.

6.1.2 Availability, Internet and Street Value

- Easy availability on the Internet and increasing street value of prescription drugs (Table 7) are major contributions (114).
- Easier availability via web-based sources or theft of legitimate prescriptions.
- The proliferation of illegal Internet pharmacies that dispense these medications without proper prescriptions and surveillance (25, 98).
- Increased web-based sources on how to tamper with medications
- This is fueled by enactment of the patient's Bill of Rights in many states and unproven regulations by JCAHO and other organizations mandating monitoring and appropriate treatment of pain, which is misunderstood by the media and the public as chronic pain rather than acute pain, and patient's right to total pain relief.
- Numerous organizations providing guidelines and standards
- Unscrupulous providers

6.1.3 Motivation for Use

The Partnership for a Drug Free America's research (28) shows that teens see distinct benefits from different drugs and choose substances based on whether their motivation is simply to get high, to deal with problems such as stress or depression, to change their body or to help with school work.

Marijuana is the classic party drug; 81% of teens used it to get high, and only 16% use it to deal with problems. In contrast, a sizable number of teens are self-medicating with these substances in order to get ahead in school or to deal with stress or depression. Forty-three percent of teens reported that they use prescription stimulants like Adderall or Ritalin without a doctor's prescription to help with school work, 31% said they use them to deal with problems, and 22% said they use them to get high. When it comes to prescription pain relievers, nearly half of the children surveyed said they use them to get high, but 40% use them to help them to deal with a problems (28).

6.2 Perceived Safety

Public perception that prescription drugs are safer than illicit street drugs (106). The fact that doctors are prescribing these drugs legitimately and with increasing frequency to treat a variety of ailments leads to the misguided and dangerous conclusion that the non-medical use should be equally safe. This misperception of safety may contribute to, for example, the casual attitude of many college students towards abusing stimulants to improve cognitive function and academic performance (29). Greater social acceptability for medicating a growing number of conditions also adds to the perception of safety (138-147). In addition, inadequate public perceptions on guarding prescription medications contributes to abuse and diversion.

6.2.1 Perception of Risk

Stephen J. Pasierb (28), president and CEO of The Partnership for a Drug-Free America stated that, "the partnership's 18th annual Partnership Attitude Tracking Study (PATS), which examines teen drug use and attitudes, showed that the intentional abuse of prescription and over-the-counter drugs to get high is now an entrenched behavior among teens." The PATS study confirmed that an alarming number of today's teenagers are more likely to have abused prescriptions and over-the-counter drugs than a variety of illegal drugs like ecstasy, cocaine, crack, and methamphetamine. According to PATS:

- Nearly 1 in 5 (19% or 4.5 million) teens has tried a prescription medication to get high;
- One in 10 (10% or 2.4 million) teens report abusing cough medicine to get high; and
- Abuse of prescription and over-the-counter medications is on par with or higher than the abuse of illegal drugs such as Ecstasy (8%), powder/crack cocaine (10%), methamphetamine (8%) and heroin (5%).

The abuse of prescription medications has become "normalized" in teen culture. With this perception that "everyone is doing it," there is great risk that the "pharming" phenomenon will only grow larger.

The Partnership's study found that

2 key factors are driving the "pharming" phenomenon: many teens have the misperception that intentionally abusing prescription and over-the-counter medicines is not harmful, and teens say there is easy access to these drugs through a medicine cabinet at home or at a friend's house or via the Internet. PATS study's findings on perception of risk are troubling, with 40%, or 9.4 million teens, believing that prescription medicines, even if they are not prescribed by a doctor, are "much safer" to use than illegal drugs; 31% or 7.3 million teens believing that there is "nothing wrong" with using prescription drugs without a prescription "once in a while"; 29% or 6.8 million teens believing prescription pain relievers, even if not prescribed by a doctor, are not addictive; and more than half of teens (55% or 13 million) not strongly agree in that using cough medicines to get high is risky.

6.3 Prescription Drug Abuse Liability

Nora D. Volkow, Director, National Institute on Drug Abuse, National Institutes of Health, US Department of Health and Human Services (33) has noted that the psychotherapeutic prescription drugs that present abuse liability fall into three broad categories:

- Stimulants, which are prescribed to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy and include drugs such as Ritalin and Adderall.
- Opioids, which are mostly prescribed to treat moderate to severe pain and include drugs such as OxyContin and Vicodin.
- CNS depressants, typically prescribed for the treatment of anxiety, panic, sleep disorders, acute stress reactions, and muscle spasms and include drugs such as Valium, Librium, and Xanax.

These drugs can have both beneficial effects in patients and serious abuse and health liabilities in people taking them for non-medical reasons due to their effects in the brain (33). There can be substantial overlap between the brain systems that mediate the therapeutic effects of psychotropic medications and those responsible for the reinforcing effects of drugs of abuse (114, 129, 132-137). However, while the molecular targets in the brain for some medications may be the same ones as those for some of the drugs of abuse, differences in how much of the drug gets into the brain and how fast it gets there determine whether desirable (therapeutic) or undesirable (abuse and addiction) effects will follow. Factors such as drug dosage, route of administration and user expectations are crucial. For example, the stimulant methylphenidate (Ritalin) has much in common with cocaine –they bind to similar sites in the brain and they both increase the brain chemical dopamine through the same molecular targets (Fig. 11) (140, 141, 143, 144). In addition, when administered intravenously, both cause a rapid and large increase in dopamine, which a person experiences as a rush or high. However, when methylphenidate is taken orally, as prescribed, it elicits a gradual and sustained increase in dopamine, which is not perceived as euphoria and instead produces the expected therapeutic effects seen in many patients.

6.4 Lack of Education

There is lack of education at all

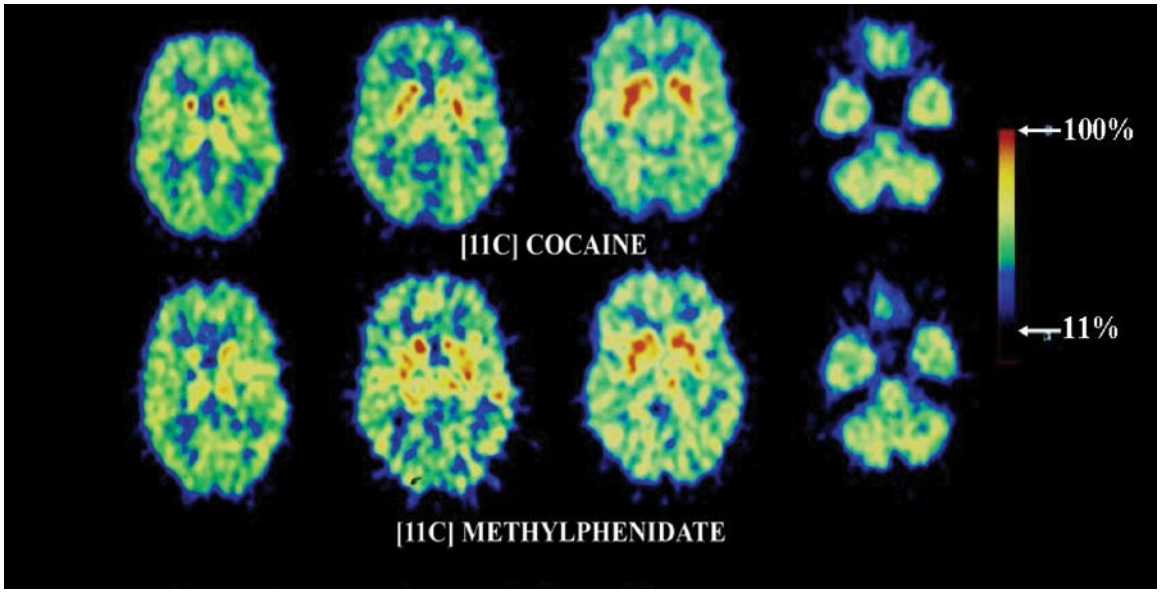

Fig. 11. *Distribution in the human brain of cocaine and Ritalin: Stimulants (Ritalin, Adderall) act like cocaine directly in the dopamine cells (33)*

levels from regulators, physicians, and pharmacists, to patients and their families. Surveys have shown that less than 40% of physicians have received any training in medical school in identifying prescription drug abuse and addiction or identification of drug diversion. In California, since October 2001, physicians have had a one-time-only requirement of 12 hours of continuing education in pain management and treatment of terminally ill and dying patients that must be completed by December 2006 (134). However, not all states require even this minimal education. In 2004, OxyContin and oxycodone were by far, some of the most widely prescribed opioid medications in the United States with an increase of 556% between 1997 and 2004. Thus, it appears that physicians are providing prescriptions without appropriate training. The physicians may not know the long-term safety and effectiveness of opioids for management of non-malignant pain as this has not been substantiated by evidence-based medicine (2). Many of the patients presenting for pain management for chronic non-malignant pain have underlying psychosocial problems and need psychological or rehabilitation services and obviously would respond well to other interventions, including interventional techniques or non-opioid drug therapy (1-3). Physicians without proper knowledge, malprescribing or abusing controlled substances, may be classified into one of the four categories indicated by the 4Ds: deficient, duped, deliberate, and dependent (Table 8).

Table 8. *Classification of a troubled physician*

Deficient (Dated Practitioner)
- ♦ Too busy to keep up with CME.
- ♦ Unaware of controlled drug categories.
- ♦ Only aware of a few treatments or medications.
- ♦ Prescribes for friends or family without a patient record.
- ♦ Unaware of symptoms of addiction.
- ♦ Remains isolated from peers.
- ♦ Only education is from drug reps.

Duped
- ♦ Always assumes the best about his patients and is gullible.
- ♦ Leaves script pads lying around.
- ♦ Falls for hydrophilic medicine excuse—fell into the toilet or the sink.
- ♦ Patients only want specific medications (i.e., OxyContin or Percocet).
- ♦ Co-dependent—cannot tell patients "No" when they ask for narcotics.

Deliberate (Dealing)
- • Practitioner becomes a mercenary.
- • Sells drugs for money, sex, street drugs, etc.
- • Office becomes a pill factory—full of drug seekers.
- • Prescribes for known addicts who will likely sell drugs to others.

Drug Dependent (Addict)
- ♦ Starts by taking controlled drug samples
- ♦ Asks staff to pick up medications in their names.
- ♦ Uses another doctor's DEA number.
- ♦ Calls in scripts in names of family members or fictitious patients and picks them up himself.

Physicians share the problems found with pharmacists. Based on the CASA survey (25), only 50% of pharmacists receive any training in identifying prescription drug diversion, abuse, or addiction. The lack of education regarding the sharing of prescriptions with friends and family is a real problem. It is extremely important to dispel the myth that taking a prescription drug is not the same as "doing drugs" (134).

6.4.1 Parents Unaware of Teens' Intentional Misuse of Medications

Parents are crucial in helping prevent the abuse of prescription and over-the-counter medications but right now there is a huge disconnect between parents and teens about "pharming." Only 1% of parents said that it is "extremely or very likely" that their own teen has tried a prescription pain killer, but 21% of teens admitted to trying this type of drug to get high (28). The same holds true for prescription stimulants: 2% of parents said it is "extremely or very likely" that their own teen has used them to get high, whereas 10% of teens actually have (28).

Today's cohort of parents is the most drug-experienced in history, but they do not understand this new drug abuse behavior among teens. As a result, they are looking for the classic signs of illegal drug use and are missing this trend and missing the signs of modern day abuse (28). Further, children who learn about the risk of drugs from their parents are up to 50% less likely to use drugs than teens who don't learn from their parents. However, 9 out of 10 parents of teens said they have talked to their child about the dangers of drugs, yet fewer than one-third of teens (31% or 7.4 million) said they "learn a lot about the risks of drugs" from their

parents. Research shows that parents are also the first place that teens turn for information about the risk of drugs (28). Fifty-six percent of teens reported that they talk to their mothers and 45% would turn to their fathers when they have a question about drugs.

6.4.2 Lack of Understanding of What Abuse of Prescription Drugs Does

When taken under the supervision of a physician, prescription drugs can be lifesaving, but when abused, they can be just as life-threatening as illicit drugs. Stimulants can elevate blood pressure, increase heart rate and respiration, cause sleep deprivation, and elicit paranoia. Their continued abuse, or even one high dose, can cause irregular heartbeat, heart failure, and seizures. Opioids and anti-anxiety medications can cause depressed respiration and even death, and CNS depressants can also induce seizures when a reduction in their chronic use triggers a sudden rebound in brain activity. Particularly dangerous is when young people indiscriminately mix and share prescription drugs, also combining them with alcohol or other drugs (31, 139-147).

6.5 Wasted Efforts on the War on Drugs

Katherine Walkenhorst (148) in a report released on June 26, 2006, described that the Office of National Drug Control Policy (ONDCP), established in 1988 by the Anti-Drug Abuse Act, in its eighteenth year of existence, has failed to reach its own established goals. It continues to fund 4 primary programs: High-Intensity Drug Trafficking Areas (HIDTA), the Counterdrug Technology Assessment Center (CTAC), the Drug Free Communities Program, and the National Youth Anti-Drug Media Campaign.

This report claims that the most wasteful program is the anti-drug media campaign. This claim is based on the findings of a government report detailing the failure of the campaign, and a study revealing that the ads provide a reverse effect. Yet, the federal government has spent $150 million in 2006. Walkenhorst claims that numerous studies done by public and private organizations have revealed the failure of this campaign. An assessment performed by the Program Assessment Rating Tool (PART) (149), set up by the federal government to determine the success of federal programs, has found since 2003 that the Youth Anti-Drug Media Campaign, has failed to produce any positive results.

Further, the ad agency involved has not provided any positive results and is not bound to provide any such results (150). The GAO also determined that the drug czar's office spent $155,000 on a series of ineffective ad campaign segments (151).

6.6 Incoherent and Ineffective Prescription Drug Monitoring Programs

Multiple prescription drug monitoring programs (PDMPs) are incoherent and ineffective including the DEA and Harold Rogers sponsored state monitoring program that was initiated by the Department of Justice in 2003 to promote the development of PDMPs. Historically, from 1940 to 1999, states have been able to establish only 15 functioning programs. The number of states with prescription drug monitoring programs has grown only slightly over the past decade from 10 in 1992 to 15 in 2002 (Fig. 12). With increased funding and resources, now there are approxi-

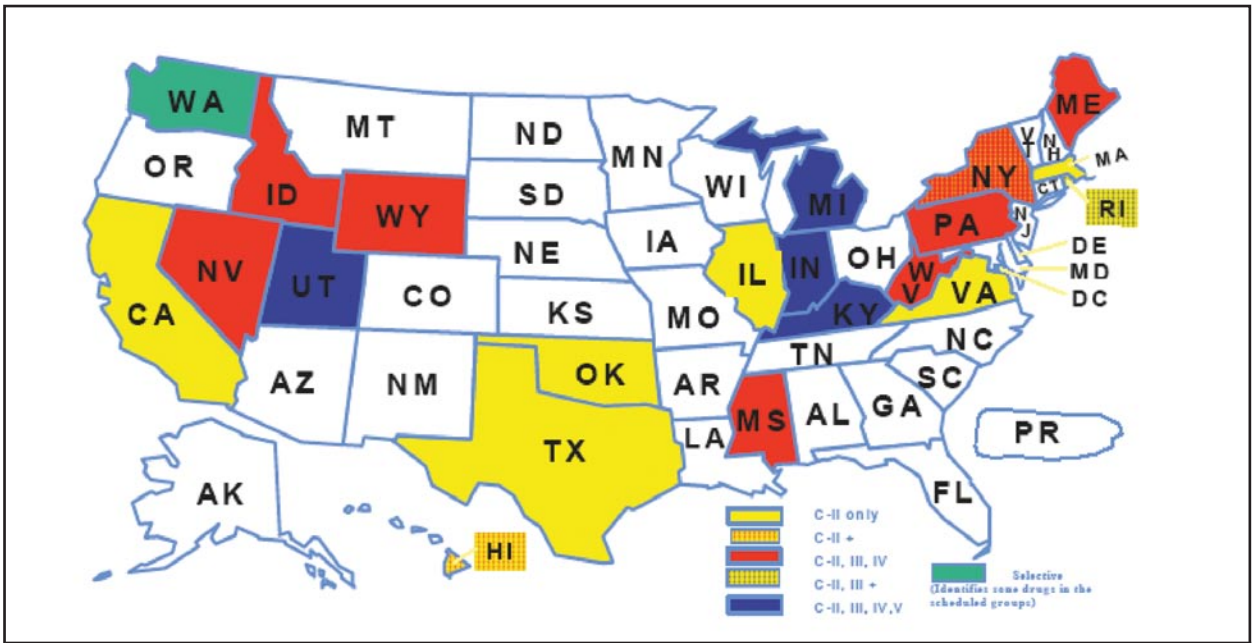

Fig. 12. *States with prescription monitoring programs (38)*

mately 35 programs in existence or in development. However, most of these programs have been a failure in terms of their lack of being proactive and in preventing doctor shopping and drug diversion. The major purpose of most of these state programs is to help the law enforcement identify and prevent prescription drug diversion. The secondary objective, which actually should be the first, is to educate and to provide information to physicians, pharmacies, and the public. Very few programs are proactive to the extent that physicians can access the necessary information to reduce or prevent abuse and diversion. Program design is highly variable across the states. Only 4 of the 15 state programs monitor Schedule IV drugs and only 5 of the 15 monitor Schedule III drugs, which are the subject of major controlled substance abuse. Of all available programs, only 3 programs are physician friendly and work proactively.

6.7 Non-Evidence Based Medical Practice and Guidelines

In response to alleged undertreatment of pain as a major health problem in the United States, numerous initiatives have been developed to address the multiple alleged barriers responsible for the undertreatment of pain (39). These responses have ranged from legislative actions to lobbying from patient advocacy groups and guidelines developed by professional organizations. However, none of these guidelines are based on evidence-based medicine. The guidelines adapted by the Federation of State Medical Boards, adapted by almost two-thirds of the state medical boards have no basis in scientific evidence (43). Thus, as one can understand, advocacy groups and professional organizations are promoting their own causes. The legislatures also have fallen tino this trap, instituting intractable pain treatment acts which further promote the concept of addressing the undertreatment of pain.

Extensive review of the literature by multiple evidence-based reviews has revealed that the effectiveness of prescription opioids for chronic nonmalignant pain is limited (2, 59-62). Extrinsic influences have forced even the DEA to take the position that clinicians should be knowledgeable about using opioids to treat pain, and should not hesitate to prescribe them when opioids are the best clinical choice of treatment (42).

7.0 Problems Facing Physicians, Pharmacists, And Patients

7.1Physicians

A CASA survey (25) of 979 physicians regarding the diversion and abuse of controlled prescription drugs showed the following:

- Physicians perceive the 3 main mechanisms of diversion to be:
  - Doctor shopping (when patients obtain controlled drugs from multiple doctors) (96%)
  - Patient deception or manipulation of doctors (88%)
  - Forged or altered prescriptions (69%).
- 59% believe that patients account for the bulk of the diversion problem.
- 47% said that patients often try to pressure them into prescribing a controlled drug.
- Only 19% of surveyed physicians received any medical school training in identifying prescription drug diversion.
- Only 40% of surveyed physicians received any training in medical school in identifying prescription drug abuse and addiction.
- 43% of physicians do not ask about prescription drug abuse when taking a patient's health history.
- One-third of physicians do not regularly call or obtain records from the patient's previous (or other treating) physician before prescribing controlled drugs on a long-term basis. HIPAA regulations have made this step much more difficult.
- 74% have refrained from prescribing controlled drugs during the past 12 months because of concern that a patient might become addicted to them.

Every day, physicians have to consider:

- Litigation for failure to treat pain
- Litigation for undertreatment
- Criminal charges for abuse, addiction, or death
- Numerous federal regulations and their implications
- Investigation or action by State Board of Medical Examiners
- Investigation or action by Drug Enforcement Agency
- Investigation or action by State Bureau of Narcotics
- Complaints by State Board of Pharmacy

Options for physicians are few and scarce.

- Referral to Pain Medicine Clinics
  - Clinics with mainstay treatment of opioids
  - Very limited resources
  - Rare option of an Interventional Pain Specialist
- Refuse to Prescribe Controlled Substances
  - Not an option for many practices
  - Inadequate treatment of pain lawsuits
  - Litigation for causing addiction
  - Criminal charges of murder
- Refer for addiction management
  - Many patients refuse detoxification
  - Inability to find addictionologists and their acceptance by patients
  - Lack of rehabilitation facilities
  - Non-coverage by most insurers
- Surrender Schedule II DEA License
  - Lose many patients
  - Lose hospital privileges
  - Lose all insurance patients
  - Not an option for interventionalists

7.2 Pharmacists

A CASA survey (25) of 1,303 pharmacists regarding diversion and abuse of controlled prescription drugs showed the following:

- When a patient presents a prescription for a controlled drug:
  - 78% of pharmacists become "somewhat or very" concerned about diversion or abuse when a patient asks for a controlled drug by its brand name;
  - 27% "somewhat or very often" think it is for purposes of diversion or abuse.
- 52% believe that patients account for the bulk of the diversion problem.
- Only about half of the pharmacists surveyed received any training in identifying prescription drug diversion

(48%) or abuse or addiction (50%) since pharmacy school.
- 61% do not regularly ask if the patient is taking any other controlled drugs when dispensing a controlled medication; 25.8% rarely or never do so.
- 29% have experienced a theft or robbery of controlled drugs at their pharmacy within the last 5 years; 20.9% do not stock certain controlled drugs in order to prevent diversion.
- 25% do not regularly validate the prescribing physician's DEA number when dispensing controlled drugs; 1 in 10 (10.5%) rarely or never do so.
- 83% have refused to dispense a controlled drug in the past year because of suspicions of diversion or abuse.

Pharmacists may be involved in prescription drug diversion, first by selling the controlled substances and then, using their database of physicians and patients to write and forge prescriptions to cover their illegal sale.

7.3 Patients

The problem list is long and extensive. A non-inclusive list is as follows:
- Undertreatment of pain.
- All patients are under suspicion.
- The interest in receiving opioids for chronic pain, fueled by advertising by pharmaceutical companies.
- Unproven, misunderstood regulations of JCAHO and other organizations mandating monitoring and appropriate treatment of pain.
- Media coverage of undertreatment of pain.
- Numerous organizations providing advocacy guidelines and standards.
- Patient advocacy groups advising them to demand more opioids.
- Access to Internet and daily bombardment of easy availability of drugs.
- Patient beliefs that they have the right to total pain relief.

8.0 What Is Being Done To Address Prescription Drug Abuse Epidemic?

8.1 Drug Enforcement Agency

On October 27, 1970, Congress passed the Comprehensive Drug Abuse Prevention and Control Act. According to the DEA, Title 2 of this Act, The Controlled Substances Act, is a "consolidation of numerous laws regulating the manufacturing and distribution of narcotics, stimulants, depressants, hallucinogens, anabolic steroids and chemicals used in the illicit production of controlled substances" and is "the legal foundation of the governments fight against drugs and other substances" (42, 110, 152).

The Act also regulates all legal and illegal substances that are recognized as having potential for abuse or addiction (152). The DEA's diversion control program oversees and regulates the legal manufacture and distribution of controlled pharmaceuticals. The DEA believes that controlled pharmaceuticals can be diverted intentionally or unintentionally by doctors, pharmacists, dentists, nurses, veterinarians, and individual users. Diversion cases may involve physicians who sell prescriptions to drug dealers or abusers, pharmacists who falsify records to obtain and then sell pharmaceuticals, employees who steal from physician or pharmacy inventories, individuals who forge prescriptions, individuals who commit armed robbery of pharmacies and drug distributors, "doctor shoppers" who routinely visit multiple doctors complaining of the same ailment to obtain multiple prescriptions for controlled substances, and individuals who establish Internet pharmacies that sell controlled pharmaceuticals without requiring prescriptions.

In 2005, Congress emphasized its concern regarding the diversion of controlled pharmaceuticals (152). The house report on the Justice Department's fiscal year (FY) 2005 appropriations stated, . . . "DEA has demonstrated a lack of effort to address this problem (152)." However, the DEA contends that diversion control is one of its strategic goals. Joseph T. Rannazzisi (110) stated that, "As the pharmaceutical controlled substances abuse problem has been growing, the DEA has significantly increased the amount of resources and manpower dedicated to investigating the diversion of controlled pharmaceuticals." The DEA has increased the number of special agent work-hours on diversion investigation by 114% between fiscal year 2003 and fiscal year 2005. The DEA has increased the number of intelligence analysts work-hours by 234% during the same period (110). Enforcement efforts undertaken by the DEA are also aimed at the economic base of drug traffickers and strong emphasis is placed on seizures of financial and other assets.

In addition, DEA's Demand Reduction office has produced an anti-drug website for teens, www.justthinktwice.com (110). This site provides young people with straightforward information on the consequences of drug use and trafficking, including health, social, legal consequences. It is continually updated to provide current information to teens and will be expanded and refined to reflect the needs of teens. The Demand Reduction Program also provides the public and school age children with a variety of demand reduction presentations on a national and local level regarding the abuse of controlled prescriptions (110).

8.2 Prescription Drug Monitoring Programs

The National All Schedules Prescription Electronic Reporting (NASPER) Act, which the American Society of Interventional Pain Physicians (ASIPP) initiated, promoted, and worked through 3 sessions of Congress to pass, was signed into law on August 11, 2005 (26). It authorizes the spending of $60 million from fiscal year 2006 to 2010 to create federal grants at the US Department of Health and Human Services to help establish or improve state-run prescription drug monitoring programs. Unfortunatley, NASPER is moving extremely slowly with no funding committed as of this writing.

The DEA and Harold Rogers sponsored a state monitoring program that was initiated by the Department of Justice in 2003 to promote the development of prescription drug monitoring programs by states (PDMPs). That commitment continues as part of the administration's National Drug Con-

trol Strategy for 2006. PDMPs have the potentional to help cut down on prescription fraud and doctor shopping by giving physicians and pharmacists more complete information about a patient's prescriptions for controlled substances as a goal. However, while these state programs have been useful, their numerous deficiencies have been described in Section 6.6.

8.3 State Regulations

The state's role is the regulation of the practice of medicine and pharmacy and the monitoring of illegal use and diversion of prescription drugs. State laws govern the prescribing and dispensing of prescription drugs by licensed healthcare professionals.

Multiple state agencies have responded to reports of drug abuse. However, complete information is not available from the directors of state Medicaid fraud control units in Kentucky, Maryland, Pennsylvania, Virginia, and West Virginia. They simply stated that drug abuse and diversion of OxyContin is a problem in their states. Figure 13 illustrates the top prescribed controlled substances by therapeutic category and dose in Kentucky (38).

State Medical Licensure Boards have also responded to complaints about physicians who were suspected of abuse and diversion of controlled substances, but like the Medicaid Fraud Control Units, the Boards generally do not maintain data on the number of investigations that were involved. Although Medical Boards may be tough, they can't always catch the bad apples. The Board reacts to complaints and cannot statutorily look for problems on its own.

8.4 Education

All organizations are making some efforts to educate authorities, physicians, pharmacists, patients and their families. The efforts directed at this are conflicting. In fact, drug companies are also allegedly promoting education to prevent diversion and abuse. However, it appears that this is tied to using more controlled substances, allegedly, "legitimately." Multiple federal organizations including the Office of the National Drug Control Policy, the National Institute on Drug Abuse to Prevent and Treat Prescription Drug abuse, the Office of the National Drug Control Policy, the Drug Enforcement Administration, the White House, the Department of Health and Human Services (HHS), the State Board of Medical Licensures, the Food and Drug Administration, the National Institutes of Health, the Substance Abuse and Mental Health Services Administration (SAMHSA), numerous state and local agencies, medical and pharmaceutical societies, and more importantly, consumer advocates such as victim's organizations, Partnership for a Drug-Free America, and numerous other organizations. However, considering the epidemic nature of the abuse and the toll on society, these efforts are at best miniscule at the present time.

8.5 Synthetic Drug Control Strategy

The Administration is concerned about the increase in the abuse of controlled substance prescription drugs. In response to the problem, the Administration released its first-ever synthet-

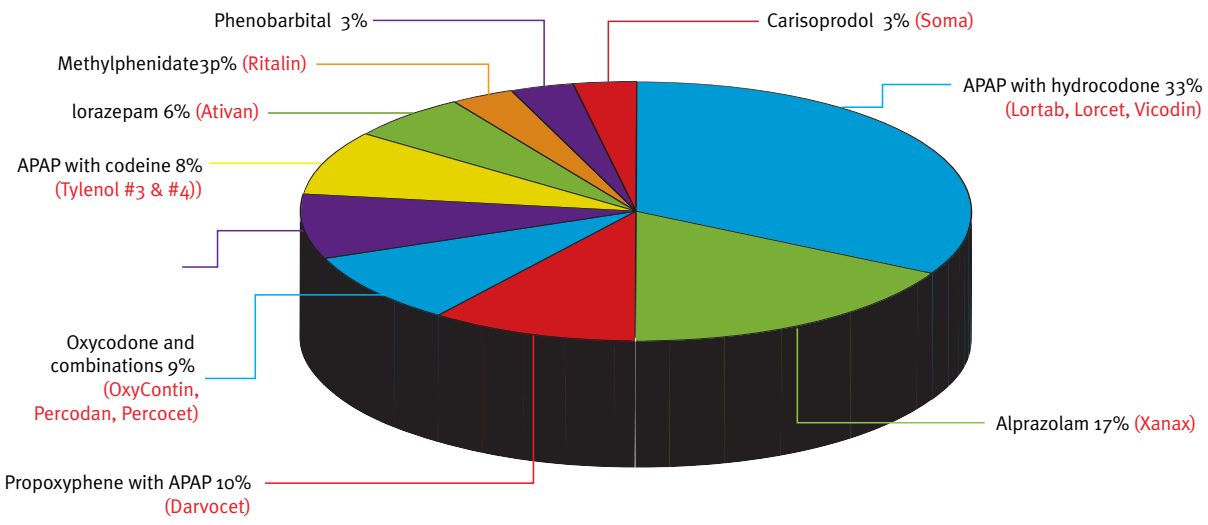

Fig. 13. *Top prescribed controlled substances by therapeutic category by doses (38)*

ic drug control strategy in June 2006, which focuses on methamphetamine and prescription drug abuse (29). With respect to prescription drug abuse, the synthetic drug control strategy calls for a 15% reduction in the illicit use of prescription drugs over the next 3 years.

The Administration also is strategizing to reduce opportunities for the diversion of controlled substance prescription drugs with identification of each method of diversion (29). Thus far, reliable data ranking each of these methods of diversion by prevalence does not exist. The Administration's synthetic drug strategy seeks to address each specific method of diversion, including doctor shopping or other prescription fraud, shipping illegal prescriptions from online pharmacies, over-prescribing, theft and burglary, selling pills to others, receiving at little or no cost from friends or family.

The National Institute on Drug Abuse (NIDA) to prevent and treat prescription drug abuse (33) has orchestrated a multi-pronged strategy intended to compliment and expand the portfolio of basic, pre-clinical, and clinical research aimed at better understanding the prescription drug phenomenon. Consequently, the NIDA started an initiative on prescription opioid use and abuse in the "treatment of pain," which encourages a multidisciplinary approach using both human and animal studies from across the sciences to examine factors (including pain itself) that predispose or protect against opioid abuse and addiction (33). Particularly important is to assess how genetic influence affects the vulnerability of an individual exposed to pain medication to become addicted.

8.6 Food and Drug Administration

The Federal Food, Drug, and Cosmetic Act requires the Food and Drug Administration (FDA) to ensure that all new drugs are safe and effective (153). Before any drug is approved for marketing in the United States, the FDA must decide whether the study submitted by the drug's sponsor, usually the manufacturer, have adequately demonstrated that the drug is safe and effective under the conditions of use proposed in the drug's labeling (153).

During the approval process, the FDA assesses a drug's products potential for abuse and misuse. Abuse liability assessments are based on a composite profile of the drug's chemistry, pharmacology, clinical manifestations, similar to other drugs in a class, and the potential for public health risks following introduction of the drug to the general population (153). Based on the abuse potential, a drug is assigned under the Controlled Substances Act, into 1 of the 5 schedules, depending upon their abuse potential and medical use.

Apart from labeling, the FDA also participates in risk minimization action plans. These are strategic safety programs designed to decrease known product risks by using one or more interventions, such as specialized education or restrictions on typical prescribing, dispensing, or use. However, a small number of risk minimization action plans that exist are largely customized programs, although consistent approaches are being sought, for example, in the control of drugs that cause birth defects, such as thalidomide and isotretinoin (153). The FDA is concerned about prescription drug abuse and its goal is to assure that patients who require opioids for pain control maintain appropriate access to them through informed providers, while limiting misuse and abuse of these products to the extent possible. Consequently, the FDA along with many federal agencies work together with professional societies, patient advocacy groups, industry, and others to share information and coordinate activities.

The FDA also seeks expert advice from non-agency experts on the medical use of opioid analgesics and monitors advertising and promotion of these drugs.

8.7 Prevention and Treatment

Approximately 35% of the federal drug control budget is targeted to prevention and treatment of drug abuse and addiction (29). These programs give states and local authorities flexibility in meeting drug-related challenges their communities face, including the mounting problem of prescription drug abuse. The strategies in prevention and treatment of prescription drugs are both targeted specifically to prescription drugs and to programs that enable prevention, intervention, and treatment of addictions, which can have a significant impact on prescription drug abuse. The goals of the Office of the National Drug Control Policy (ONDCP) are to eliminate diversion and abuse of potentially addictive prescription medications, by engaging federal, private, legal, and medical sectors in the creation of effective strategies and policies (29). It is reported that the President's drug control policy is characterized by vigilance, flexibility, adaptability, and innovative strategies to address emerging drug threats (29).

The National Institute on Drug Abuse to prevent and treat prescription drug abuse identifies treatment and prevention of drug abuse and addiction as key goals (34). The agency's efforts to identify effective treatments for prescription opioid abuse and addiction include conducting a multicenter study of more than 600 participants, employing clinical trials network (CTN) to evaluate treatment regimens using oral buprenorphine-naloxone. In addition, behavioral therapies, an integral part of all treatment strategies, continue to be a mainstay for treating stimulant addiction (33).

8.8 Changing Controlled Substance Formulations

For abusers, the appeal of a prescription drug typically depends on its dose, strength, ease with which it can be abused, and purity of the drug. One of the most commonly abused, branded, prescription-controlled substances in the United States is OxyContin (27). The active ingredient in OxyContin is oxycodone, a potent opioid which is a Schedule II controlled substance.

Hypothetically, OxyContin contains a very high dose of oxycodone that when used properly is intended to be slowly released over 12 hours. However, drug abusers, can quickly and simply disable OxyContin's controlled-release mechanism, usually by crushing, breaking, or chewing the tablet or by stirring it in high-proof alcohol for a few minutes (27). The extracted oxycodone is then ingested, snorted, or injected immediately releasing a dose of drug into the body that was intended to be slowly delivered over a 12-hour period. Consequently, the abuser experiences a very powerful and immediate high, leading to further addiction.

The DEA reported that criminal activity related to OxyContin abuse and diversion is rapidly depleting the resources of law enforcement (154). The DEA also reported record theft of 1,369,667 dosage units of OxyContin between January 2000 and June 2003 (155). Further, approximately 25% of the Schedule II investigations conducted by the DEA between 2001 and 2003 involved OxyContin (152).

The use of normal pharmaceutical technology can help combat the problem of prescription drug abuse by using chemical advances to develop a tamper-resistant capsule that provides long-acting effective pain relief when used properly, while also resisting degradations under conditions of abuse (27). An investigational drug product Remoxy is a form of long-acting OxyContin, developed by Pain Therapeutics Inc., which contains oxycodone in a highly viscous fluid, is formulated to be resistant to tampering or accidental misuse. Even though a sophisticated chemical laboratory might still manage to extract its active ingredient, it cannot be readily broken, chewed, or crushed, which are the principle means by which abusers disable the extended-release mechanism of OxyContin and other sustained-release opioid drug products.

A second approach to reducing prescription drug abuse by altering the synthesis and consequently, the therapeutics of a drug, is by combining an opioid agonist and antagonist. Oxitrex is one such drug being developed using oxycodone and an ultra-low-dose of an opioid antagonist (27). The synthetic drug control strategy of the Office of the National Drug Control Policy lists as its third of forty-six recommendations: continue to support the efforts of firms that manufacture frequently diverted pharmaceutical products to reformulate their products so as to reduce diversion and abuse (27, 156).

The development of new pain medications or formulations with minimum abuse potential has already witnessed some remarkable advances in this area of research with the introduction of buprenorphine-naloxone, a combined formulation for the treatment of opioid addiction with dramatically reduced abuse liability (157). Further, the FDA also intends to develop guidance for the industry on both assessment of abuse potential of drugs and also on developing analgesic products for the treatment of pain.

9.0 National All Schedules Prescription Electronic Reporting Act

9.1 Background

The National All Schedules Prescription Electronic Reporting (NASPER) Act of 2005 is a law that provides for the establishment of a controlled substance monitoring program in each state, with communication between state programs (26). It amends the Public Health Service Act to require the United States Secretary of Health and Human Services to award one-year grants to each state that has an approved application to establish, or improve, a state-controlled substance monitoring program.

The concept for the National All Schedules Prescription Electronic Reporting (NASPER) Act of 2005 was provided by the American Society of Interventional Pain Physicians (ASIPP) whose members and leadership saw a such a need for the information exchange program.

Efforts that resulted in NASPER's approval were initiated with three major and important goals:

1) Physicians and pharmacists' access to state monitoring programs
2) Monitoring of Schedule II to IV drugs
3) Information sharing across state lines

Modeled on a highly successful state monitoring program in Kentucky (Kentucky All Schedule Prescription Electronic Reporting Act – KASPER), the proposed national legislation was introduced during the 107th Congress in the US House of Representatives in September 2002. After multiple hearings and passages through the House and Senate, it passed both Houses in 2005 and became law in 2005.

9.2 Purpose

The purpose of the NASPER (158, 159) is to:

(1) Foster the establishment of state-administered controlled substance monitoring systems in order to ensure that health care providers have timely access to accurate prescription history information for use in the early identification of patients at risk of addiction or diversion in order to initiate appropriate medical interventions and avert the tragic personal, family, and community consequences of untreated addiction; and

(2) Establish, based on the experience of existing state-controlled substance monitoring programs, a set of best practices to guide the establishment of new state programs and the improvement of existing programs.

9.3 Federal Grants

Each fiscal year, the US Secretary of Health and Human Services shall award a grant to each state to establish and implement a state-controlled substance monitoring program or to make improvements to an existing state-controlled substance monitoring program.

9.4 Minimum Requirements

The Secretary also shall establish minimum requirements for criteria to be used by states including an application approval process, state legislation, interoperability, and minimum reporting requirements.

9.5 Database

Each state shall establish and maintain an electronic database containing information reported to the state on Schedule II, III and IV drugs, a database interoperable between the monitoring programs of various states.

9.6 Drug Diversion

In consultation with practitioners, dispensers, and other relevant and interested stakeholders, a state receiving a grant shall establish a program to notify practitioners and dispensers of information that will help identify and prevent the unlawful diversion or misuse of controlled substances; and may, to the extent permitted under state law, notify the appropriate authorities responsible for carrying out drug diversion investigations if a state determines that information in the database maintained by the state indicates an unlawful diversion or abuse of controlled substances.

9.7 Privacy

In implementing or improving a controlled substance monitoring program, a state shall limit the information provided pursuant to a valid request to the minimum necessary to accomplish the intended purpose of the request; and shall limit information requested for research of a non-investigative nature by state or federal agencies or law enforcement to non-identifiable information. Information is available in an electronic format for the reporting, sharing, and disclosure of information.

The Secretary, based on the review of existing state-controlled substance monitoring programs and other relevant information, shall determine whether the implementation of such programs has had a substantial negative impact on patient access to treatment, including therapy for pain or controlled substance abuse; pediatric patient access to treatment; or patient enrollment in research or clinical trials involving controlled substances. A state may establish an advisory council to assist in the establishment, implementation, or improvement of a controlled substance monitoring program.

9.8 Funding Authorization

Funding authorized under the law is $15 million for fiscal years 2006 and 2007, and $10 million for fiscal years 2008, 2009, and 2010.

However, due to conflicts with an unauthorized program by the Harold Rogers Grant, the funding for NASPER has been obstructed and, instead, funding is being spent on ineffective programs. The new proposed budget includes approximately $5 to 10 million for fiscal year 2007.

9.9 Effectiveness of Prescription Drug Monitoring Programs

Prescription drug monitoring programs capture information that may be shared with law enforcement agencies, health care and regulatory agencies, and in some states, health care practitioners, to help identify inappropriate or illegal activities involving controlled prescription drugs. It has been stated that the scrutiny of professional boards and monitoring programs has, in some cases, created fear that legal action will be taken against physicians and pharmacists regarding their prescribing and dispensing practices (37, 104, 124, 160-165). As a result, practitioners may undertreat patients or use less appropriate medications that are not covered by a monitoring program.

The US Government Accountability Office (GAO) conducted a study on state monitoring programs of prescription drugs (152). They concluded that state monitoring programs provide a useful tool to reduce diversion.

The first prescription drug monitoring program (PDMP) was established in California in 1940. The number of states with PDMPs has grown only slightly over the past decade, from 10 in 1992 to 15 in 2002. These 15 programs cover 47% of the nation's population and DEA-registered practitioners, and about 45% of the nation's pharmacies. Since the GAO report on state monitoring systems was published, PDMPs have been increasing gradually.

The National Alliance for Model State Drug Laws, established in 1993, has served as a resource center for states interested in identifying legislative and program improvements in drug abuse reduction and prevention. Each year since fiscal year 1995, the alliance has received a $1 million grant from the US Department of Justice. The funds are used to identify legislative, policy, and program initiatives to address the supply of, abuse of, and addiction to, alcohol and other drugs. However, prescription drug monitoring programs vary as to objectives, design, and operation, even though the primary objective of PDMPs is to assist law enforcement in detecting and preventing drug diversion.

In addition to helping law enforcement identify and prevent prescription drug diversion, state programs may include educational objectives to provide information to physicians, pharmacies, and the public. The programs are also highly variable with regards to monitoring scheduled substances from Schedule II to Schedule IV. Only 4 states - Utah, Nevada, Kentucky, and Idaho - monitor Schedule II to IV drugs; the majority monitor only Schedule II drugs. Also, the majority of these programs are retroactive with after-the-fact identification of abuse as reported by public health departments, pharmacy boards, and law enforcement. The major disadvantage of these programs is lack of communication among the state programs. Conse-

quently, only a few programs operate proactively, while most operate reactively (160-162).

A few states routinely analyze prescription data collected by PDMPs to identify individuals, physicians, or pharmacies that have unusual use, prescribing, or dispensing patterns that may suggest potential drug diversion, abuse, or doctor shopping (160-162). However, only 3 states provide this information proactively to physicians. The GAO report cited many advantages, as well as disadvantages, to PDMPs. States with PDMPs experience considerable reductions in the time and effort required by law enforcement and regulatory investigators to explore leads and the merits of possible drug diversion cases. However, while the presence of a PDMP may help one state reduce its illegal drug diversion, diversion activities may actually increase in contiguous states without PDMPs. All 3 of the states providing access to physicians - Kentucky, Nevada, and Utah – have helped reduce the unwarranted prescribing and subsequent diversion of abused drugs in their states. In both Kentucky and Nevada, an increasing number of PDMP reports are being used by physicians to check the prescription drug utilization history of current and prospective patients to determine whether it is necessary to prescribe certain drugs that are subject to abuse (Figs. 14 and 15).

The Cabinet for Health and Family Services described the need for Kentucky All Schedule Prescription Electronic Reporting (KASPER) Program (38).

- Healthcare professionals need a tool to help identify patient prescription drug problems and when intervention may be needed.
- Diversion of controlled substances is reaching epidemic proportions.
  - Diverters cover large areas to obtain drugs.
  - Agencies need efficiency and value in their investigative tools.
- KASPER was designed as a tool to help address the problem of prescription drug abuse and diversion by providing:
  - A source of information for practitioners and pharmacists.
  - An investigative tool for law enforcement.
- KASPER is not designed to:
  - Prevent people from getting prescription drugs.
  - To decrease the number of doses dispensed.
- A 2004 KASPER satisfaction survey (38) showed the following:
  - 86% of physicians used KASPER to request patient reports.
  - 81% of the physicians were satisfied, whereas, 6% were neutral or somewhat dissatisfied, in contrast to 13% without any response.
  - 84% of the physicians felt KASPER was effective, whereas 13% did not respond, with 4% feeling it was ineffective.
  - 86% of the respondents felt that KASPER is an excellent tool for identifying potential "doctor shoppers," with 12% of the physicians not responding.
  - 63% of the physicians responded that KASPER was important when treating a patient in helping make a medical decision about which drug to prescribe, whereas, 25% did not respond.

10.0 Strategies To Combat The Epidemic

10.1 Funding and Implementation of NASPER

Multiple strategies to combat the epidemic of drug abuse include educa-

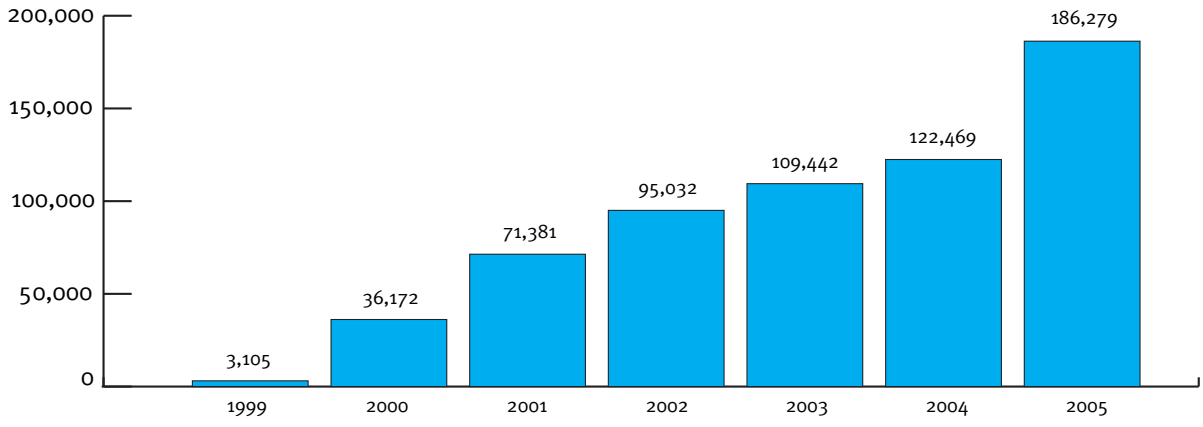

Fig. 14. *The number of KASPER reports produced per year (38)*

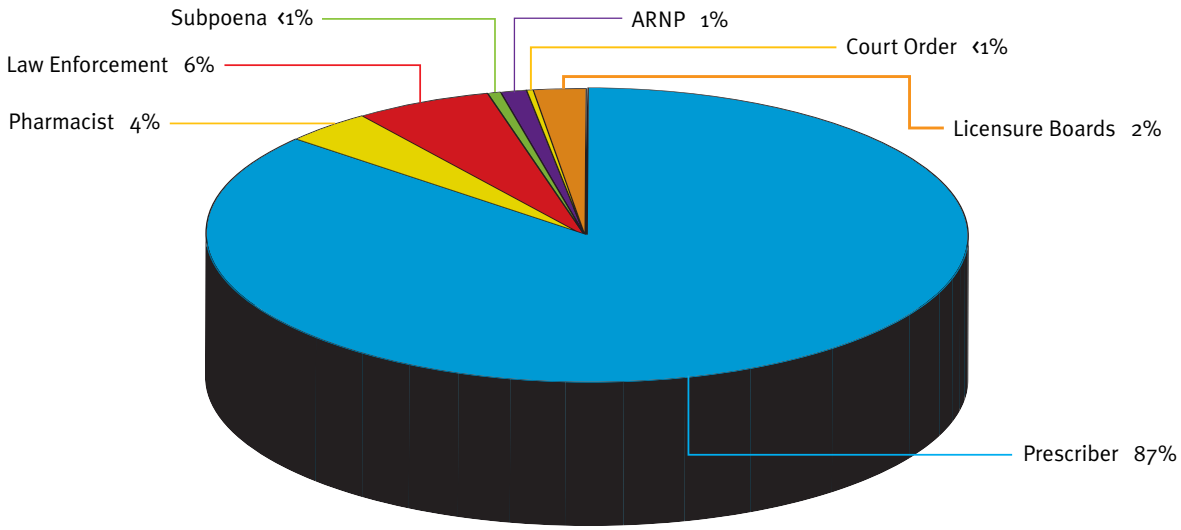

Fig. 15. *Percentage of KASPER report requests by type (38)*

tion at all levels, including public, physicians, and pharmacists; enactment of NASPER in all states; improved relationship between the DEA and providers; increased scrutiny of methadone clinics; and increased number of comprehensive drug rehabilitation programs, with buprenorphine detoxication and other modalities; and elimination of Internet pharmacies.

10.2 Education

Education is required at all levels including physicians, pharmacists, and public.

10.2.1 Physicians

With regards to physician education, surveys have shown that less than 40% of physicians have received any training in medical school in identifying prescription drug abuse and addition or identification of drug diversion. While the July 2005 report of CASA (25) stated that 4 in 10 doctors surveyed say they received no training in medical school on prescribing controlled substances. Van Rooyan (134) described the present state of affairs as follows:

- The majority of physicians do not know that the long-term safety and effectiveness of opioids for management of non-malignant pain have NOT been substantiated.
- The majority of physicians do not know that patients seeking pain relief for chronic, non-malignant pain often have underlying psycho-social problems and need psychological or rehabilitation services or would respond well to other non- drug interventions.
- In busy medical practices, particularly primary care and family practice office settings, a thorough diagnosis of the cause and type of pain and a balanced, multifaceted pain treatment program are often difficult to achieve. The result is that often pain therapy is based not on science but on intuition or hearsay, and ends up aggravating rather than ameliorating prescription pain medication abuse and addiction.
- Many good physicians relied upon false marketing information regarding OxyContin from an aggressive Purdue Pharma sales force that was prompted by greed. The result was an expansion of opioid therapy for patients who might benefit more from non-drug interventions or alternate drugs, without the accompanying risks of opioids.

The medical profession has been alerted through a number of organizations, meetings, medical journals, and medical associations and via pharmaceutical companies of the mounting problem of prescription drug abuse (29). Notwithstanding the response of the medical community, current statistics indicate that a more concerted effort is required to diminish this escalating public health problem in our society. The administration recognizes the need for a closer partnership between the general medical community, and pain and addiction specialists. The Office of the National Drug Control Policy (ONDCP) as planned should organize several events to facilitate the dissemination of pain and addiction information to the general medical commu-

nity. Representatives of the medical and pharmaceutical communities should be called together to develop and concerted, effective strategy of change to address this public health problem. This should encourage medical professionals, pharmacists, and pharmaceutical companies to take a leading role in educating physicians and patients as to the importance of retaining control of prescription medications with abuse liability. ONDCP has planned to convene a medical conference to assemble leading medical professional associations to focus on medical eduction on addictions, and specifically on prescription medications. While this is a noble effort, the effort should be tripled or quadrupled and the educational efforts should reach not only the people who are preaching to the community, resulting in increases in drug abuse, but also to all the physicians in every corner of the United States (135).

Consequently, controlled substance education must be mandated in medical schools, residency training programs, and supported by continuing education each year, variable from 20 hours in the first year to 10 hours in subsequent years. The training must be accredited and approved and may be monitored mainly by the DEA or State Board of Medical Licensure. Finally, a separate residency program is needed and must be instituted in the near future in interventional pain management, which will not only train the physicians about comprehensive programs and other modalities of treatments other than narcotics, but also will provide appropriate safety training and guidelines.

10.2.2 Pharmacists

Controlled substance education must be mandated in pharmacy schools, and training programs, and also should be supported by continuing education each year, variable from 20 hours in the first year to 10 hours in subsequent years. The training must be accredited and approved and may be monitored mainly by the DEA or State Boards of Pharmacy.

Education for pharmacists is also extremely crucial. Based on the CASA survey (25), only 50% of pharmacists receive any training in identifying prescription drug diversion, abuse, or addiction.

10.2.3 Public

The most important aspect of the training is the public. The public must be educated on non-opiate techniques of chronic pain management. In addition, the public should be educated about overall ineffectiveness of opioid use, prevalence of misuse and adverse effects, even if used properly. The education should stress the disastrous consequences of misuse and abuse. Further, public education should include youth and family education, prevention strategies specific for people with access to controlled prescription drugs with media campaigns, community coalitions, Partnership for a Drug-Free America, prescription drug tracking, prevention and intervention by biometric identification at various levels, students and employees, etc.; screening, brief intervention, referral and treatment.

In the area of education, youth and family education is extremely important. Van Rooyan (134) illustrated the problems among youngsters as follows:

- Many young people think taking a prescription drug is not the same as "doing drugs."
- Many teachers, counselors and administrators are not aware of the abuse of prescription drugs, the scope of the problem, nor the signs of misuse (no odor, no paraphernalia = no drugs)
- Many young people have a friend or relative who was prescribed OxyContin for an injury, back pain or arthritis and now is unable to stop taking the drug.
- High school health classes include segments on illicit drugs but in most classes prescription drug abuse is not addressed.
- Some people obtain OxyContin from their own family doctors by "faking pain."
- Most physicians have very little training in opioid prescribing or addiction; as a result many are not selective in prescribing opioids nor do they make adequate use of non-drug interventions.
- Easy availability of prescription drugs from doctors, family medicine cabinets and the Internet, combined with young people's feelings of invincibility has led to more deaths and addictions than ever imagined.
- Prescription drug abuse education needs to target parents as well as youth.

10.2.4 Funding and Conduct of Education Programs

The present system of education is too little and too broken. This education should reach each and every person. The agencies must coordinate among themselves so that the government dollars (federal and state) are used appropriately. These agencies should cooperate and thus encourage private and advocacy organizations deterring abuse and diversion and they should also fund these programs. In addition, substantial unrestricted grants from pharmaceutical companies are essential, along with increased federal appropriations for youth and family prescription drug abuse education, increased mandatory physician education regarding selective opioid prescribing and a balanced multifaceted approach to pain management, treatment and rehabilitation programs, and nationwide prescription monitoring programs (NASPER) (134).

10.3 Coordination of Efforts by Agencies

There are more than 10 federal agencies and approximately 5 to 6 agencies in each state, followed by local agencies, attempting to curb the drug epidemic. Each organization functions in its own way duplicating efforts. One such example is the undermining of the recently passed public law, NASPER, and the funding for an unauthorized program. There must be stronger collaborations between physician's orga-

nizations, the ONDCP, SAMHSA, the National Institute on Drug Abuse, the DEA, the FDA, and other federal and state agencies, and local authorities, as well as professional and private associations with a strong interest in preserving public health to accomplish this mission of curbing drug abuse rather than encouraging it.

Of specific importance is the relationship between DEA and the provider community, including pharmacies, which is currently, at best, lukewarm. For proper implementation of effective policies, this relationship has to improve.

Consequently, the DEA should encourage the rapid implementation of the NASPER program as it is proactive, physician-friendly, includes all drug schedules and shares information among all participating states. Further, Medicaid coverage for controlled substances should be looked at and regulated appropriately. The DEA should spend more of its time on educating the public and physician community and working with all organizations rather than only the major organizations. Many of the organizations now involved are physician and patient advocacy organizations and may not be focused on the goals of reducing the drug epidemic.

10.4 Elimination of Internet Pharmacies

Falco (106) expressed several concerns with regards to the sales of psychoactive prescription drugs over the Internet, which is becoming a major enterprise, and presenting a new challenge to drug abuse prevention and treatment; prevalence of adolescent substance abuse in the United States, which is increasing; increasing non-prescription use of addictive pharmaceutical drugs by adolescents; perception of non-medical prescription drug use among adolescents; ease of finding Internet drug pharmacies; difficulty in shutting down these websites; intercepting NPW deliveries; enforcement; and increasing awareness of drug availability online. She outlined the next steps in developing a comprehensive strategy which included more research on accurate information of the extent of controlled substances availability without a prescription over the Internet; data on the Internet's role in supplying prescription drug abusers; new treatment and prevention strategies; and public and private enforcement strategies.

10.5 Abuse-Resistant Prescriptions

The development of abuse-resistant formulations is one of the first and foremost strategies to combat or eliminate the epidemic of drug abuse. A second important strategy is the development of new pain medications or formulations with minimum abuse potential. Compounds that act on a combination of two distinct opioid receptors (mu and delta), have been shown in preclinical studies to provide strong analgesia without producing tolerance or dependence. Development of drugs with lower abuse liability and tamper resistant formulations, along with the development of a new generation of non-opioid-based medications for severe pain would circumvent or greatly reduce abuse potential.

10.6 Monitoring of Methadone Clinics

Increased scrutiny of methadone clinics is essential. Methadone is becoming a drug of choice for abuse, as well as resulting in increasing deaths. Many of these deaths cannot be explained on the sole basis that they are from physician prescriptions.

10.7 Improved Labeling

A warning may be provided on all controlled substance prescriptions, stating that it is not only dangerous but illegal to give, share or sell a controlled substance to a family member, relative, friend or any other person, except in an emergency.

10.8 Prescribing Guidelines

The authorities promoting uncontrolled use of opioids for unproven management of chronic non-cancer pain are not only vocal, but have been provided a forum at various agencies, organizations, and journals. The pendulum has swung from real undertreatment to real overtreatment (still perceived as undertreatment by some), and the time has arrived for balancing the concept of adequate pain management based on effectiveness and safety (1, 2, 26, 39, 163-165). Properly developed prescribing guidelines using either consensus or evidence-based medicine principles will assist not only physicians and patients, but also curtail diversion and abuse. These guidelines should be without bias, with proper evaluation of the literature, and consensus developed by reasonable parties without prejudice or economic benefit for a particular group. Such guidelines describing the prevalence of chronic pain; the prevalence of opioid use and abuse; the issues related to diversion and abuse; the evaluation of chronic pain patients, with or without drug abuse; the assessment and needs of chronic pain patients to be provided with opioids; the following of appropriate principles in the diagnosis and management of chronic pain; utilizing precautions in providing controlled substances; and finally, recognizing abuse, diversion, and taking appropriate actions at each level are described in Table 9 (2).

Table 9. *Ten step process: An algorithmic approach for long-term opioid therapy in chronic pain*

STEP I	**Comprehensive initial evaluation**
STEP II	**Establish diagnosis** ♦ X-rays, MRI, CT, neurophysiological studies ♦ Psychological evaluation ♦ Precision diagnostic interventions
STEP III	**Establish medical necessity (lack of progress or as supplemental therapy)** ♦ Physical diagnosis ♦ Therapeutic interventional pain management ♦ Physical modalities ♦ Behavior therapy
STEP IV	**Assess risk-benefit ratio** ♦ Treatment is beneficial
STEP V	**Establish treatment goals**
STEP VI	**Obtain informed consent and agreement**
STEP VII	**Initial dose adjustment phase (up to 8-12 weeks)** ♦ Start low dose ♦ Utilize opioids, NSAIDS, and adjuvants ♦ Discontinue due to • Lack of analgesia • Side effects • Lack of functional improvement
STEP VIII	**Stable phase (stable – moderate doses)** ♦ Monthly refills ♦ Assess for four As • Analgesia • Activity • Aberrant behavior • Adverse effect ♦ Manage side effects
STEP IX	**Adherence monitoring** ♦ Prescription monitoring programs ♦ Random drug screens ♦ Pill counts
STEP X	**Outcomes** ♦ Success – continue • Stable doses • Analgesia, activity • No abuse, side effects ♦ Failed – discontinue if • Dose escalation • No analgesia • No activity • Abuse • Side effects • Non-compliance

Adapted with permission from American Society of Interventional Pain Physicians and author (2)

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