



California State Board of Pharmacy

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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY

DEPARTMENT OF CONSUMER AFFAIRS

GOVERNOR EDMUND G. BROWN JR.

Prescription Medication Abuse Subcommittee

Ramon Castellblanch, PhD, Chair

Rosalyn Hackworth, Board Member

Amy Gutierrez, PharmD, Board Member

Darlene Fujimoto, PharmD, Volunteer

Materials for the October 7, 2013 Meeting

This is the first meeting of the Prescription Medication Abuse Subcommittee of the Communication and Public Education Committee. The subcommittee was formed following the February 2013 Joint California Medical Board and Board of Pharmacy Appropriate Prescribing and Dispensing Forum. The Medical Board has formed its own subcommittee to work on similar issues.

1. **FOR DISCUSSION: Development of Proposed Mission Statement for the Subcommittee**

This subcommittee was formed to continue to explore ways to address the misuse and abuse of prescription medication, particularly of controlled substances. At the end of the forum, a list of possible items were mentioned in the closing ceremony. This list is provided as **Attachment 1**.

The subcommittee has various issue areas:

- Educate the public and licensees about the dangers of prescription drug abuse
- Collaborate with prescribing boards to promote strengthen the sharing of information among practitioners (prescribers and dispensers)
- Promote the use of CURES by practitioners
- Continue to work with the Medical Board and other prescribing boards on topics in this area

Chair Castellblanch has suggested that a mission statement be developed for this committee. For reference, the mission and general goals of the board are provided below. The board has only one mission:

The Board of Pharmacy protects and promotes the health and safety of Californians by pursuing the highest quality of pharmacists care and the appropriate use of pharmaceuticals through education, communication, licensing, legislation, regulation and enforcement.

Each of the five committees have general goals:

- Enforcement: Exercise oversight on all pharmacy and drug distribution activities
- Licensing: Ensure the qualifications of applicants and licensees advance the vision and mission of the Board of Pharmacy
- Communication and Public Education: Provide relevant information to consumers and licensees
- Organizational Development: Achieve regulatory efficiency, customer service and consumer protection

2. Review and Discussion of Statistics Documenting the Issues of Prescription Drug Abuse

A number of references are pointing to the increasing incidence of controlled substances being misused by individuals.

Attachment 2 contains a several statistics highlighting the prescription drug abuse impacts and several articles to provide background about prescription drug abuse. The slides are from a DEA presentation.

3. Discussion of Joint Efforts with the Medical Board of California to Address and Educate Licensee and the Public About Prescription Medication Abuse

The Medical Board has also formed a subcommittee to work on the issue of prescription medication abuse and perhaps to coordinate another forum in the future in Southern California. The first meeting of their task force was September 23. A copy of the agenda and general project plan is provided as **Attachment 3**.

We have invited representatives from the Medical Board to attend this meeting to join in this discussion.

4. Discussion of the Enhanced CURES Program (as established by SB 809, Chapter 400, Statutes of 2013)

In California, the Controlled Substance Utilization Review and Evaluation System (CURES) is an electronic tracking program that reports all pharmacy (and specified types of prescriber) dispensing of controlled drugs in Schedules II, III, and IV by drug name, quantity, prescriber, patient, and pharmacy.

Data from CURES aids this board in efforts to identify, prosecute and reduce prescription drug diversion. CURES provides invaluable information that offers the ability to identify if a person is “doctor shopping” (when a prescription drug addict visits multiple doctors to obtain multiple prescriptions for drugs, or uses multiple pharmacies to obtain prescription drugs). Information tracked in the system contains the patient name, prescriber name, pharmacy name, drug name, amount and dosage, and is available to law enforcement agencies, regulatory bodies and qualified researchers. The system can also report on the top drugs prescribed for a specific time period, drugs prescribed in a particular county, doctor prescribing data, pharmacy dispensing data and is a critical tool for assessing whether multiple prescriptions for the same patient may exist.

CURES now has more than 100 million controlled substance prescriptions electronically filed. The system has been key in investigations of doctor shoppers, pharmacies and prescribers. For the board, this data is critical in allowing for the identification of pharmacies involved in massive dispensing of controlled substances, which can be a potential sign of drug diversion, and serves as a trigger for important investigations.

In addition to CURES' value to regulatory and law enforcement agencies, CURES also has a prescription drug monitoring component whereby DOJ-preapproved providers may access reports on specific patients to see what controlled substances have been dispensed to the patient by various pharmacies. Use of this system can prevent prescribers from prescribing and pharmacies from dispensing medications to doctor and pharmacy shoppers. However, the computer system supporting CURES in the DOJ needs upgrading.

Governor Brown signed requirements to upgrade the CURES system last Friday. The Department of Consumer Affairs and the health care boards that use CURES should benefit from the new parameters once the new computer system is available in about two years. A copy of SB 809 is provided as **Attachment 4**.

5. Discussion on the Corresponding Responsibility of a Pharmacist and the Board's Recent Precedential Decision in this Area

Corresponding responsibility is defined in federal and state law, and California's Health and Safety Code 11153 provides that:

11153. Responsibility for Legitimacy of Prescription; Corresponding Responsibility of Pharmacist; Knowing Violation

(a) A prescription for a controlled substance shall only be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his or her professional practice. The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription. Except as authorized by this division, the following are not legal prescriptions: (1) an order purporting to be a prescription which is issued not in the usual course of professional treatment or in legitimate and authorized research; or (2) an order for an addict or habitual user of controlled substances, which is issued not in the course of professional treatment or as part of an authorized narcotic treatment program, for the purpose of providing the user with controlled substances, sufficient to keep him or her comfortable by maintaining customary use.

At the July Board Meeting, the board voted to make its decision in Pacifica Pharmacy a precedential decision regarding a pharmacist's corresponding responsibility. This decision is now posted on the board's website as a precedential decision, and has been the subject of a subscriber alert. Recently, Supervising Deputy Attorney Joshua Room did a summary of the decision which is provided as **Attachment 5**.

The board will highlight this decision in a future *The Script*. It will also add this decision as a topic in prescription drug abuse presentations made by staff, and specifically call it to the attention of

prosecuting DAGs when seeking discipline for a licensee's failure to adhere to corresponding responsibility.

6. Discussion on the Board of Pharmacy's Previously Published *Health Notes on Pain*, a Monograph for Pharmacy Practitioners

In the mid 1990s and ending in the early 2000s, this board published a series of eight monographs for pharmacists whereby the board could ensure the consistency of education being available on specific topics, and for which a pharmacist could earn continuing education credit by completing and passing an exam on the materials' content. The board generally subcontracted with pharmacist experts in the field, and relied on academic editors to develop the articles. Each issue was attractive, but development of each issue was relatively expensive and time consuming.

The first issue was on treating pain, including appropriate pain management, and other topics. This was developed following the then Administration's work in addressing under-treatment of pain.

This monograph is still available on our website:

http://www.pharmacy.ca.gov/publications/health_notes_pain_mgmt.pdf However, a recent review of the monograph indicates that the messages in this issue may be at odds with federal and state thinking about pain management.

During this segment of the meeting, the subcommittee will have a chance to discuss future use and availability of this issue.

7. Discussion about Public Education Efforts for Prescription Drug Abuse, and Community Outreach

During the April Board Meeting discussion on the success of the February Joint Forum with the Medical and the need for greater public activity with respect to prescription drug abuse led the board to form this subcommittee. An excerpt of the minutes from this meeting is provided as **Attachment 6**.

Some of the items suggested include a brochure for pharmacists on corresponding responsibility, sharing information on improving opioid use in hospitals (see **Attachment 6** for a fact sheet developed by Dr. Gutierrez's facility), and possible curriculum development for use in schools to advise students and parents of the dangers of prescription drug abuse and the attraction such drugs hold for youth.

The DEA has developed such a curriculum and we hope to obtain a copy for the next meeting.

8. Public Outreach to Address Prescription Drug Abuse

Over the last two years, the board has hosted several one-day seminars for pharmacists and other interested parties on drug diversion, prescription drug abuse and corresponding responsibility for pharmacists. The board's partner in this has been the Los Angeles Office of the Drug Enforcement Administration. Six hours of CE is awarded for this training, which is well attended and receives high evaluation scores. Two such sessions were provided in June and July 2013. Later in 2013, we hope to host another training in Orange County.

Also in mid August 2013, this board joined with the Washington, DC headquarters office of the DEA to co-host with them four, one-day seminars for pharmacists in California on controlled substances issues, prescription drug abuse, corresponding responsibility and other matters related to curtail drug diversion. Two were held in San Diego, and two held in San Jose. At least 300 pharmacists have attended each of these presentations.

Attachment 1

Medical and Pharmacy Boards' Joint Forum
to Promote Appropriate Prescribing and Dispensing
February 21-22, 2013

CHART OF RECOMMENDATIONS

RECOMMENDATION	FROM	ACTION?
Will bring back information to Senator DeSaulnier	Linda	
Continuing this dialogue and interaction	Linda	
Education	Linda	
Examination of enforcement models	Linda	
Revision of guidelines	Linda	
New and revised/enhanced laws	Linda	
Addressing CURES	Linda	
Addressing unused prescription drugs	Linda	
Try to influence the manufacturers to not have the 30 tab of vicodin be the default pre-packaged size; educate doctors/dentist to order less	Sharon	
CURES – work with solving problem of CURES registrants	Sharon	
Need for pharmacist to work more closely with the practitioner	Ginny	
CURES – funding	Ginny	
Need for education	Ginny	
PMP across state lines: Interlink Interconnect Program to link	Ginny	
PMP needs upgrades – enhancement to CURES system; more user friendly	Ginny	
Add reporting of Schedule V Drugs to PMP (CURES)	Ginny	
<ul style="list-style-type: none"> ➤ Increase education for healthcare providers regarding their role in prevention and detection <ul style="list-style-type: none"> • Appropriate prescribing and dispensing • Identification of common drugs of abuse • How to detect fraudulent prescriptions • How to recognize substance abuse • How to effectively use CURES 	Amy	
<ul style="list-style-type: none"> ➤ Promote use of patient pain management contracts <ul style="list-style-type: none"> • Circulate effective examples among providers 	Amy	
Establish standard prescribing practices for urgent care and emergency departments	Amy	
Establish public education materials focused on increasing awareness --increase community education (parents, youth) on the dangers of the misuse and abuse of prescription drugs	Amy	

Increase pain management training on healthcare provider professional training curricula	Amy	
Secure increased options for consumer disposal of unwanted medications	Amy	
Establish increased security measures for prescription dispensing, e.g. require photo identification at point of dispensing	Amy	
Appropriately fund and strengthen the capabilities of the State's CURES system	Amy	
Consider potential alert system to advise pharmacies of large volume of stolen prescription pads	Amy	
<u>Doctor shoppers and misdemeanor penalties</u>	Amy	
provide a link to la county paper: http://publichealth.lacounty.gov/sapc/resources/PrescriptionWEB3.pdf	Amy	
expanding our recruitment of public health resources	P-2	
MBC representative speak to CA Conference of local health officers (could get CURES support letter)	P-2	
Create a sub-category for controlled substances specialty pharmacist	P-4	
provide a downloadable PowerPoint presentation to educate	P-5	
Implementing through the workman's comp system: MTUS providers on MPM lists = acknowledge that they will at least read the MT list--all savings should go to CURES	P-6	
RX board to look into wine pain cocktails and using when patient has addiction and diversion issues	P-6	
sent out an email to "everybody" (pharmists/ pharmacies) letting them know that they have access to the CURES program; perhaps a link to the CURES registration Web page	P-7	
push be made to make it a requirement for every PIC to sign up for the CURES program	P-7	
look at ways to deal with pain management doctor advertising.	P-9	
Pick a "cut-point" on what drug level would cause the coroners to report	P-11	
more education on the requirements of pain management; must be seen twice a year, required documentation, urine drug screening, etc. this is a huge knowledge gap we need to close; <i>Recend/re-notice on Pain Management Guidelines</i>	P-11	
tighten up the outpatient requirements to align with the inpatient requirements with regards to prescribing perimeters and control	P-11	
CURES cost should be funded by the public.	P-12	
Use machine to dispense medication; technological restrictions	P-12	

that logs, track, etc.; change how patients get access therefore discouraging diversion; Biometrics		
Seek other therapeutic ways to help patients	P-13	
RX board consider informing through email system inappropriate prescribing cases without details so they are aware to be on the watch out	P-14	
Provide a PowerPoint presentation that he could use to train his fellows	P-15	
interactive process that allows RX prescription entry to provide historical information of last few months without logging into CURES	P-16	

Attachment 2

In 2010, approximately 38,329 unintentional drug overdose deaths occurred in the United States, one death every 14 minutes.

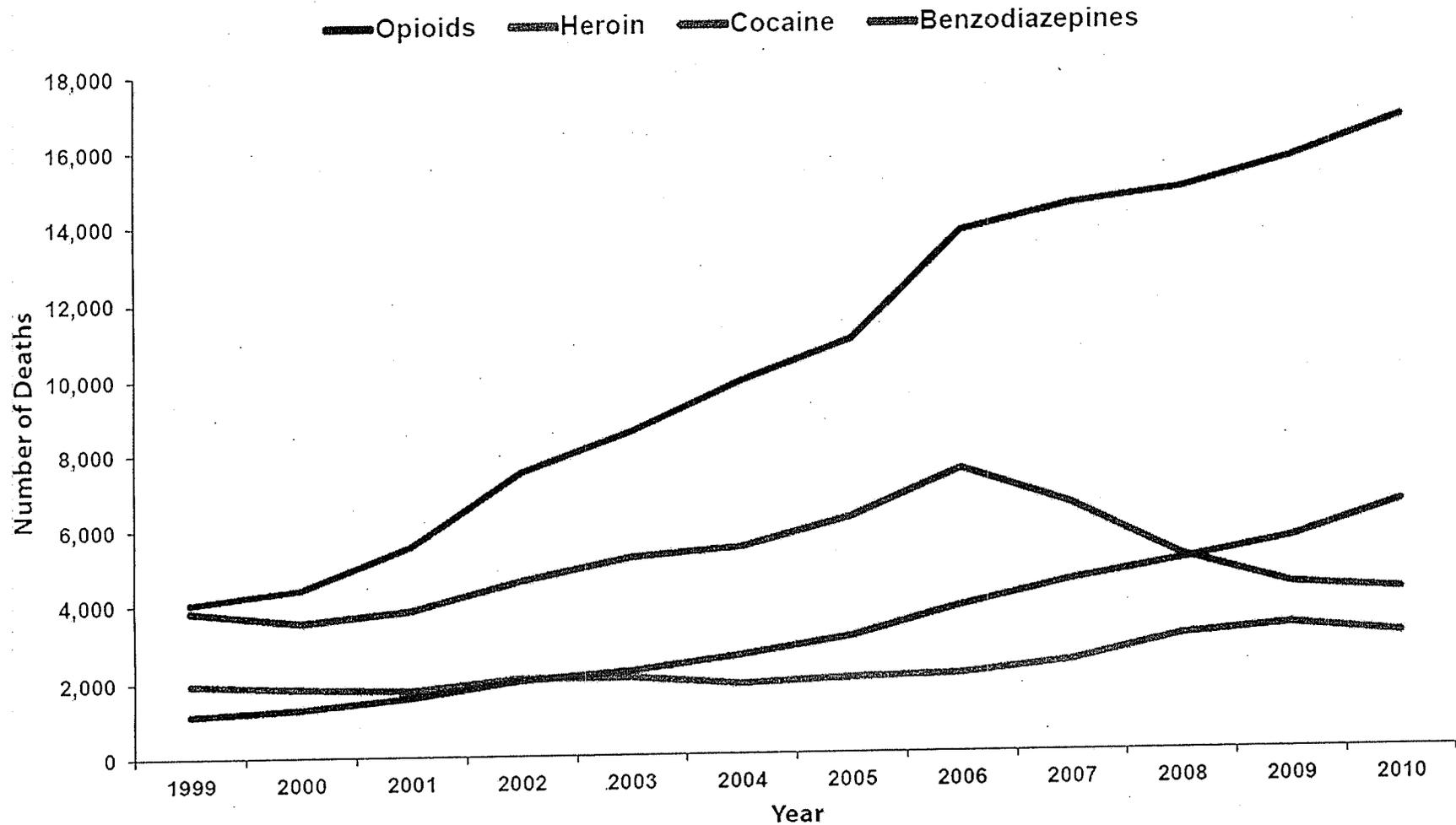
Of this number, 22,134 of these deaths were attributed to Prescription Drugs (16,651 attributed to opioid overdoses/ 75.2 %).

Prescription drug abuse is the fastest growing drug problem in the United States.

Source: CDC Drug Overdose Deaths in the United States, 2010 (October 2012)

U.S. Drug Enforcement Administration / Operations
Division / Office of Diversion Control

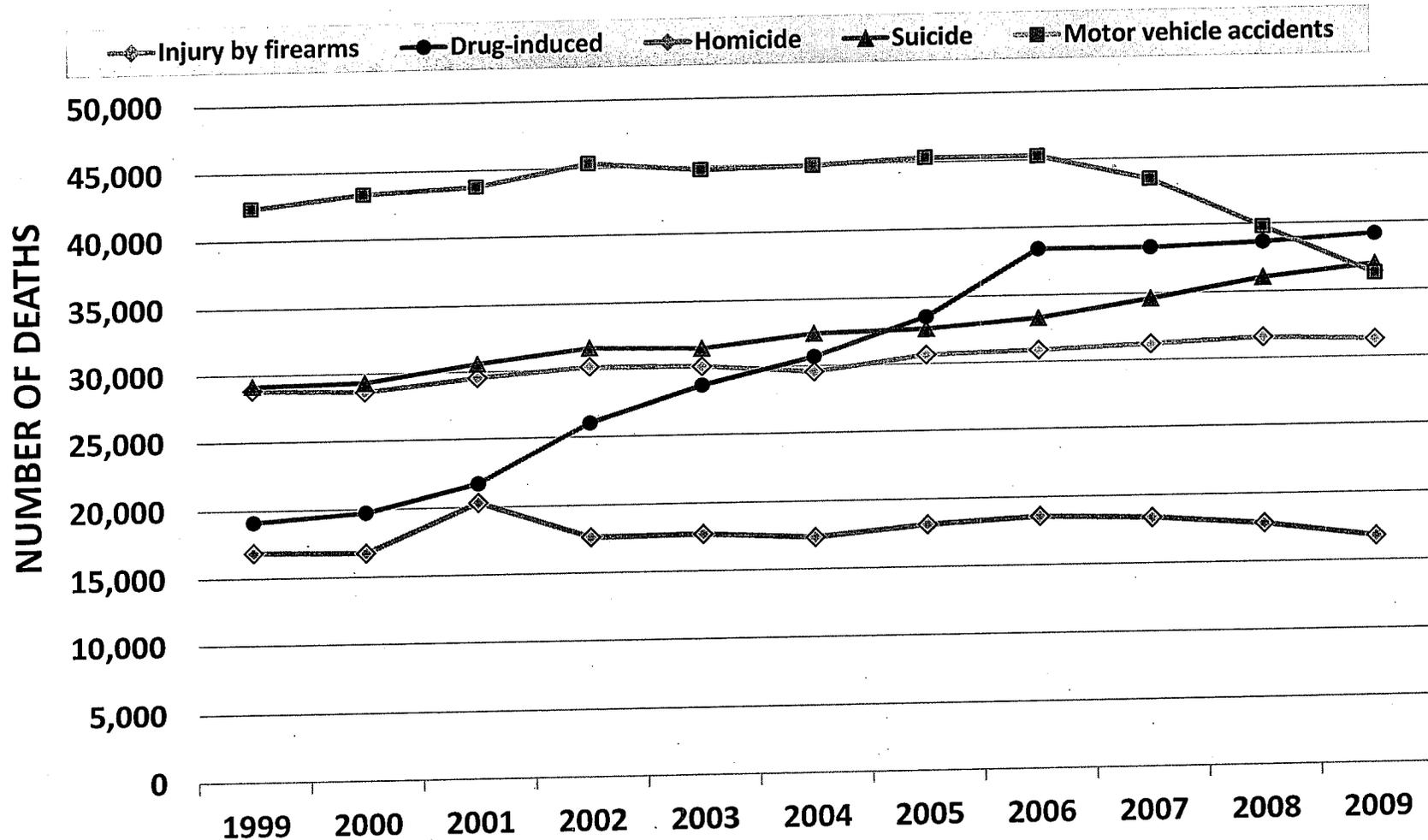
U.S. Drug Overdose Deaths by Major Drug Type, 1999-2010



U.S. Drug Enforcement Administration /
Operations Division / Office of Diversion
Control

Source: CDC/NCHS, NVSS

Drug-Induced Deaths vs. Other Injury Deaths (1999–2009)



Causes of death attributable to drugs include accidental or intentional poisonings by drugs and deaths from medical conditions resulting from chronic drug use. Drug-induced causes exclude accidents, homicides, and other causes indirectly related to drug use. Not all injury cause categories are mutually exclusive.

Source: National Center for Health Statistics, Centers for Disease Control and Prevention. National Vital Statistics Reports *Deaths: Final Data* for the years 1999 to 2009 (January 2012).

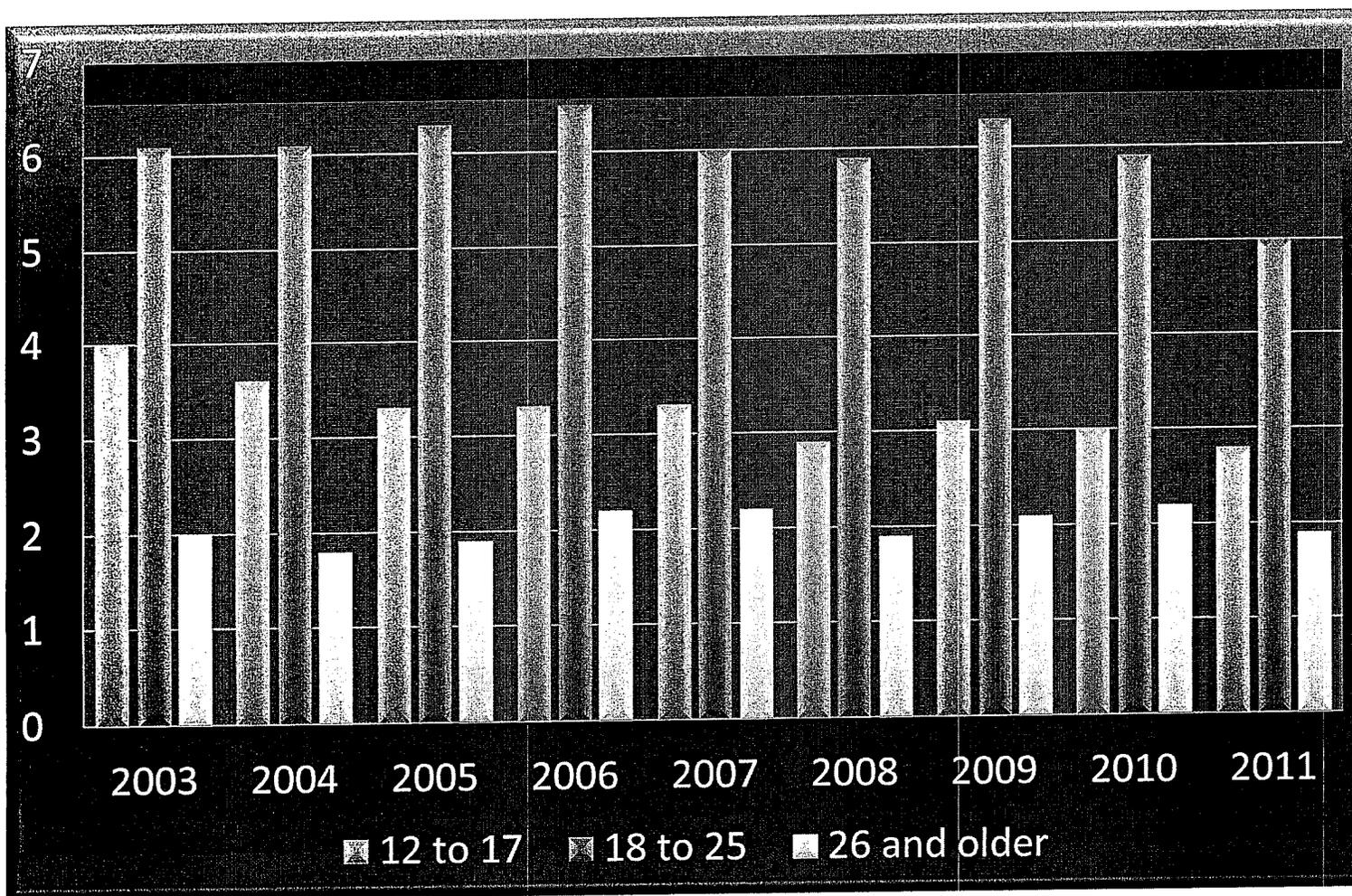
2006 estimated cost in the United States from
nonmedical use of prescription opioids

\$53.4 BILLION

- \$42 billion – Lost productivity
- \$8.2 billion – Criminal Justice costs
- \$2.2 billion – Treatment costs
- \$944 million – Medical complications

Five drugs – OxyContin, oxycodone, hydrocodone,
propoxyphene, and methadone accounted for two-thirds
of the economic burden

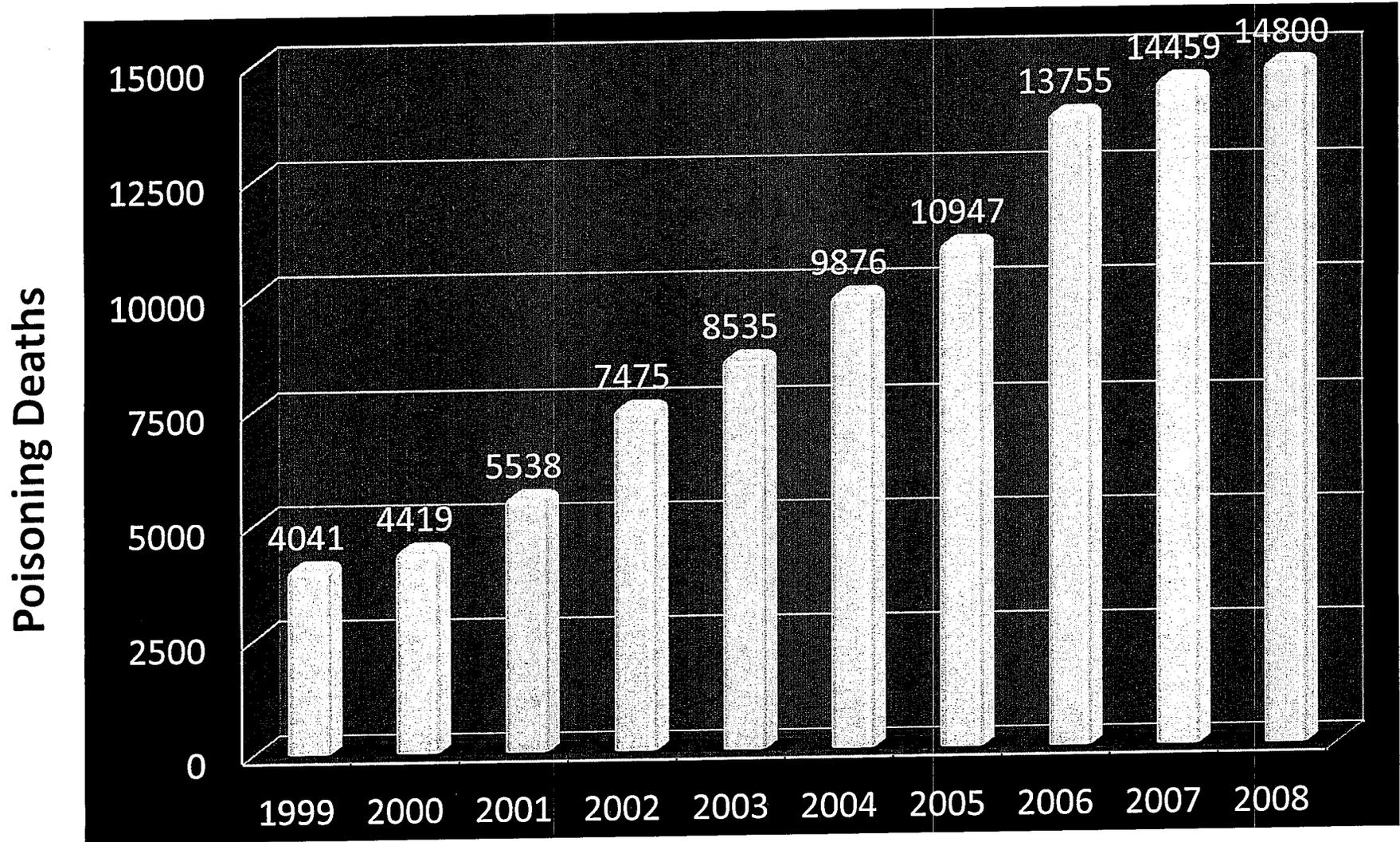
Percentage of High School Seniors Using Prescription Drugs by Age, 2003-2011



Source: 2011 National Survey on Drug Use and Health

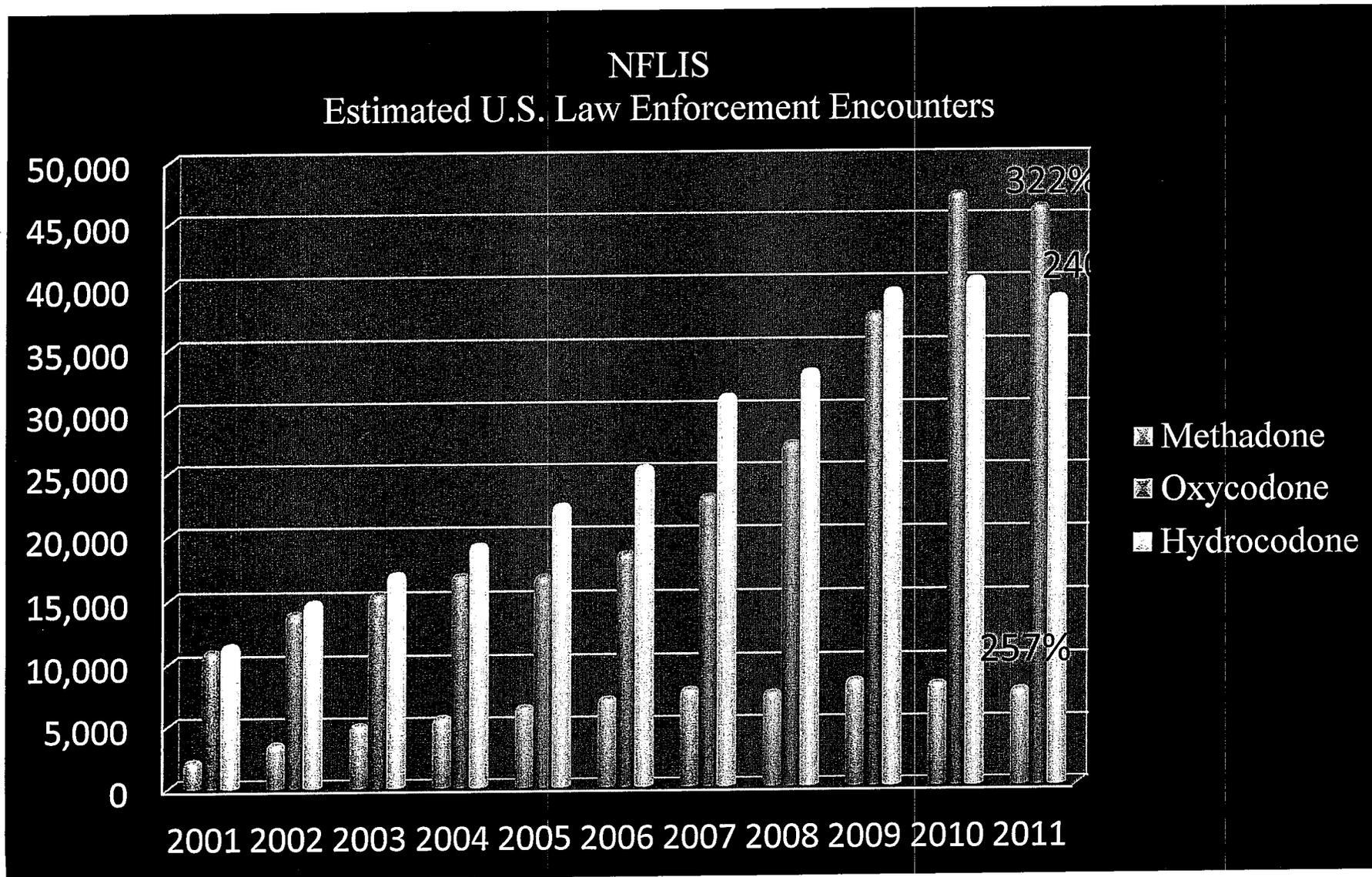
- Increase of 115%: ER visits attributable to pharmaceuticals alone
(*i.e.*, with no other type of drug or alcohol) (626,472 to 1,345,645)
 - No Significant Change: ER visits attributable to cocaine, heroin, marijuana, or methamphetamine
- Rx Drugs most frequently implicated:
 - **Opiates/Opioids pain relievers**
 - Oxycodone products 255% increase
 - Hydrocodone products 149% increase
- **Emergency room data 2004 - 2009**
 - Fentanyl products 117.5% increase
 - **Insomnia or Anti-Anxiety medications**
 - Zolpidem 154.9% increase
 - Alprazolam 148.3% increase
 - Clonazepam 114.8% increase
 - **Carisoprodol 100.6% increase**

Poisoning Deaths: Opioid Analgesics



Source: CDC/NCHS, National Vital Statistics System

Number of Forensic Cases 2001-2011



ONDCP Strategy

“Epidemic: Responding To America’s Prescription Drug Abuse Crisis” (Released in April 2011)



- Education
 - Healthcare Provider Education
 - Parent, Youth, and Patient Education
- Tracking and Monitoring
 - Work with states to establish effective PDMPs
 - Support NASPER
 - Explore reimbursements to prescribers who check PDMPs before writing a prescription
- Proper Medicine Disposal
- Enforcement
 - Assist states address doctor shopping and pill mills
 - Increase HIDTA intelligence-gathering and investigation of prescription drug trafficking
 - Expand the use of PDMPs to identify criminal prescribers and clinics

DEA Response

Enforcement

- Regulatory/Administrative/Civil/Criminal
- Stepped-up inspection program
- TDS program

National Take-back Initiative

- Proposed regulations

Education

- Pharmacist Diversion Awareness Conferences (PDAC)
- Participation in conferences for healthcare professionals
- Registrant conferences

Large-Scale Diversion

- In 2009, the average purchase for all oxycodone products for all pharmacies in US – 63,294 d.u.
- In 2010, the average was – 69,449 d.u.
- In 2009, the average purchase for all oxycodone products for the top 100 pharmacies in Florida – 1,226,460 d.u.
- In 2010, the average was – 1,261,908 d.u.

Purchases of Oxycodone 30mg

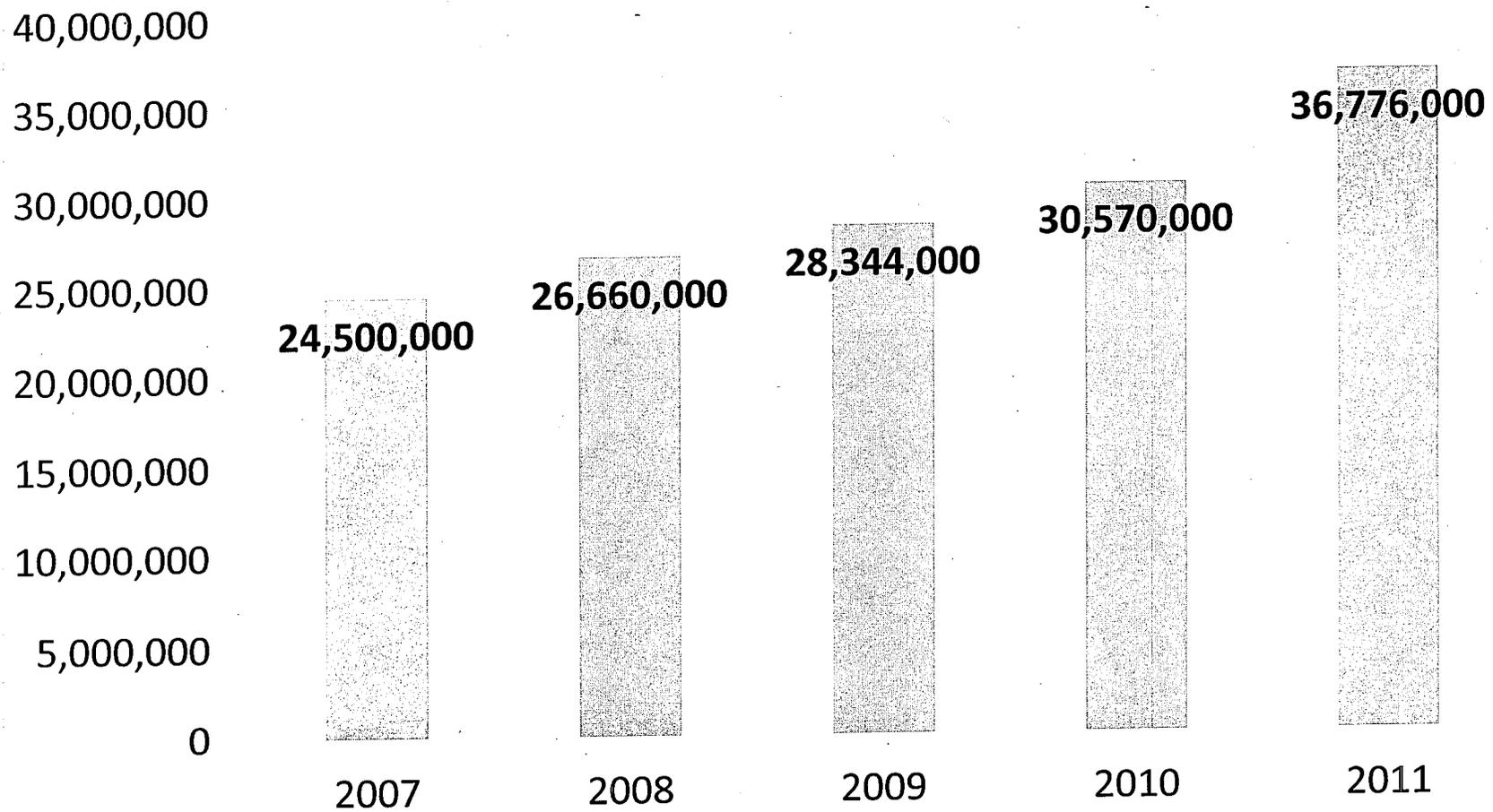
- In 2009, 44% of all oxycodone 30mg products were distributed to Florida
- In 2010, 43% of all oxycodone 30mg products were distributed to Florida



Non-Controlled Substances

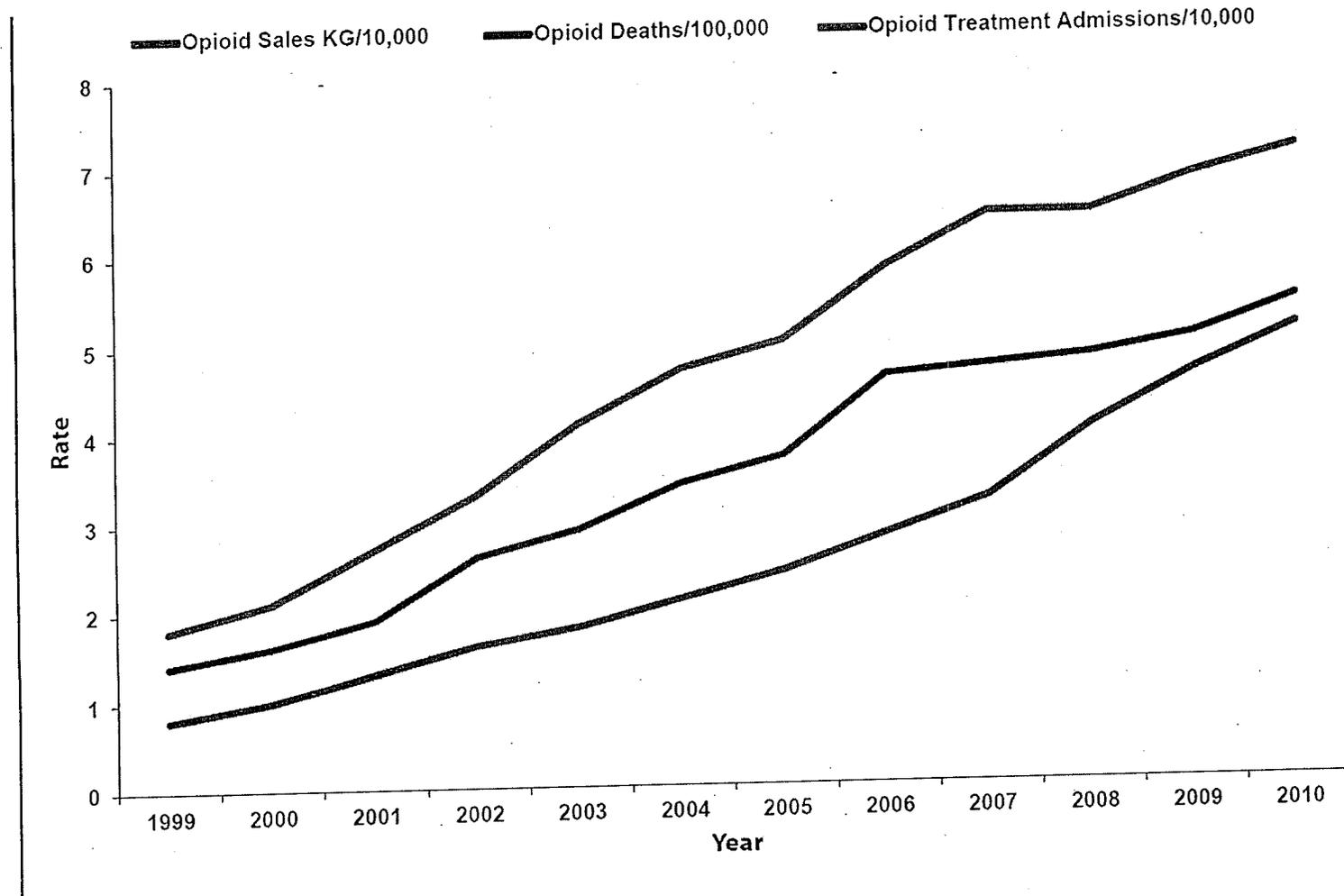
- Analgesic:
 - Tramadol (Ultram®), Ultracet®)
- Muscle Relaxant:
 - Cyclobenzaprine (Flexeril®)

Tramadol Prescriptions



Source: IMS Health National Prescription Audit Plus downloaded 6/5/2012

U.S. Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, 1999-2010



Source: National Vital Statistics System (NVSS),
DEA's Automation of Reports and
Consolidated Orders System, SAMHSA's
Treatment Episode Data Set

U.S. Drug Enforcement Administration /
Operations Division / Office of Diversion
Control

Top 25 U.S. Pharmaceutical Products Dispensed by Prescription*

	Total RX in Millions				
	2007	2008	2009	2010	2011
Total US Prescription Market	9,825	9,866	9,949	9,993	4,024
1 hydrocodone/acetaminophen	119.2	124.1	128.2	131.2	136.0
2 simvastatin	47.9	67.5	83.8	94.1	96.6
3 lisinopril	71.1	76.8	82.8	87.4	88.6
4 levethyroxine sodium	54.6	61.2	66.0	70.5	74.1
5 amlodipine besylate	27.9	44.6	51.9	57.2	62.1
6 omeprazole (RX)	26.6	35.1	45.4	53.4	59.3
7 azithromycin	46.3	51.0	53.8	52.6	55.3
8 amoxicillin	59.2	50.9	52.4	52.3	53.8
9 metformin HCL	40.2	42.9	44.3	46.9	48.4
10 hydrochlorothiazide	48.5	48.5	47.9	47.8	48.1
11 abiraterone	39.8	41.7	49.9	46.3	47.8
12 furosemide	44.2	44.1	49.5	49.4	42.1
13 Lipitor®	65.8	58.5	51.7	45.3	40.8
14 rosuvastatin tartrate	16.0	29.9	35.1	38.0	39.4
15 metoprolol tartrate	31.6	32.6	41.1	38.9	37.8
16 citalopram HBR	17.8	22.4	27.1	32.1	37.7
17 sertraline HCL	31.6	32.7	34.2	35.7	37.2
18 metoprolol succinate	21.0	41.5	26.9	33.0	34.5
19 prednisone	25.9	27.1	27.8	28.7	33.7
20 atenolol	44.7	41.8	39.9	36.3	33.3
21 gabapentin	20.0	22.2	25.4	29.3	33.2
22 tramadol HCL	19.1	21.8	24.1	26.8	32.9
23 oxycodone/acetaminophen	25.9	28.4	30.2	31.9	32.8
24 ibuprofen (RX)	27.7	28.5	30.3	31.1	32.6
25 warfarin sodium	28.8	30.2	31.6	32.0	30.9

*

Source:



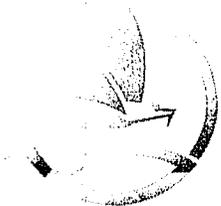
National Prescription Audit™

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Updated February 23, 2012

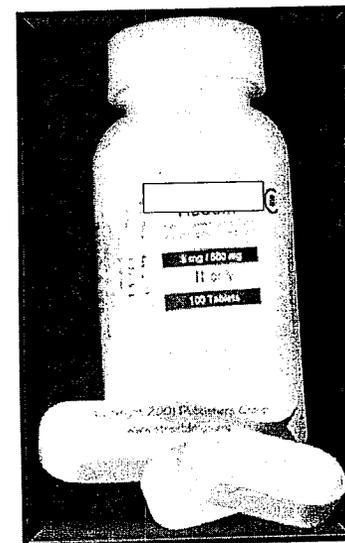
Top 50 Generic Drugs by Total Prescriptions 2010

Rank	Drug	Total Rxs	Change from Previous Year	Rank	Drug	Total Rxs	Change from Previous Year
1	Hydrocodone/APAP	122,806,850	2.10%	26	Lorazepam	23,428,627	3.70%
2	Lisinopril	76,901,813	4.30%	27	Warfarin	23,388,338	1.50%
3	Simvastatin	76,771,821	4.90%	28	Clonazepam	23,085,065	4.00%
4	Levothyroxine	68,222,152	8.20%	29	Fluticasone nasal	22,447,832	19.70%
5	Amoxicillin	51,083,822	-0.60%	30	Cyclobenzaprine	22,240,071	7.30%
6	Amlodipine besylate	50,186,652	11.70%	31	Cephalexin	21,943,482	2.70%
7	Azithromycin	48,756,188	-2.10%	32	Trimethoprim/sulfa	21,345,723	4.50%
8	Alprazolam	46,201,182	3.90%	33	Fexofenadine	20,430,430	27.50%
9	Hydrochlorothiazide	45,838,017	-0.80%	34	Amoxicillin/pot clav	20,234,873	1.20%
10	Omeprazole	44,795,175	15.40%	35	Ciprofloxacin HCl	20,063,382	1.80%
11	Metformin	41,932,689	4.70%	36	Pravastatin	20,026,786	17.90%
12	Furosemide oral	36,583,895	-0.10%	37	Trazodone HCl	18,786,495	6.50%
13	Metoprolol tartrate	34,707,807	-0.50%	38	Lovastatin	17,509,951	13.50%
14	Atenolol	33,839,806	-11.00%	39	Triamterene/HCTZ	17,201,037	-7.00%
15	Sertraline	33,409,838	8.90%	40	Carvedilol	16,681,336	8.30%
16	Metoprolol succinate	32,224,000	12.00%	41	Alendronate	16,177,014	-6.90%
17	Zolpidem tartrate	29,719,569	-2.80%	42	Ranitidine HCl	14,699,414	6.60%
18	Oxycodone/APAP	28,705,243	6.80%	43	Meloxicam	14,645,167	2.90%
19	Citalopram HBR	27,993,635	9.40%	44	Diazepam	14,584,147	7.10%
20	Gabapentin	26,865,557	14.00%	45	Naproxen	14,297,759	10.30%
21	Ibuprofen	26,256,548	3.20%	46	Propoxyphene-N/APAP	14,274,354	-18.70%
22	Prednisone oral	25,529,463	-2.70%	47	Fluconazole	13,938,887	4.60%
23	Tramadol	25,527,796	10.30%	48	Methylprednisolone tabs	13,659,852	11.30%
24	Lisinopril/HCTZ	24,538,247	8.00%	49	Doxycycline	13,199,430	1.90%
25	Fluoxetine	24,473,994	6.80%	50	Paroxetine	12,979,366	-14.40%



Hydrocodone, APAP C-III

- Hydrocodone / Acetaminophen (toxicity)
- Similarities:
 - Structurally related to codeine
 - Equal to morphine in producing opiate-like effects
- Brand Names: Vicodin[®], Lortab[®], Lorcet[®]
- “Cocktail” or “Holy Trinity”
 - Hydrocodone
 - Soma[®] / carisoprodol
 - Alprazolam / Xanax[®]
- Street prices: \$2 to \$10+ per tablet depending on strength & region



State Ranking* - Hydrocodone

January 1– September 30, 2012

RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL
1	CA	23,776,920	12	MD	741,978	23	OH	346,787	34	AK	159,271	45	NE	50,104
2	GA	2,409,068	13	TX	701,126	24	HI	345,827	35	MN	139,325	46	SD	42,280
3	IL	2,050,379	14	CO	620,493	25	MS	330,759	36	IA	112,594	47	ME	37,500
4	TN	1,647,726	15	NV	564,154	26	NJ	325,776	37	ND	106,930	48	RI	22,667
5	PA	1,646,148	16	NC	500,302	27	WA	310,658	38	KS	93,795	49	DC	21,110
6	AL	1,324,943	17	MO	493,318	28	WI	266,806	39	DE	85,458	50	VT	14,900
7	MI	883,366	18	NY	456,281	29	LA	244,062	40	UT	79,160	51	NH	11,818
8	IN	850,550	19	OK	408,606	30	OR	224,877	41	MA	69,290	52	GU	3,500
9	VA	812,750	20	KY	405,044	31	ID	176,600	42	WY	68,450	53	PR	2,500
10	AZ	806,259	21	SC	374,024	32	WV	167,788	43	AR	66,270	54	VI	700
11	FL	754,979	22	CT	360,517	33	NM	161,810	44	MT	54,800	55	AS	0

*** Business Activity-Practitioners**

State Ranking* - Hydrocodone

January 1 – September 30, 2012

RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL	RANK	STATE	TOTAL
1	CA	752,243,210	12	PA	179,880,349	23	MS	95,040,930	34	MA	45,146,650	45	NH	11,372,160
2	TX	616,744,356	13	KY	174,997,631	24	AR	91,577,120	35	MD	39,757,136	46	WY	9,801,690
3	TN	372,321,936	14	NC	168,721,190	25	OR	89,644,605	36	ID	39,144,850	47	AK	8,914,452
4	MI	316,860,884	15	MO	155,533,410	26	WI	83,864,540	37	NM	34,014,930	48	ND	8,192,140
5	FL	272,756,535	16	OK	142,561,470	27	KS	72,465,169	38	NE	28,350,230	49	DE	7,154,030
6	IL	233,059,530	17	LA	128,601,625	28	WV	68,151,620	39	CT	26,188,240	50	VT	5,672,450
7	OH	224,079,845	18	SC	119,274,940	29	CO	60,518,800	40	ME	22,443,390	51	DC	1,795,600
8	IN	216,475,192	19	NV	117,109,135	30	IA	53,580,034	41	MT	20,483,720	52	PR	1,421,520
9	GA	197,245,775	20	WA	113,082,770	31	MN	53,502,119	42	RI	15,836,670	53	VI	344,030
10	NY	191,672,460	21	VA	111,391,716	32	UT	46,820,190	43	HI	14,422,340	54	GU	183,400
11	AL	190,924,530	22	AZ	108,617,660	33	NJ	46,479,750	44	SD	12,077,710	55	AS	0

**** Business Activity – Retail Pharmacies***

Circle of Addiction & the Next Generation

Oxycodone
Combinations

Percocet®

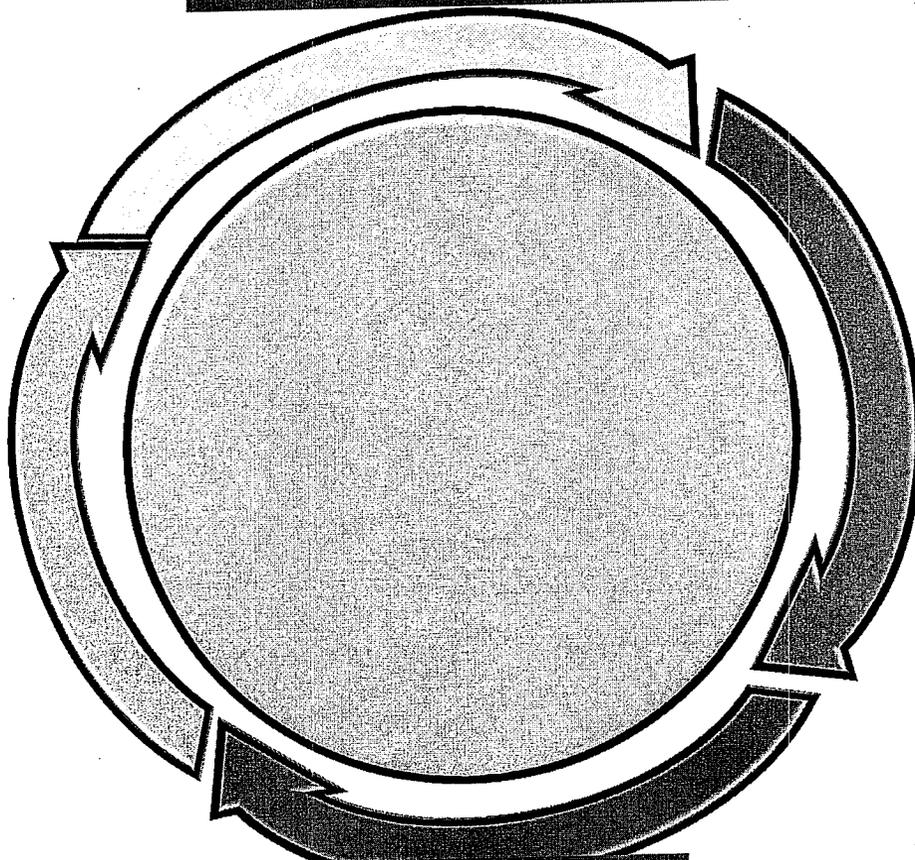
\$7-\$10/tab

OxyContin®
\$80/tab

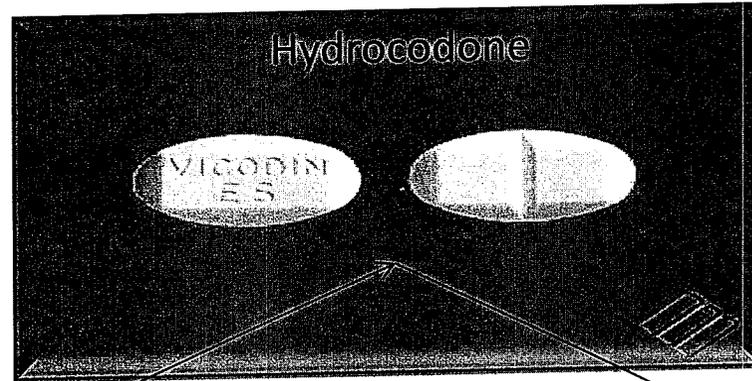
Roxicodone®
Oxycodone IR
15mg, 30mg
\$30-\$40/tab

Hydrocodone
Lorcet®
\$5-\$7/tab

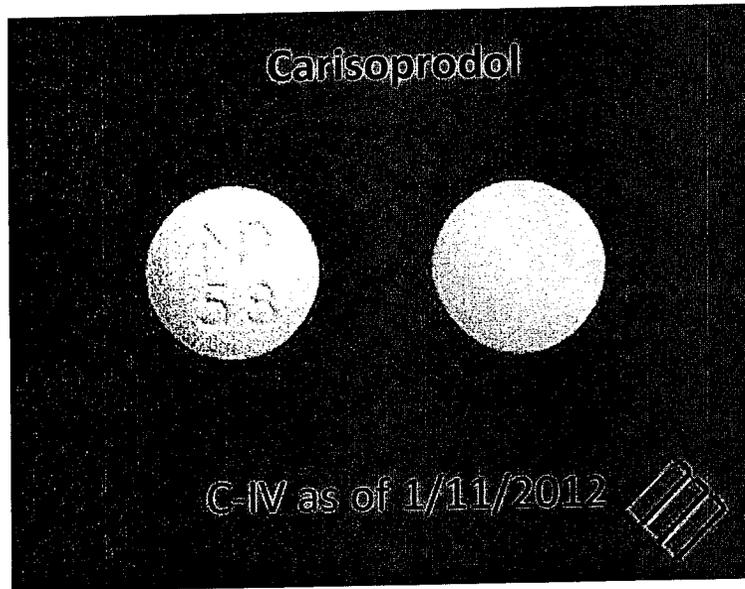
Heroin
\$10/bag



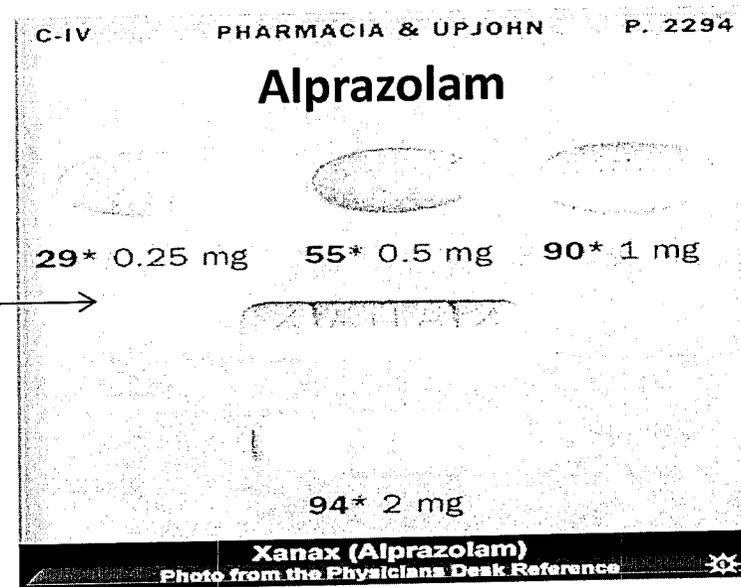
The Trinity



Opiate



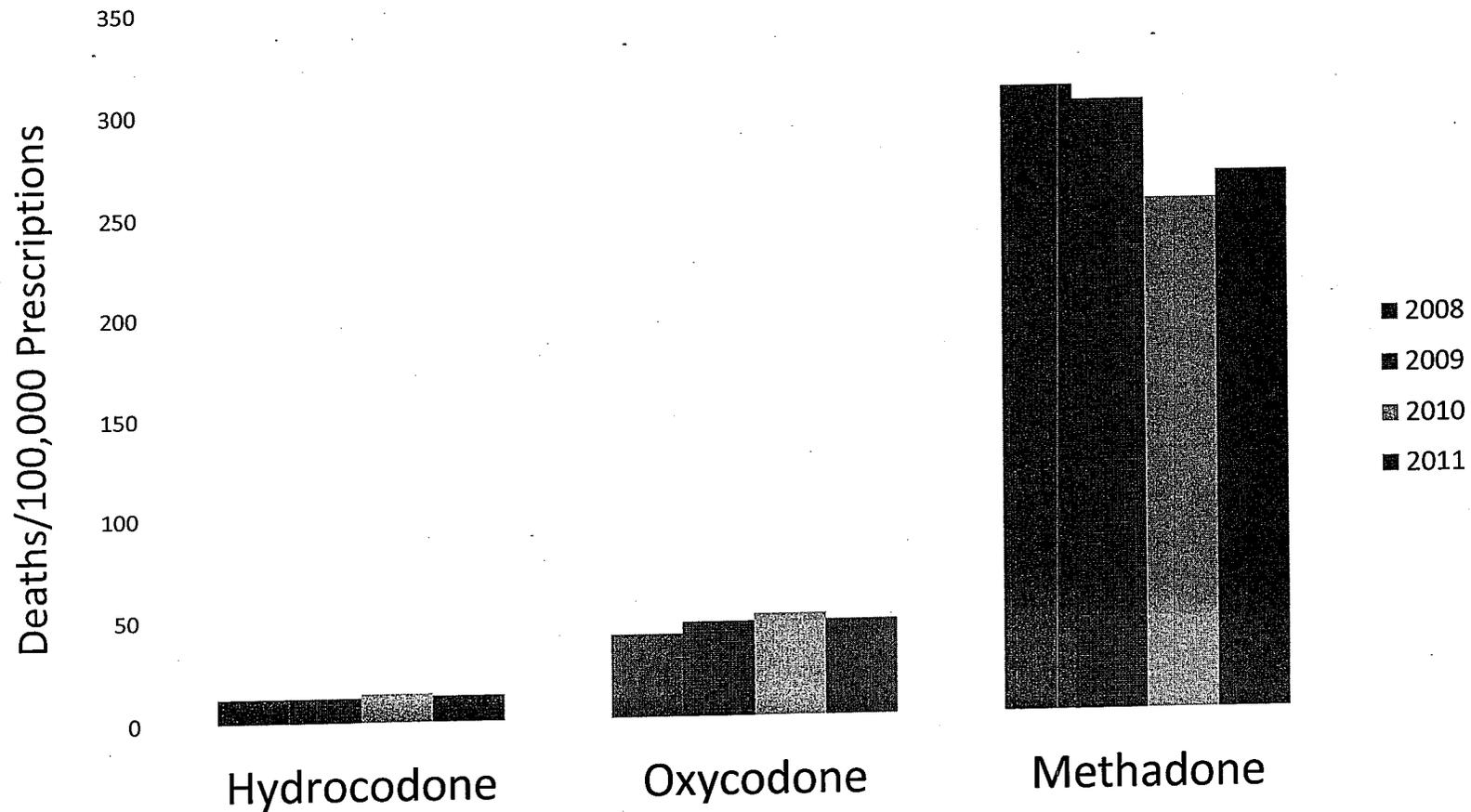
Muscle Relaxant



Benzodiazepine

Florida Deaths Per 100,000 Prescriptions

2008-2011



- Sources:
- Death Data : Florida Department of Law Enforcement, "Drugs Identified in Deceased Persons by Florida Medical Examiners"
- Prescription Data: IMS Exponent, State Level: Florida Retail Prescription Data

Overdose... Why?

- Patients not taking the drug as directed
- Physicians not properly prescribing the drug
- Non medical users ingesting with other substances
- Opiate naive



Preventing and recognizing prescription drug abuse
See page 10

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

from the director:

The nonmedical use and abuse of prescription drugs is a serious public health problem in this country. Although most people take prescription medications responsibly, an estimated 52 million people (20 percent of those aged 12 and older) have used prescription drugs for nonmedical reasons at least once in their lifetimes. Young people are strongly represented in this group. In fact, the National Institute on Drug Abuse's (NIDA) Monitoring the Future (MTF) survey found that about 1 in 12 high school seniors reported past-year nonmedical use of the prescription pain reliever Vicodin in 2010, and 1 in 20 reported abusing OxyContin—making these medications among the most commonly abused drugs by adolescents.

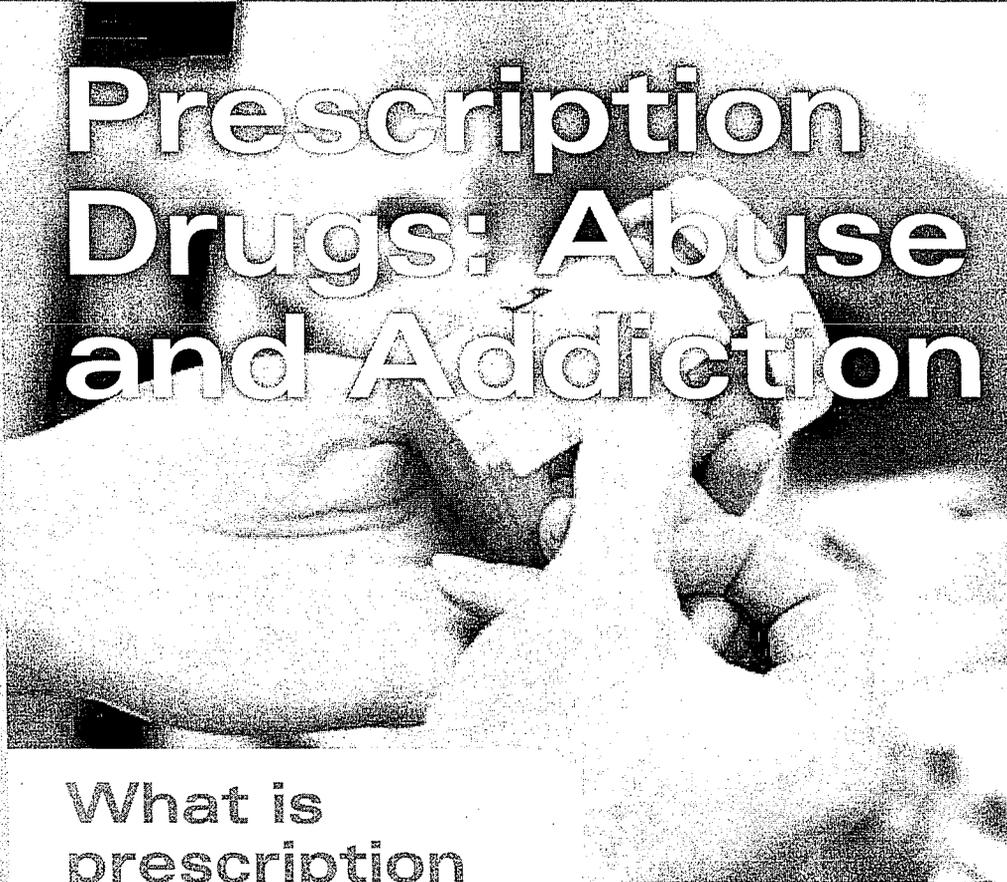
The abuse of certain prescription drugs—opioids, central nervous system (CNS) depressants, and stimulants—can lead to a variety of adverse health effects, including addiction. Among those who reported past-year nonmedical use of a prescription drug, nearly 14 percent met criteria for abuse of or dependence on it. The reasons for the high prevalence of prescription drug abuse vary by age, gender, and other factors, but likely include greater availability.

The number of prescriptions for some of these medications has increased dramatically since the early 1990s (see figures, page 2). Moreover, a consumer culture amenable to “taking a pill for what ails you” and the perception of prescription drugs as less harmful than illicit drugs are other likely contributors to the problem. It is an urgent one: unintentional overdose deaths involving opioid pain relievers have quadrupled since 1999, and by 2007, outnumbered those involving heroin and cocaine.

NIDA hopes to change this situation by increasing awareness and promoting additional research on prescription drug abuse. Prescription drug abuse is not a new problem, but one that deserves renewed attention. It is imperative that as a Nation we make ourselves aware of the consequences associated with abuse of these medications.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

Research Report Series



Prescription Drugs: Abuse and Addiction

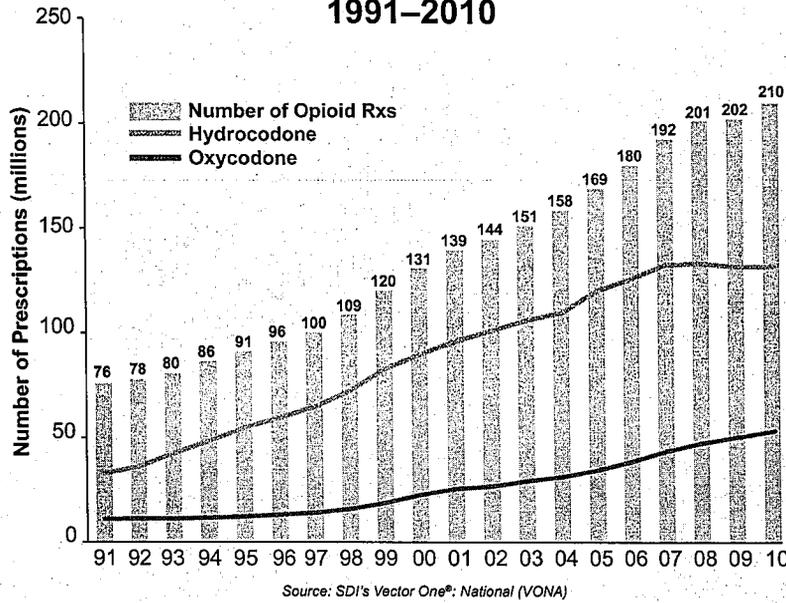
What is prescription drug abuse?

Prescription drug abuse¹ is the use of a medication without a prescription, in a way other than as prescribed, or for the experience or feelings elicited. According to several national surveys, prescription medications, such as those used to treat pain, attention deficit disorders, and anxiety, are being abused at a rate second only to marijuana among illicit drug users. The consequences of this abuse have been steadily worsening, reflected in increased treatment admissions, emergency room visits, and overdose deaths.

continued inside

¹ Prescription drug abuse, as defined in this report, is equivalent to the term “nonmedical use,” used by many of the national surveys or data collection systems. This definition does not correspond to the definition of abuse/dependence listed in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV).

Total Number of Opioid Prescriptions Dispensed by U.S. Retail Pharmacies, 1991–2010

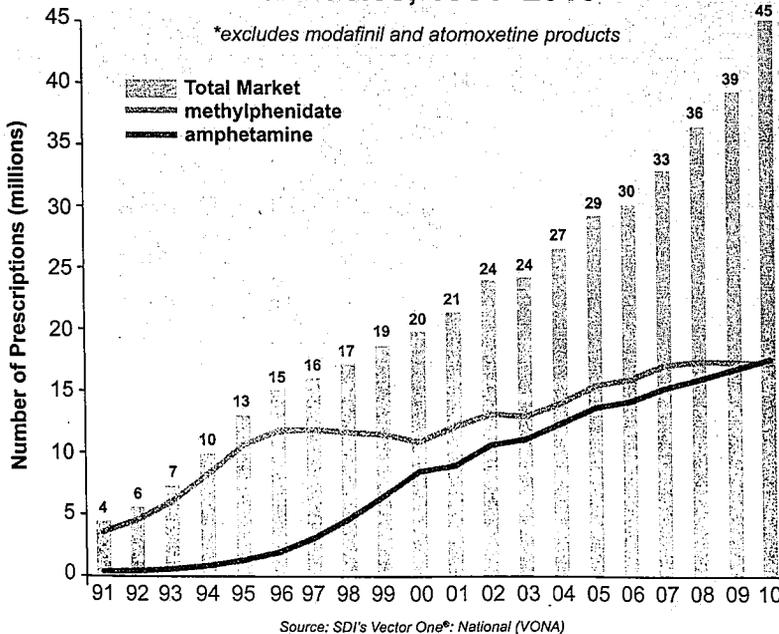


What are some of the commonly abused prescription drugs?

Although many medications can be abused, the following three classes are most commonly abused:

- Opioids—usually prescribed to treat pain;
- Central nervous system (CNS) depressants—used to treat anxiety and sleep disorders; and
- Stimulants—most often prescribed to treat attention-deficit hyperactivity disorder (ADHD).

Total Number of Prescriptions for Stimulants* Dispensed by U.S. Retail Pharmacies, 1991–2010



Opioids—

What are opioids?

Opioids are medications that relieve pain. They reduce the intensity of pain signals reaching the brain and affect those brain areas controlling emotion, which diminishes the effects of a painful stimulus. Medications that fall within this class include hydrocodone (e.g., Vicodin), oxycodone (e.g., OxyContin, Percocet), morphine (e.g., Kadian, Avinza), codeine, and related drugs. Hydrocodone products are the most commonly prescribed for a variety of painful conditions, including dental and injury-related pain. Morphine



is often used before and after surgical procedures to alleviate severe pain. Codeine, on the other hand, is often prescribed for mild pain. In addition to their pain-relieving properties, some of these drugs—codeine and diphenoxylate (Lomotil) for example—can be used to relieve coughs and severe diarrhea.

How do opioids affect the brain and body?

Opioids act by attaching to specific proteins called opioid receptors, which are found in the brain, spinal cord, gastrointestinal tract, and other organs in the body. When these drugs attach to their receptors, they reduce the perception of pain. Opioids can also produce drowsiness, mental confusion, nausea, constipation, and, depending



In 2007, the number of overdose deaths from prescription opioids outnumbered deaths from heroin and cocaine combined.

² Changing the route of administration also contributes to the abuse of other prescription medications, including stimulants, a practice that can lead to serious medical consequences.

Dependence vs. Addiction

Physical dependence occurs because of *normal* adaptations to chronic exposure to a drug and is not the same as addiction. Addiction, which can include physical dependence, is distinguished by compulsive drug seeking and use despite sometimes devastating consequences.

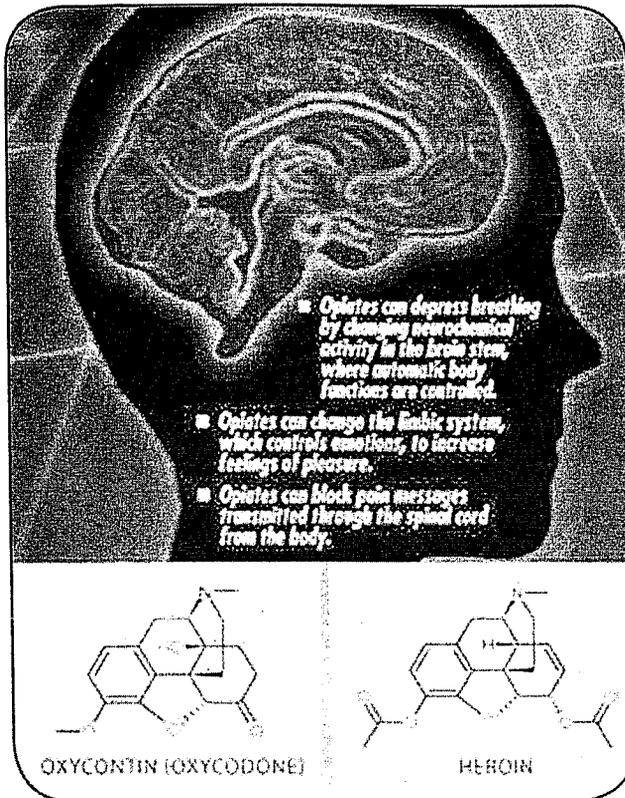
Someone who is physically dependent on a medication will experience withdrawal symptoms when use of the drug is abruptly reduced or stopped. These symptoms can be mild or severe (depending on the drug) and can usually be managed medically or avoided by using a slow drug taper.

Dependence is often accompanied by tolerance, or the need to take higher doses of a medication to get the same effect. When tolerance occurs, it can be difficult for a physician to evaluate whether a patient is developing a drug problem, or has a real medical need for higher doses to control their symptoms. For this reason, physicians need to be vigilant and attentive to their patients' symptoms and level of functioning to treat them appropriately.

upon the amount of drug taken, can depress respiration. Some people experience a euphoric response to opioid medications, since these drugs also affect the brain regions involved in reward. Those who abuse opioids may seek to intensify their experience by taking the drug in ways other than those prescribed. For example, OxyContin is an oral medication used to treat moderate to severe pain through a slow, steady release of the opioid. People who abuse OxyContin may snort or inject it,² thereby increasing their risk for serious medical complications, including overdose.

What are the possible consequences of opioid use and abuse?

Taken as prescribed, opioids can be used to manage pain safely and effectively. However, when abused, even a single large dose can cause severe respiratory depression and death. Properly managed, short-term medical use of opioid analgesics rarely causes addiction—characterized by compulsive drug seeking and use despite serious adverse consequences. Regular (e.g., several times a day, for several weeks or more) or longer term use or abuse of opioids can lead to physical dependence and, in some cases,



OxyContin and heroin have similar chemical structures and bind to the same receptors in the brain.

Is it safe to use opioid drugs with other medications?

Only under a physician's supervision can opioids be used safely with other drugs. Typically, they should not be used with other substances that depress the CNS, such as alcohol, antihistamines, barbiturates, benzodiazepines, or general anesthetics, because these combinations increase the risk of life-threatening respiratory depression.

CNS depressants—

What are CNS depressants?

CNS depressants, sometimes referred to as sedatives and tranquilizers, are substances that can slow brain activity. This property makes them useful for treating anxiety and sleep disorders. Among the medications commonly prescribed for these purposes are the following:

- **Benzodiazepines**, such as diazepam (Valium) and alprazolam (Xanax), are sometimes prescribed to treat anxiety, acute stress reactions, and panic attacks. The more sedating benzodiazepines, such as triazolam (Halcion) and estazolam (ProSom) are prescribed for short-term treatment of sleep disorders. Usually, benzodiazepines are not prescribed for long-term use because of the risk for developing tolerance, dependence, or addiction.

addiction. Physical dependence is a *normal* adaptation to chronic exposure to a drug and is not the same as addiction (see text box on "Dependence vs. Addiction" on page 3). In either case, withdrawal symptoms may occur if drug use

is suddenly reduced or stopped. These symptoms can include restlessness, muscle and bone pain, insomnia, diarrhea, vomiting, cold flashes with goose bumps ("cold turkey"), and involuntary leg movements.

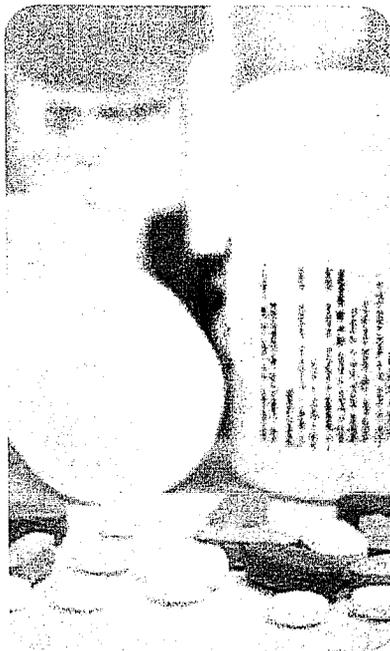
Over-the-Counter Medicines

Over-the-counter (OTC) medications, such as certain cough suppressants, sleep aids, and antihistamines, can be abused for their psychoactive effects. This typically means taking doses higher than recommended or combining OTC medications with alcohol, or with illicit or prescription drugs. Either practice can have dangerous results, depending on the medications involved. Some contain aspirin or acetaminophen (e.g., Tylenol), which can be toxic to the liver at high doses. Others, when taken for their "hallucinogenic" properties, can cause confusion, psychosis, coma, and even death.

Cough syrups and cold medications are the most commonly abused OTC medications. In 2010, for example, 6.6 percent of high school seniors took cough syrup "to get high." At high doses, dextromethorphan—a key ingredient found in cough syrup—can act like PCP or ketamine, producing dissociative or out-of-body experiences.

- **Non-benzodiazepine sleep medications**, such as zolpidem (Ambien), eszopiclone (Lunesta), and zalepon (Sonata), have a different chemical structure, but act on some of the same brain receptors as benzodiazepines. They are thought to have fewer side effects and less risk of dependence than benzodiazepines.
- **Barbiturates**, such as mephobarbital (Mebaral), phenobarbital (Luminal Sodium), and pentobarbital sodium (Nembutal), are used less frequently to reduce anxiety or to help with sleep problems because of their higher risk of overdose compared to benzodiazepines. However, they are still used in surgical procedures and for seizure disorders.

How do CNS depressants affect the brain and body? Most CNS depressants act on the brain by affecting the neurotransmitter gamma-aminobutyric acid (GABA). Neurotransmitters are brain chemicals that facilitate communication between brain cells. Although the different classes of CNS depressants work in unique ways, it is through their ability to increase GABA—and thereby inhibit brain activity—that they produce a drowsy or calming effect beneficial to those suffering from anxiety or sleep disorders.



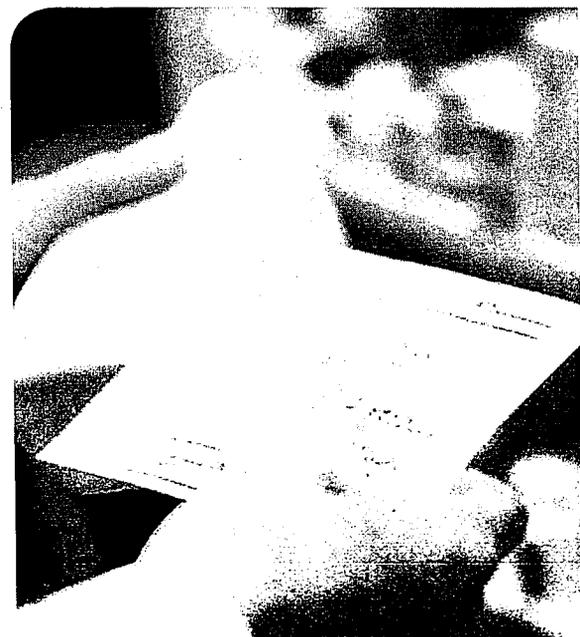
What are the possible consequences of CNS depressant use and abuse?

Despite their many beneficial effects, benzodiazepines and barbiturates have the potential for abuse and should be used only as prescribed. The use of non-benzodiazepine sleep aids is less well studied, but certain indicators have raised concern about their abuse liability as well. During the first few days of taking a prescribed CNS depressant, a person usually feels sleepy and uncoordinated, but as the body becomes accustomed to the effects of the drug and tolerance develops, these side effects begin to disappear. If one uses these drugs long term, larger doses may be needed to achieve the therapeutic effects. Continued use can also lead to physical dependence and withdrawal when use is abruptly reduced or stopped (see text box on “Dependence vs. Addiction” on page 3). Because all CNS depressants work by slowing the brain’s activity, when

an individual stops taking them, there can be a rebound effect, resulting in seizures or other harmful consequences. Although withdrawal from benzodiazepines can be problematic, it is rarely life threatening, whereas withdrawal from prolonged use of barbiturates can have life-threatening complications. Therefore, someone who is thinking about discontinuing CNS depressant therapy or who is suffering withdrawal from a CNS depressant should speak with a physician or seek immediate medical treatment.

Is it safe to use CNS depressants with other medications?

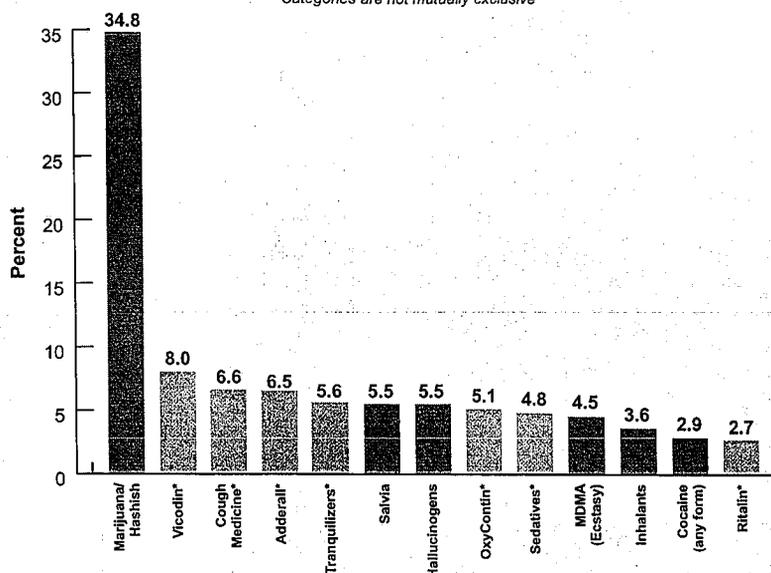
Only under a physician’s supervision is it safe to use CNS depressants with other medications. Typically, they should not be combined with any other medication or substance that causes CNS depression, including prescription pain medicines, some OTC cold and allergy medications, and alcohol. Using CNS depressants with these other substances—particularly alcohol—can affect heart rhythm, slow respiration, and even lead to death.



After Marijuana, Prescription and Over-the-Counter Medications* Account for Most of the Commonly Abused Drugs

Prevalence of Past-Year Drug Use Among 12th Graders

Categories are not mutually exclusive



SOURCE: University of Michigan, 2010 Monitoring the Future Study

* Nonmedical Use

only a few health conditions, including ADHD, narcolepsy, and occasionally depression—in those who have not responded to other treatments.

How do stimulants affect the brain and body?

Stimulants, such as dextroamphetamine (Dexedrine and Adderall) and methylphenidate (Ritalin and Concerta), act in the brain similarly to a family of key brain neurotransmitters called monoamines, which include norepinephrine and dopamine. Stimulants enhance the effects of these chemicals in the brain. The associated increase in dopamine can induce a feeling of euphoria when stimulants are taken nonmedically. Stimulants also increase blood pressure and heart rate, constrict blood vessels, increase blood glucose, and open up breathing passages.

Stimulants—

What are stimulants?

As the name suggests, stimulants increase alertness, attention, and energy, as well as elevate blood pressure, heart rate, and respiration. Stimulants historically were used to treat asthma and other respiratory problems, obesity, neurological disorders, and a variety of other ailments. But as their potential for abuse and addiction became apparent, the medical use of stimulants began to wane. Now, stimulants are prescribed to treat

Cognitive Enhancers

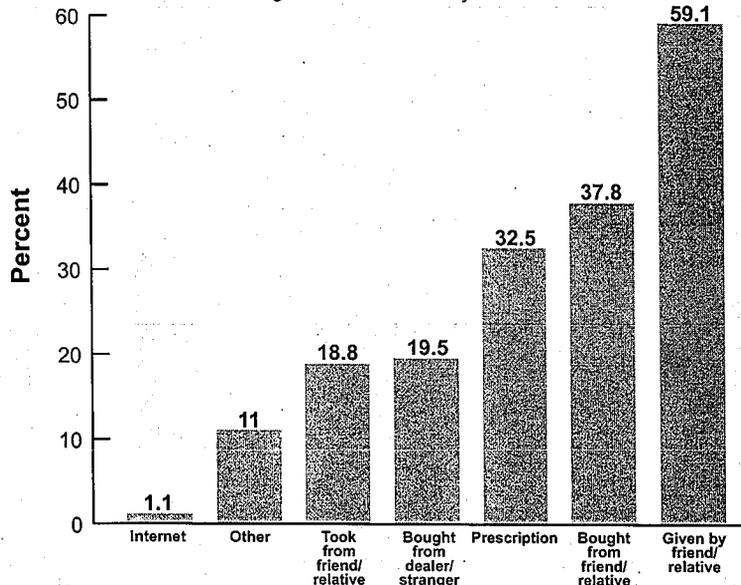
The dramatic increases in stimulant prescriptions over the last 2 decades have led to their greater environmental availability and increased risk for diversion and abuse. For those who take these medications to improve properly diagnosed conditions, they can be transforming, greatly enhancing a person's quality of life. However, because they are perceived by many to be generally safe and effective, prescription stimulants, such as Concerta or Adderall, are increasingly being abused to address nonmedical conditions or situations. Indeed, reports suggest that the practice is occurring among some academic professionals, athletes, performers, older people, and both high school and college students. Such nonmedical cognitive enhancement poses potential health risks, including addiction, cardiovascular events, and psychosis.



Youth who abuse prescription medications are also more likely to report use of other drugs.

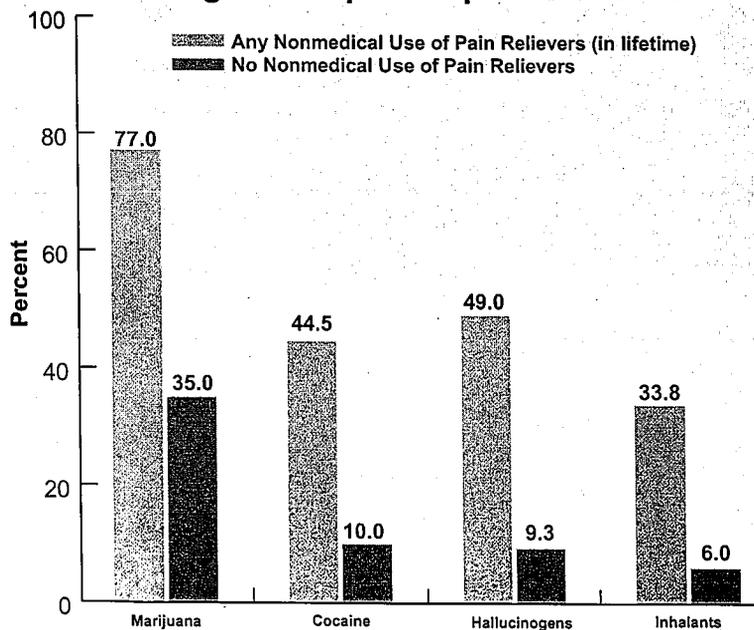
Source of Prescription Narcotics among Those Who Used in the Past-Year, 12th Grade*

* Categories are not mutually exclusive



SOURCE: University of Michigan, 2010 Monitoring the Future Study

Greater Lifetime Use of Illicit Drugs among Prescription Opiate Abusers



The rate of use of other drugs is significantly higher among those who have abused prescription drugs in their lifetimes. The same is true for past-year users.

SOURCE: SAMHSA. Misuse of prescription drugs: Data from the 2002, 2003, and 2004 National Surveys on Drug Use and Health. HHS Pub. No. (SMA)06-4192. Rockville, MD: Office of Applied Studies, 2006.

What are the possible consequences of stimulant use and abuse?

As with other drugs of abuse, it is possible for individuals to become dependent upon or addicted to stimulants. Withdrawal symptoms associated with discontinuing stimulant use include fatigue, depression, and disturbance of sleep patterns. Repeated abuse of some stimulants (sometimes within a short period) can lead to feelings of hostility or paranoia, even psychosis. Further, taking high doses of a stimulant may result in dangerously high body temperature and an irregular heartbeat. There is also the potential for cardiovascular failure or seizures.

Is it safe to use stimulants with other medications?

Stimulants should not be used with other medications unless authorized by a physician. Patients also should be aware of the dangers associated with mixing stimulants and OTC cold medicines that contain decongestants, as combining these substances may cause blood pressure to become dangerously high or lead to irregular heart rhythms.

Trends in prescription drug abuse

How many people abuse prescription drugs?

According to results from the 2010 National Survey on Drug Use and Health (NSDUH), an estimated 2.4 million Americans used prescription drugs nonmedically for the first time within the past year,

which averages to approximately 6,600 initiates per day. More than one-half were females and about a third were aged 12 to 17. Although prescription drug abuse affects many Americans, certain populations, such as youth, older adults, and women, may be at particular risk.

Adolescents and young adults

Abuse of prescription drugs is highest among young adults aged 18 to 25, with 5.9 percent reporting nonmedical use in the past month (NSDUH, 2010). Among youth aged 12 to 17, 3.0 percent reported past-month nonmedical use of prescription medications.

According to the 2010 MTF, prescription and OTC drugs are among the most commonly abused drugs by 12th graders (see figure on page 6), after alcohol, marijuana, and tobacco. While past-year nonmedical use of sedatives and tranquilizers decreased among 12th graders over the last 5 years, this is not the case for the nonmedical use of amphetamines or opioid pain relievers.

When asked how prescription opioids were obtained for nonmedical use, more than half of the 12th graders surveyed said they were given the drugs or bought them from a friend or



relative. Interestingly, the number of students who purchased opioids over the Internet was negligible (see top chart on previous page).

Youth who abuse prescription medications are also more likely to report use of other drugs. Multiple studies have revealed associations between prescription drug abuse and higher rates of cigarette smoking; heavy episodic drinking; and marijuana, cocaine, and other illicit drug use among adolescents, young adults, and college students in the United States (see bottom chart on previous page).

Older adults

Persons aged 65 years and older comprise only 13 percent of the population, yet account for more than one-third of total outpatient spending on prescription medications in the United States. Older patients are more likely to be prescribed long-term and multiple prescriptions, and some experience cognitive decline, which could lead to improper use of medications. Alternatively, those on a fixed income may abuse another person's remaining medication to save money.

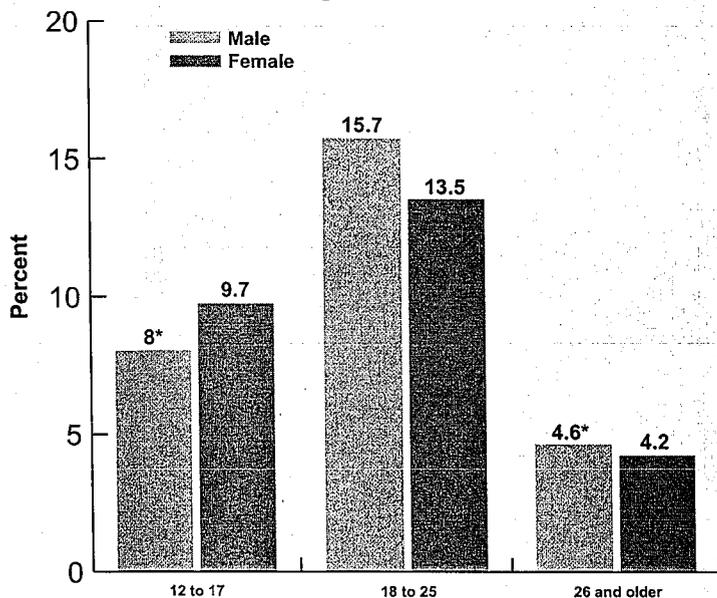
The high rates of comorbid illnesses in older populations, age-related changes in drug metabolism, and the potential for drug interactions may make any of these practices more dangerous than in younger populations. Further, a large percentage of older adults also use OTC medicines and dietary supplements, which (in addition to alcohol) could compound any adverse health consequences resulting from prescription drug abuse.



Older patients are more likely to be prescribed long-term and multiple prescriptions, which could lead to improper use of medications.

Past-Year Nonmedical Use of Psychotherapeutics Among Persons 12 or Older, by Gender and Age Group

Annual averages based on 2002-2005

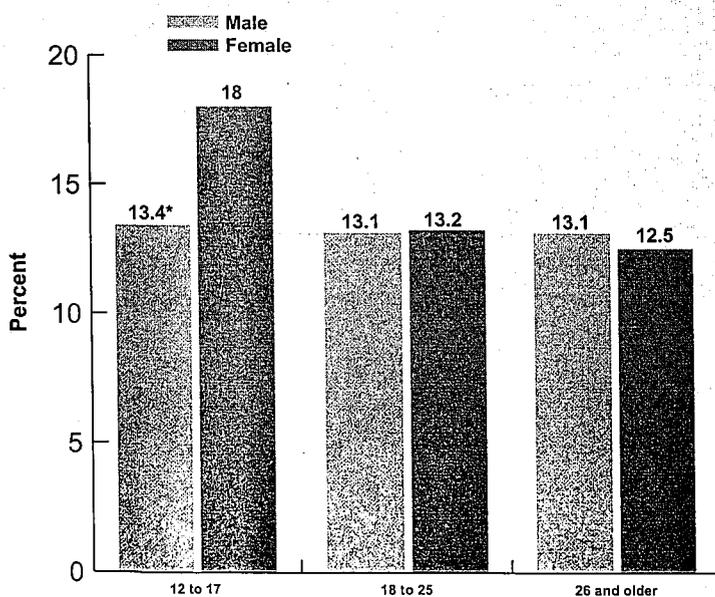


* Difference from male to female significant at $p < 0.01$.

SOURCE: Cotto, J.H, et al. Gender effects on drug use, abuse, and dependence: An analysis of results from the National Survey on Drug Use and Health. *Gen Med* 7(5):402-413, 2010.

Past-Year Dependence or Abuse of Psychotherapeutics Among Past-Year Nonmedical Users 12 or Older, by Gender and Age Group

Annual averages based on 2002-2005



* Difference from male to female significant at $p < 0.01$.

SOURCE: Cotto, J.H, et al. Gender effects on drug use, abuse, and dependence: An analysis of results from the National Survey on Drug Use and Health. *Gen Med* 7(5):402-413, 2010.

Gender differences

Overall, more males than females abuse prescription drugs in all age groups except the youngest (aged 12 to 17 years); that is, females in this age group exceed males in the nonmedical use of *all* psychotherapeutics, including pain relievers, tranquilizers, and stimulants. Among *nonmedical users* of prescription drugs, females 12 to 17 years old are also more likely to meet abuse or dependence criteria for psychotherapeutics (see figure, left).

How many people suffer adverse health consequences from abusing prescription drugs?

The Drug Abuse Warning Network (DAWN), which monitors emergency department (ED) visits in selected areas across the Nation, reported that approximately 1 million ED visits in 2009 could be attributed to prescription drug abuse. Roughly 343,000 involved prescription opioid pain relievers, a rate more than double that of 5 years prior. ED visits also more than doubled for CNS stimulants, involved in nearly 22,000 visits in 2009, as well as CNS depressants (anxiolytics, sedatives, and hypnotics), involved in 363,000 visits. Of the latter, benzodiazepines (e.g., Xanax) comprised the vast majority. Rates for a popular prescribed non-benzodiazepine sleep aid, zolpidem (Ambien), rose from roughly 13,000 in 2004 to 29,000 in 2009. More than half of ED visits for prescription drug abuse involved multiple drugs.



To ensure proper medical care, patients should discuss any and all drug use—including prescription and over-the-counter medications—with their doctors.

Preventing and recognizing prescription drug abuse

The risks for addiction to prescription drugs increase when they are used in ways other than as prescribed (e.g., at higher doses, by different routes of administration, or combined with alcohol or other drugs). Physicians, their patients, and pharmacists all can play a role in identifying and preventing prescription drug abuse.

Physicians. More than 80 percent of Americans had contact with a healthcare professional in the past year, placing doctors in a unique position, not only to prescribe medications, but also to identify abuse (or nonmedical use) of prescription drugs and prevent the escalation to addiction. By asking about *all* drugs, physicians can help their patients recognize that a problem exists, set recovery goals, and seek appropriate treatment. Screening for prescription drug abuse can be incorporated into routine medical

visits. Doctors should also take note of rapid increases in the amount of medication needed or frequent, unscheduled refill requests. Doctors should be alert to the fact that those addicted to prescription drugs may engage in “doctor shopping”—moving from provider to provider—in an effort to obtain multiple prescriptions for the drug(s) they abuse.

Preventing or stopping prescription drug abuse is an important part of patient care. However, healthcare providers should not avoid prescribing stimulants, CNS depressants, or opioid pain relievers if needed. (See text box on “Chronic Pain Treatment and Addiction” on page 13.)

Patients. For their part, patients can take steps to ensure that they use prescription medications appropriately: always follow the prescribed directions, be aware of potential interactions with other drugs, never stop or change a dosing regimen without first discussing it with a healthcare provider, and never use another person’s prescription. In addition to describing their medical problem, patients should always inform their healthcare professionals about all the prescriptions, OTC medicines, and dietary and herbal supplements they are taking, before they obtain any other medications. Additionally, unused or expired medications should be properly



Prescription Drug Monitoring Programs allow physicians and pharmacists to track prescriptions and help identify patients who are “doctor shopping.”

discarded per U.S. Food and Drug Administration (FDA) guidelines or at U.S. Drug Enforcement Administration collection sites.

Pharmacists. Pharmacists dispense medications and can help patients understand instructions for taking them. By being watchful for prescription falsifications or alterations, pharmacists can serve as the first line of defense in recognizing prescription drug abuse. Some pharmacies have developed hotlines to alert other pharmacies in the region when a fraudulent prescription is detected. Moreover, prescription drug monitoring programs (PDMPs), which require physicians and pharmacists to log each filled prescription into a State database, can assist medical professionals in identifying patients who are getting prescriptions from multiple sources. As of May 2011, 48 States and 1 territory have enacted legislation authorizing PDMPs, 34 of which are operational.

Treating prescription drug addiction

Years of research have shown that addiction to any drug (illicit or prescribed) is a brain disease that can be treated effectively. Treatment must take into account the type of drug used and the needs of the individual. Successful treatment may need to incorporate several components, including detoxification, counseling, and sometimes the use of addiction medications. Multiple courses of treatment may be needed for the patient to make a full recovery.



Although a behavioral or pharmacological approach alone may be sufficient for treating some patients, research shows that a combined approach may be best.

The two main categories of drug addiction treatment are behavioral and pharmacological. Behavioral treatments help patients stop drug use by teaching them strategies to function without drugs, deal with cravings, avoid drugs and situations that could lead to drug use, and handle a relapse should it occur. When delivered effectively, behavioral treatments, such as individual counseling, group or family counseling, contingency management, and cognitive-behavioral therapies, also can help patients improve their personal relationships and their ability to function at work and in the community.

Some addictions, such as opioid addiction, can be treated with medications. These pharmacological treatments counter the effects of the drug on the brain and behavior, and

can be used to relieve withdrawal symptoms, help overcome drug cravings, or treat an overdose. Although a behavioral or pharmacological approach alone may be sufficient for treating some patients, research shows that a combined approach may be best.

Treating addiction to prescription opioids

Several options are available for effectively treating prescription opioid addiction. These options are drawn from research on the treatment of heroin addiction and include medications (e.g., naltrexone, methadone, and buprenorphine) as well as behavioral counseling approaches.

Naltrexone is an *antagonist* medication that prevents opioids from activating their receptors. It is used to treat overdose and addiction, although its use for addiction has been limited due to



poor adherence and tolerability by patients. Recently, an injectable, long-acting form of naltrexone (Vivitrol), originally approved for treating alcoholism, has also received FDA approval to treat opioid addiction (i.e., heroin or other opioids). Because its effects last for weeks, Vivitrol is ideal for patients who do not have ready access to healthcare or who struggle with taking their medications regularly. Methadone is a synthetic opioid *agonist* that eliminates withdrawal symptoms and relieves drug cravings by acting on the same brain targets as other opioids like heroin, morphine, and opioid pain medications. It has been used successfully for more than 40 years to treat heroin addiction, but must be dispensed through opioid treatment programs. Buprenorphine is a partial opioid agonist (i.e., it has agonist and antagonist properties), which can be prescribed by certified physicians in an office setting. Like methadone, it

can reduce cravings and is well tolerated by patients. NIDA is supporting research needed to determine the effectiveness of these medications in treating addiction to opioid pain relievers.

Treating addiction to CNS depressants

Patients addicted to barbiturates and benzodiazepines should not attempt to stop taking them on their own. Withdrawal symptoms from these drugs can be problematic, and—in the case of certain CNS depressants—potentially life-threatening. Research on treating barbiturate and benzodiazepine addiction is sparse; however, addicted patients should undergo medically supervised detoxification because the dosage they take should be gradually tapered. Inpatient or outpatient counseling can help individuals through this process. Cognitive-behavioral therapy, which focuses on modifying the patient's thinking,

expectations, and behaviors while increasing skills for coping with various life stressors, also has been used successfully to help individuals adapt to discontinuing benzodiazepines.

Often barbiturate and benzodiazepine abuse occurs in conjunction with the abuse of other drugs, such as alcohol or cocaine. In such cases of polydrug abuse, the treatment approach should address the multiple addictions.

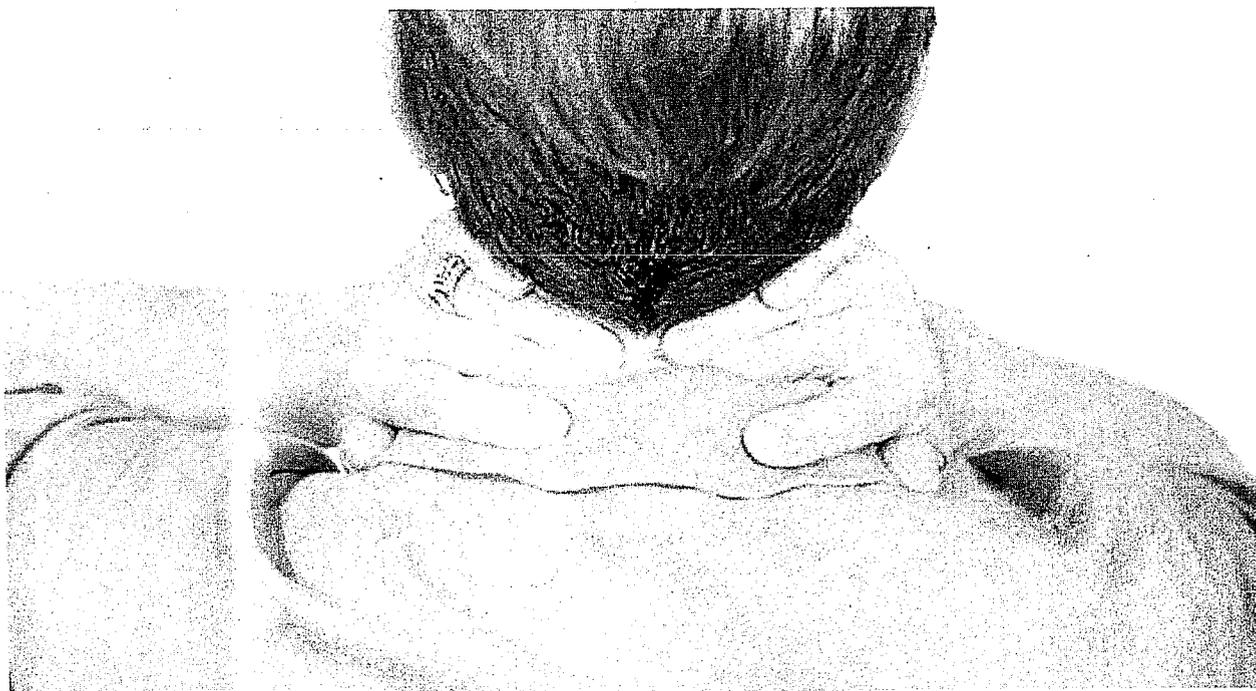
Treating addiction to prescription stimulants

Treatment of addiction to prescription stimulants, such as Adderall and Concerta, is based on behavioral therapies used in treating cocaine and methamphetamine addiction. At this time, there are no medications that are FDA-approved for treating stimulant addiction. Thus, NIDA is supporting research in this area.

Depending on the patient's situation, the first steps in treating prescription stimulant addiction may be to taper the drug dosage and attempt to ease withdrawal symptoms. The detoxification process could then be followed by behavioral therapy. Contingency management, for example, uses a system that enables patients to earn vouchers for drug-free urine tests. (These vouchers can be exchanged for items that promote healthy living.) Cognitive-behavioral therapy also may be an effective treatment for addressing stimulant addiction. Finally, recovery support groups may be helpful in conjunction with behavioral therapy.

Chronic Pain Treatment and Addiction

Healthcare providers have long wrestled with how best to treat patients who suffer from chronic pain, roughly 116 million in this country. Their dilemma stems from the potential risks involved with long-term treatment, such as the development of drug tolerance (and the need for escalating doses), hyperalgesia (increased pain sensitivity), and addiction. Patients themselves may even be reluctant to take an opioid medication prescribed to them for fear



of becoming addicted. Estimates of addiction among chronic pain patients vary widely—from about 3 percent to 40 percent. This variability is the result of differences in treatment duration, insufficient research on long-term outcomes, and disparate study populations and measures used to assess abuse or addiction.

To mitigate addiction risk, physicians should screen patients for potential risk factors, including personal or family history of drug abuse or mental illness. Monitoring patients for signs of abuse is also crucial, and yet some indicators can signify multiple conditions, making accurate assessment challenging. Early or frequent requests for prescription pain medication refills, for example, could represent illness progression, the development of drug tolerance, or the emergence of a drug problem.

The development of effective, nonaddicting pain medications is a public health priority. A growing elderly population and an increasing number of injured military only add to the urgency of this issue. Researchers are exploring alternative medications that can alleviate pain but have less abuse potential. More research is needed to better understand effective chronic pain management, including identifying factors that predispose some patients to addiction and developing measures to prevent abuse.

Glossary

Addiction: A chronic, relapsing disease characterized by compulsive drug seeking and use, despite serious adverse consequences, and by long-lasting changes in the brain.

Agonist: A chemical entity that binds to a receptor and activates it, mimicking the action of the natural (or abused) substance that binds there.

Antagonist: A chemical entity that binds to a receptor and blocks its activation. Antagonists prevent the natural (or abused) substance from activating its receptor.

Barbiturate: A type of CNS depressant prescribed to promote sleep (usually in surgical procedures) or as an anticonvulsant.

Benzodiazepine: A type of CNS depressant prescribed to relieve anxiety and sleep problems. Valium and Xanax are among the most widely prescribed medications.

Buprenorphine: A mixed opiate agonist/antagonist medication approved by the FDA in October 2002 for the treatment of opioid addiction (e.g., heroin).

Central Nervous System: The brain and spinal cord.

CNS Depressants: A class of drugs that slow CNS function (also called sedatives and tranquilizers), some of which are used to treat anxiety and sleep disorders; includes barbiturates and benzodiazepines.

Comorbidity: The occurrence of two disorders or illnesses in the same person, also referred to as co-occurring conditions or dual diagnosis. Patients with comorbid illnesses may experience a more severe illness course and require treatment for each or all conditions.

Detoxification: A process in which the body rids itself of a drug (or its metabolites). During this period, withdrawal symptoms can emerge that may require medical treatment. This is often the first step in drug abuse treatment.

Dopamine: A brain chemical, classified as a neurotransmitter, found in regions that regulate movement, emotion, motivation, and pleasure.

Methadone: A long-acting synthetic opioid medication that is effective in treating opioid addiction and pain.

Narcolepsy: A disorder characterized by uncontrollable episodes of deep sleep.

Norepinephrine: A neurotransmitter present in the brain and the peripheral (sympathetic) nervous system; and a hormone released by the adrenal glands. Norepinephrine is involved in attention, responses to stress, and it regulates smooth muscle contraction, heart rate, and blood pressure.

Opioid: A compound or drug that binds to receptors in the brain involved in the control of pain and other functions (e.g., morphine, heroin, hydrocodone, oxycodone).

Physical Dependence: An adaptive physiological state that occurs with regular drug use and results in a withdrawal syndrome when drug use is stopped; often occurs with tolerance. Physical dependence can happen with chronic—even appropriate—use of many medications, and by itself does not constitute addiction.

Polydrug Abuse: The abuse of two or more drugs at the same time, such as CNS depressants and alcohol.

Prescription Drug Abuse: The use of a medication without a prescription; in a way other than as prescribed; or for the experience or feeling elicited. This term is used interchangeably with “nonmedical” use, a term employed by many of the national surveys.

Psychotherapeutics: Drugs that have an effect on the function of the brain and that often are used to treat psychiatric/neurologic disorders; includes opioids, CNS depressants, and stimulants.

Respiratory Depression: Slowing of respiration (breathing) that results in the reduced availability of oxygen to vital organs.

Sedatives: Drugs that suppress anxiety and promote sleep; the NSDUH classification includes benzodiazepines, barbiturates, and other types of CNS depressants.

Stimulants: A class of drugs that enhances the activity of monoamines (such as dopamine) in the brain, increasing arousal, heart rate, blood pressure, and respiration, and decreasing appetite; includes some medications used to treat attention-deficit hyperactivity disorder (e.g., methylphenidate and amphetamines), as well as cocaine and methamphetamine.

Tolerance: A condition in which higher doses of a drug are required to produce the same effect achieved during initial use; often associated with physical dependence.

Tranquilizers: Drugs prescribed to promote sleep or reduce anxiety; the NSDUH classification includes benzodiazepines, barbiturates, and other types of CNS depressants.

Withdrawal: Symptoms that occur after chronic use of a drug is reduced abruptly or stopped.

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Where Can I Get More Scientific Information on Prescription Drug Abuse?

To learn more about prescription drugs and other drugs of abuse, or to order materials on these topics free of charge in English or Spanish, visit the NIDA Web site at www.drugabuse.gov or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).



What's New on the NIDA Web Site

- Information on drugs of abuse
- Publications and communications (including *NIDA Notes* and *Addiction Science & Clinical Practice journal*)
- Calendar of events
- Links to NIDA organizational units
- Funding information (including program announcements and deadlines)
- International activities
- Links to related Web sites (access to Web sites of many other organizations in the field)

NIDA Web Sites

drugabuse.gov
backtoschool.drugabuse.gov
clubdrugs.gov
teens.drugabuse.gov

For Physician Information

NIDAMED

www.drugabuse.gov/nidamed

Other Web Sites

Information on prescription drug abuse is also available through the following Web site:

- Substance Abuse and Mental Health Services Administration Health Information Network:
www.samhsa.gov/shin

U.S. Department of Health and Human Services

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Opioid Pharmacotherapy for Chronic Noncancer Pain: The American Experience

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Chronic noncancer pain is a significant and growing public health challenge in the United States. Lacking effective alternative interventions for effective chronic noncancer pain management, many physicians have turned to opioid pharmacotherapy. Increased opioid prescribing brings not only gains in therapeutic benefit but also a higher incidence of adverse drug events including increased medication misuse and opioid related mortality. Currently the United States must confront the dual problems of widespread undertreated chronic noncancer pain and a prescription opioid abuse crisis. Withholding pain relieving drugs from patients in need is unjustifiable, yet drug diversion, abuse and adverse drug events have become major social as well as medical problems. At the heart of this crisis is the lack of definitive evidence about the risk to benefit ratio of opioid pharmacotherapy for chronic noncancer pain both on an individual case and on a population basis. This article describes the extent and severity of the American chronic noncancer pain problem and the history of opioid pharmacotherapy for chronic noncancer pain in the United States. It then discusses the concept of evidence based practice and reviews current evidence supporting opioid pharmacotherapy for chronic noncancer pain as well as adverse drug events related to opioid pharmacotherapy including misuse and abuse. Finally, it considers the conflict of providing pain relief versus protecting society and reviews steps that governmental agencies, industry and others are taking to contain and ultimately resolve the problems of excessive prescribing and conflicting priorities. (Korean J Pain 2013; 26: 3-13)

Key Words:

chronic pain, evidence-based practice, noncancer pain, opioid pharmacotherapy.

INTRODUCTION

Chronic noncancer pain is a significant and growing public health challenge in the United States. About one third of Americans suffer from chronic noncancer pain [1]. The pain is moderate to severe for about 25% of the population, and it is disabling for approximately 10% [2]. Society

incurs substantial costs for chronic pain, not only in medical expenditures but also in disability compensation, lost work productivity, reduced family incomes and degraded quality of life. Lacking alternative interventions for effective chronic noncancer pain management, many physicians have turned to opioid pharmacotherapy, traditionally the mainstay of palliative care for patients with advanced

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cancer. The opioids prescribed in the United States, both immediate and extended release, are the μ agonists codeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, oxycodone, and oxycodone. Opioid prescription for acute pain, recurring pain and chronic pain has increased substantially over the last quarter century.

Opioids are among the most prescribed classes of medication in America. The United States, which has 5% of the world's population, now consumes 56% of the world's opioid medications, [3] while in many developing countries patients suffering with cancer related pain must do without them because of restrictive policies. Increased opioid prescribing brings not only gains in therapeutic benefit but also a higher incidence of adverse drug events including increased medication misuse and opioid related mortality. Moreover, unused prescribed opioids have become increasingly available in American homes and communities, providing unprecedented opportunity for diversion of prescription medications. Currently the United States must confront the dual problems of widespread undertreated chronic noncancer pain and the prescription opioid abuse crisis. Withholding pain relieving drugs from patients in need is unjustifiable, yet drug diversion, abuse and adverse drug events have become a major social as well as medical issues. At the heart of this crisis is the lack of definitive evidence about the risk to benefit ratio of opioid pharmacotherapy for chronic noncancer pain both on an individual case and on a population basis.

The purposes of this paper are to describe: 1) The extent and severity of the American chronic noncancer pain problem; 2) The history of opioid pharmacotherapy for chronic noncancer pain in the United States; 3) The concept of evidence based practice and current evidence supporting opioid pharmacotherapy for chronic noncancer pain; 4) Adverse drug events related to opioid pharmacotherapy including misuse and abuse; 5) The conflict of providing pain relief versus protecting society; and 6) Steps that governmental agencies, industry and others are taking to contain and ultimately resolve the problems of excessive prescribing and conflicting priorities.

CHRONIC PAIN IN THE UNITED STATES

Like other developed nations, the United States has a major problem with chronic pain. Despite major advances

at the scientific level in defining the nature and mechanisms of pain and the development of interventions for relieving pain, the chronic pain problem continues to grow [1]. Several contributing factors exist. In developed nations, older populations increase because more people live longer. Longer lifespans mean that more people will develop diseases associated with chronic pain. In addition, more people survive catastrophic traumatic injuries that are likely to leave them with chronic pain. As the risk for chronic pain increases, the prevalence of chronic pain conditions continues to grow. Moreover, obesity is becoming a problem in developed countries and particularly in the United States. Obesity is a pro-inflammatory condition that increases the risk of chronic pain [4,5]. The estimated prevalence of obesity in Americans aged 60 years and older was 37% for 2010 [6]. Related to this is the lack of exercise and generally poor level of physical fitness in the United States, which are also associated with chronic pain.

The population of the United States is currently 313 million people. Of these, over 100 million suffer some form of chronic pain [1]. Examination of the nation's priority health conditions reveals that 25.8 million Americans have diabetes, 16.3 million have coronary heart disease and 11.9 million have cancer. Clearly, chronic pain represents an enormous problem that is more prevalent than diabetes, heart disease and cancer combined. Physicians in most specialties regularly encounter chronic pain problems.

The cost of chronic noncancer pain to American society is at least \$560-\$635 billion annually, and this includes the loss of work productivity [7]. This means that society loses about \$2,000 per American citizen per year. In 2008 federal and state governments paid about \$99 billion for pain related medical expenditures. The costs of chronic pain exceed those of diabetes, heart disease and cancer combined. Clearly, chronic pain is a major burden to American society.

The impact of undermanaged chronic noncancer pain on the patient is complex and serious [1]. It compromises the individual's normal activities of daily living, interferes with sleep, reduces the productivity of the patient in the workplace, and degrades quality of life. Studies show that the risk of suicide among patients with chronic pain is approximately twice that for control groups. Moreover, chronic pain affects the families, friends and coworkers of individual patients. Family roles change when pain disables one of the family members, and loss of productivity

can impose a financial burden on the family.

The growing epidemic of chronic pain in America has set the stage for the opioid pharmacotherapy dilemma. Chronic pain, by definition, is neither self-limiting nor curable, and patients require skilled, effective pain management. By and large, chronic noncancer pain patients in the United States and elsewhere are under managed. The literature suggests that psychological interventions and physical therapies are effective, and interdisciplinary approaches appear to be the most cost-effective and definitive solutions to disabling chronic pain [8]. Nonetheless, in the United States providers and payers resist these approaches, forcing patients to undergo mono-disciplinary medical treatment in most cases. Apart from certified pain specialists, most American physicians are poorly prepared to diagnose, monitor and manage chronic pain conditions. Simple, straightforward, monotherapeutic pharmacological interventions, such as opioid pharmacotherapy, appeal in many settings.

THE EMERGENCE OF OPIOID PHARMACOTHERAPY FOR CHRONIC NONCANCER PAIN

Prior to about 1990, the use of opioid pharmacotherapy for chronic noncancer pain was rare, although it was the mainstay of palliative care for patients with advanced cancer. Portenoy and Foley [9] conducted a landmark study that ultimately shifted the indication for opioid pharmacotherapy beyond palliative care in the cancer setting to chronic noncancer pain. They studied 38 patients with chronic noncancer pain, and most received less than 20 mg/day (morphine equivalent). Of these, 19 had four years or more of treatment, and six had used opioids for more than seven years. Although 14 of these patients reported inadequate pain relief, 24 described partial but acceptable or fully adequate pain relief with opioid pharmacotherapy. Management problems occurred in only two cases, and these patients both had histories of prior drug abuse. The patients did not report improvement in employment or social function. A number of positive case studies subsequently appeared in the literature, and these showed that opioid medications can reduce disabling chronic pain to manageable levels for some patients.

The pharmaceutical industry quickly realized that opioid

pharmacotherapy for chronic noncancer pain represented an enormous marketing opportunity. Multiple companies began to develop extended release opioid products and to market them aggressively. Industry claimed that such products could, in principle, produce more consistent pain relief, generate less euphoria with administration, reduce the rate of tolerance development and offer better side effect profiles. Industry marketing, supported by their development of patient advocacy programs and physician education efforts added substantially to the momentum of opioid prescribing for chronic noncancer pain.

In 1997, the American Pain Society and the American Academy of Pain Medicine published a joint consensus statement supporting opioid pharmacotherapy for chronic noncancer pain [10]. Shortly thereafter, the Federation of State Medical Boards of the United States liberalized the medical guidelines for opioid prescribing for chronic noncancer pain [11]. Advocates of opioid pharmacotherapy were able to ride on various campaigns to make pain control a priority in medicine, although most such efforts were independent of opioid advocacy. At that time, the short-term risks and long-term adverse drug events associated with opioid pharmacotherapy received little attention.

EVIDENCE BASED PRACTICE

American medicine aspires to evidence based practice. The definition of this, according to its chief pioneering advocate, Dr. David Sackett, is "... the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient. It means integrating individual clinical expertise with the best available external clinical evidence from systematic research" [12]. Best evidence comes from systematic review of published research that has sound methodology, as the Cochrane Collaboration advocates. The Cochrane Collaboration is an international network of more than 28,000 participants in more than 100 nations that prepares systematic literature reviews of published evidence. Cochrane standards are the highest for evidence based health care. Their meta-analytic reviews synthesize information from multiple primary randomized controlled trials, using rigorous methodologies and strategies that minimize bias and random error.

EFFICACY AND EFFECTIVENESS

Evidence based practice means that American physicians should link opioid prescribing for chronic noncancer pain patients to an extensive body of literature comprising multiple randomized controlled trials collectively analyzed, following Cochrane standards, with meta-analysis. Every product offered should have sound published evidence for both efficacy and effectiveness. Efficacy exists when an intervention proves successful when implemented properly under controlled conditions. Randomized controlled trials can demonstrate efficacy for various opioid products using well-defined protocols and highly selected patients recruited with stringent exclusion criteria. Efficacy is short term. It simply shows that an intervention can work for a given clinical condition. In contrast, effectiveness means that an intervention is successful in actual practice with typical patient populations. Trials demonstrating efficacy need mixed patient populations, take place under conditions of everyday practice, and are long term. The United States Food and Drug Administration requires evidence of efficacy to approve putting a new product on the market. Consequently, all existing opioid pharmacotherapy products have demonstrated efficacy, but there is no requirement for demonstrating effectiveness. Because opioid pharmacotherapy is a long-range intervention, typically prescribed for patients with multiple comorbidities, demonstrated effectiveness is crucial for a meaningful evidence base.

The literature should clearly define the nature and extent of therapeutic benefit, the adverse drug events and the risks associated with each of them, and the risk to benefit ratio. Ideally, the literature should guide the practicing physician in determining which patients are likely to benefit from opioid pharmacotherapy, which patients are likely to derive no benefit, which patients are at risk for harm, and which patients are at risk for misuse or diversion of opioid medication.

THE CLINICAL TRIALS EVIDENCE BASE FOR OPIOID PHARMACOTHERAPY

Portenoy et al. [13] undertook an open-label, multi-site, uncontrolled prospective longitudinal investigation of opioid pharmacotherapy for chronic noncancer pain. Patients used controlled-release oxycodone for up to 36

months to control chronic pain, returning at three-month intervals. They completed the Brief Pain Inventory at each return visit. Of the 233 patients enrolled, 39 completed the 36-month study. Of the 127 patients that discontinued therapy, 38 cited an adverse event, 17 reported ineffective pain relief, 24 were lost to follow up, and 48 left the study for other reasons. Of those who left the study, most did so during the first year. For those who remained, scores for worst pain decreased from 7.7 (\pm 1.6) at baseline to 5.4 (\pm 2.5) at the end of month three. The beneficial pain relieving effects of the drug proved largely stable over study duration. None of the patients met the DSM-IV criteria for drug dependence or abuse. This open-label, uncontrolled study lacks a comparison group and has other limitations, but it demonstrates that at least a subgroup of patients with chronic noncancer pain can sustain long-range benefits from opioid pharmacotherapy without complications.

To evaluate the state of knowledge about opioid pharmacotherapy for chronic noncancer pain up to 2008, the Evidence-Based Practice Center and Health Technologies Assessment Group (ECRI Institute) undertook a systematic review of all studies that looked at patients who used opioids for chronic noncancer pain for six or more months. This included transdermal and intrathecal in addition to oral routes of administration. Overall, patients reported a reduction in pain intensity of at least 30% on an 11-point numerical rating scale. It is not clear what this means, as no standards exist for a meaningful change in chronic pain [14]. Importantly, many patients ultimately discontinued opioid pharmacotherapy due to insufficient pain relief or adverse drug events. The panel noted the paucity of studies in the evidence base, the narrow outcome assessments, and the short-term nature of the studies that inform about efficacy but not effectiveness.

Papaleontiou et al. [15] published a systematic review of the evidence on the efficacy, safety and abuse/misuse potential of opioids for chronic noncancer pain in older adults. Forty-three randomized studies provided efficacy data. Eighteen of the studies compared opioid pharmacotherapy to placebo. Meta-analyses revealed significant pain intensity reduction and parallel reductions in physical disability. One patient in four discontinued opioid pharmacotherapy due to an adverse drug event, and 8% withdrew from the study due to insufficient drug efficacy. This report did not look at effectiveness. The authors concluded that

short-term opioid pharmacotherapy in patients aged 60–73 years who had no significant co-morbidities produced modest but favorable outcomes on both pain and physical functioning. Patients with neuropathic pain derived more benefit than patients with osteoarthritis-related pain. No significant improvements in sleep or quality of life occurred. Advancing age was associated with lower risk for abuse and misuse, but some of the studied excluded patients with substance abuse histories.

Carson et al., [16] at the Oregon Evidence-based Practice Center examined the comparative efficacy and harms of several long and short-acting opioids in adults with chronic noncancer pain. The main outcomes were pain intensity, pain relief and function. They identified 41 randomized trials that examined the effects of opioid pharmacotherapy on chronic noncancer pain. Nearly all of the trials proved to be of short duration, ranging from five days to 24 weeks, although one study had a 13 month duration. The heterogeneity in study populations constrained interpretation. It was not possible to demonstrate meaningful differences in outcomes across products or between long and short acting forms of particular drugs.

In summary, the evidence base for the effectiveness of opioid analgesic drugs for chronic noncancer pain is nearly nonexistent. Some evidence does exist for the efficacy of these medications. The literature is weak because the outcome measures are, with a few exceptions, limited mostly to pain rating scales. Restoring functional capability, improving quality of life, return to work, reduced health care utilization, improving sleep and several other outcomes are important therapeutic targets for opioid pharmacotherapy. The great deficiency in the evidence base is that only weak evidence exists to show that opioid pain medications are effective for chronic noncancer pain in some patients over months or years. Nonetheless, a large volume of anecdotal reports of successful long-term therapy from clinical practice cannot be easily dismissed. The major limiting issue is predicting who will benefit and who will be harmed by opioid pharmacotherapy over the long run.

ADVERSE DRUG EVENTS

1. Known and emerging adverse effects

Palliative care physicians have long known that opioid medications can produce opioid-induced bowel dysfunction,

nausea, vomiting, dry mouth and sedation. The first of these is usually treatable and the others tend to resolve over time as tolerance develops. Most efficacy studies have assessed these adverse drug events, although some have looked at cognitive function and drug misuse. Moore and McQuay [17] examined the incidence of common adverse drug events in over 4,000 patients undergoing opioid pharmacotherapy for chronic noncancer pain. Dry mouth affected 25% of patients, nausea 21%, and constipation 15%. As noted above, patients in randomized trials of opioid pharmacotherapy often discontinue participation because of adverse drug events.

Several additional adverse drug events have emerged over the last two decades that were not evident in the acute pain and palliative care settings. They include opioid-induced endocrine deficiencies with increased risks for osteoporosis and bone fracture and diabetes [18,19], cardiac complications [20], hyperalgesia [21], and immunosuppression [22]. Misuse of medications including addiction, drug diversion and abuse of medications are also adverse drug events, and they have become the fastest growing drug problem in the United States. The most alarming adverse drug event is fatal prescription drug overdose [23]. Although the literature identifies these adverse drug events, large scale, randomized controlled studies of opioid pharmacotherapy have yet to include and quantify these events comprehensively. Comprehensive systematic reviews of the emerging opioid adverse events are not currently possible. Until more definitive information emerges about who is at how much risk for which adverse drug events, the risk benefit ratio for opioid pharmacotherapy in chronic noncancer pain patients must remain undefined.

2. The prescription opioid abuse crisis

From 1997 to 2010 in the United States, sales of opioid analgesic drugs quadrupled.

Physicians prescribed 96 mg morphine equivalent per person in 1997 but 710 mg morphine equivalent in 2010 [24]. With this increased prescribing rate, the societal costs of prescription opioid abuse and misuse also grew. Birnbaum et al. [25] estimated the societal costs of prescription opioid abuse in the United States to be \$55.7 billion in 2007. Workplace costs were \$25.6 billion, health care expenditures accounted for \$25.0 billion, and criminal justice expenses totaled \$5.1 billion. Clearly, prescription

opioid misuse and abuse has imposed a significant burden on American society. Yet, the total of these expenditures is only 5–10% of the total costs associated with chronic pain in the United States.

3. Aberrant drug behaviors

Patients who have a prescribed opioid can engage in abuse in multiple ways, collectively termed aberrant drug behaviors [26]. Instead of following instructions, they can take the drug at more or less than prescribed doses, take it more or less often than instructed, take the medication for purposes other than pain relief such as sedation or to cope with interpersonal stress, chew, crush or snort medications, hoard medication, or seek prescriptions from multiple prescribers (doctor shopping). Several community practice surveys estimate the overall rates of opioid misuse and abuse in a range from 4–26% [27]. In an 18-month study of more than 25 million patients, Cepeda et al., [28,29] estimated that three of 1,000 patients exposed to opioids exhibit doctor shopping behavior, typically eight months after first exposure.

4. Addiction and opioid use disorder

Virtually all patients taking extended release opioid medications over long periods of time will develop drug dependence. This decreases volitional control over drug use because cessation of drug intake will cause withdrawal symptoms. This dependence is not drug addiction, but it can compel patients to seek urgent prescription refills if they have consumed their medication ahead of the scheduled refill.

Patients qualify as addicted to prescribed medication when they engage in compulsive use of a substance despite obvious harm. Addicts typically deny that a drug use problem exists, become obsessed with obtaining the medication, neglect vocational and family responsibilities, and they often use more of the medication than planned. Opioid addicts may exaggerate or lie about an acute or chronic pain condition in order to obtain a prescription. The identification of true addiction in the chronic non-cancer pain population is complex and challenging.

Fishbain et al. [30] conducted an evidence based structured review of 67 studies to determine the percentage of patients using chronic opioid pharmacotherapy that developed abuse/addiction or aberrant drug related behaviors. They estimated an abuse/addiction rate of 3.27%. If pa-

tients had no previous or current history of abuse or addiction, the rate was 0.19%. The aberrant drug related behavior rate was 11.5%, but those with no previous abuse/addiction history had a rate of only 0.59%. They concluded that long-term exposure to chronic opioid pharmacotherapy would lead to abuse or addiction in a low percentage of patients, particularly if this treatment were confined to those with no history of substance abuse or addiction.

Subsequently, Boscarino et al. [31] classified a sample of 705 chronic noncancer pain patients using opioid pharmacotherapy according the proposed Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) criteria for Opioid Use Disorder. Opioid use disorder is a maladaptive pattern of opioid use leading to clinically significant impairment of distress. They reported that 21.7% qualified as moderate and 13.2% as severe on Opioid Use Disorder. Although not synonymous with classical concepts of addiction and abuse, Opioid Use Disorder gauges patients on dependence and nontherapeutic compulsive use.

5. Diversion

Increased opioid prescribing rates have also led to increased diversion of opioid medications. Prescription drug diversion is the unlawful channeling of regulated pharmaceutical drugs from legal sources to the community or an illegal market place. The 2010 National Survey on Drug Use and Health [24] estimated that 22.6 million or 8.9% of Americans older than 12 years were current illicit drug users. New nonmedical users of prescription pain relievers numbered 2.0 million, and 55.0% of these reported that they had received prescription pain killer for free from a friend or relative. Another 11.4% bought the drug from a friend or relative, while 4.8% took them from a friend or relative without permission. Other forms of drug diversion include strategic doctor shopping on the part of patients with subsequent selling or release of the drugs in the community, theft on the part of pharmacy employees, and the purchase of prescribed medications for indigent patients [32]. Financially impoverished patients may sell all or part of their opioid medications to meet the costs of basic needs such as food, housing or even other medications.

6. Accidental opioid related overdose deaths

The most salient prescribed opioid misuse problem in the United States is accidental drug poisoning death. Warner et al. [23] examined death rates in the United States

from 1980–2008. They reported that in 2008, the number of drug poisoning deaths exceeded for the first time the number of deaths by motor vehicle accident in the United States. Opioid analgesics were involved in more accidental poisoning deaths than other drugs, including cocaine. The accidental drug poisoning death rate has nearly tripled since 1980. In 2008, opioid medications were involved in nearly 15,000 deaths. This problem is apparently related to medication diversion. Hall et al. [33] studied 295 patients who had died from unintentional drug overdose. Of these decedents, 275 took opioids (93.2%) but only 122 (44.4%) had prescriptions for opioid medication. From 2004–2008, the rate of emergency medicine visits for the nonmedical use of opioid medications doubled from 49 per 100,000 to 101 per 100,000. Patients at risk for accidental opioid-related overdose death may be those using methadone, those who have co-morbid substance abuse disorders, those using sedatives, anti-depressants or alcohol, and those with sleep-disordered breathing [34,35].

CONTAINING AND RESOLVING THE PROBLEM

1. The problem

A significant ethical and legal conflict exists in the United States. Chronic noncancer pain disables people, degrades quality of life, increases risk of suicide, and imposes a large economic burden on society. Opioid medications offer a time- and cost-efficient way to manage many chronic noncancer pain patients who do not respond to non-opioid drugs (e.g., nonsteroidal anti-inflammatory medications, acetaminophen, and other adjuvant analgesics), who do not have access to comprehensive interdisciplinary pain care (involving medical, rehabilitative and behavioral interventions or who are otherwise under-managed. Despite the lack of an adequate evidence base for opioid pharmacotherapy in chronic noncancer pain patients, opioid prescribing in the United States has steadily escalated over the last quarter century. With escalated opioid prescribing has come a set of problems related to partly unanticipated adverse drug events. These include widespread drug misuse by patients and others share these drugs, medication diversion, Opioid Use Disorder and alarming increases in the rate of opioid-related overdose deaths. Prescribed opioids are rapidly becoming the primary misused medications in the United States and the

primary cause of accidental death. Protecting the public against illicit use of opioid medications has become a high priority. This area of clinical practice remains highly controversial, with patient advocates on both sides of the issue voicing strong opinions.

The root cause of the problem is that prescribing patterns have outpaced the availability of evidence to support such prescribing, and without such evidence adequate education of prescribers on proper assessment, patient selection and management practices is impossible [27,36]. Sound evidence-based practice requires that physicians administer interventions according to knowledge gleaned from synthesized information in the literature. This knowledge should characterize both the potential benefits of a treatment and the potential harms. Most importantly, this characterization should go beyond simple efficacy to include effectiveness. It is crucial to determine the potential long-range benefits of opioid pharmacotherapy for typical patients and also the potential long-range harms. This information is simply unavailable in the literature, and there are no comprehensive federal or other funding initiatives in place to strategically generate the needed knowledge base in the foreseeable future.

2. Regulatory laws and bodies

In the United States, federal and state laws and regulations govern both the distribution and prescription of opioid medications. State regulatory agencies enforce these regulations. The federal Controlled Substances Act of 1970 is a subset of the Comprehensive Drug Abuse Prevention and Control Act of 1970. It is the major federal law controlling the prescribing of opioid medications, which are controlled substances. Under this law licensed medical practitioners can prescribe controlled substances for legitimate medical purposes according to standard medical practice. There are five classifications for controlled substances. Schedule I substances have no medical benefit coupled with extreme potential for abuse, and physicians cannot prescribe them. Heroin falls under this classification. Schedule II drugs have medical benefit but also have high potential for abuse. Opioid medications for chronic noncancer pain such as morphine and oxycodone fall under this classification. Drugs scheduled as III, IV and V have medical benefit but incrementally lower potentials for abuse, although hydrocodone, the most abused opioid, is a schedule III drug currently under review for possible rescheduling to

Schedule II due to its demonstrated abuse liability.

The Drug Enforcement Agency (DEA) is a part of the United States Department of Justice. Its job is to assure an adequate supply of controlled substances for legitimate medical use and research while also assuring that the prescription, dispensing, and administration of controlled substances is solely for legitimate medical purposes. American physicians who prescribed opioid medications must obtain DEA registration. The DEA may investigate individual physicians to determine whether their prescribing patterns reflect legitimate medical practice. It can revoke a physician's controlled substances registration. This happens infrequently.

Individual states have licensing boards that license and oversee medical practitioners. In general, state medical boards regulate opioid prescribing through licensure screening and promulgating medical practice guidelines. Such boards keep abreast of emerging findings in the literature and the development of new interventions or drug formulations. The Federation of State Medical Boards helps assure continuity in policy across states. In the late 1990s it produced a policy template, "Use of Controlled Substances for the Treatment of Pain" and produced its "Model Policy for the Use of Controlled Substances" [11], and it has commissioned a guide for clinicians [37].

Currently 43 states have adopted prescription drug monitoring programs. Such programs maintain a statewide electronic database that collects specific information on drugs dispensed within a state. The program can provide feedback to authorized professionals. Some states require physicians to report every controlled substance prescription they write, while others require pharmacist reporting. A doctor shopping patient seeking to fill multiple prescriptions for opioid medication will find that the dispensing pharmacist knows from the database that the patient is doing this. The United States Department of Justice fosters these programs. State licensing boards are increasingly instructing clinicians in the use of prescription monitoring program databases and asking them to query these sites on a regular basis before prescribing. An ongoing challenge is to have these databases fully secure to protect patient privacy, yet readily accessible with current information for all practitioners in routine clinical settings.

3. Steps toward resolving the opioid prescribing dilemma

The United States Executive Branch of the federal

government under President Obama has taken action on the opioid pharmacotherapy problem through the Office of National Drug Control Policy. In 2011, it announced the Prescription Drug Abuse Prevention Plan, a set of guidelines to address the misuse of prescription opioid medications [38]. This plan encourages stakeholders to take action in four domains: 1) Education; 2) Tracking and Monitoring; 3) Proper Medication Disposal; and 4) Enforcement. The education effort aims to increase awareness of the dangers of prescription drug abuse among patients, young people, parents and providers. The tracking and monitoring effort focuses on state prescription drug monitoring programs. It seeks to improve and empower such programs by giving clinicians greater access and increasing inter-state operability and communication. The effort directed at proper medication disposal is concerned with the home storage of unused opioid medication. Patients need convenient ways to dispose of opioid medications that they do not intend to use and secure ways to store medications they are using. This requires the development of environmentally save options for medication disposal. Finally, the enforcement effort recognizes that a small minority of opioid prescribing physicians act outside of standard medical practice and often enable doctor shopping. Their actions are a threat to the patients in their care and to the communities in which they practice. The guidelines put forward a plan for more aggressive pharmaceutical crime investigation and prosecution. The goals of this five year plan include reducing nonmedical use of opioids among young people, implementing a Risk Evaluation and Mitigation Strategy, implement regulations for medication disposal, enhance the registration of controlled substances information and achieve prescription drug monitoring programs in all 50 states, and decrease the number of unintentional overdose deaths.

The Food and Drug Administration (FDA), an agency within the Department of Health and Human Services, has introduced a risk evaluation and mitigation strategy for both extended release and long-acting opioid medications [39]. The 20 companies that produce opioid medications must contribute to provider and patient education by providing educational grants to continuing education trainers. This is part of the agency's efforts to address the epidemic of prescription drug abuse and accidental overdose. The goals of this strategy are to assure that prescribers know how to prescribe safely and that patients understand the

risks of opioid pharmacotherapy. There are three components: 1) Training for prescribers according to an FDA blueprint; 2) A consumer friendly updated medication guide and patient counseling document; and 3) Assessment and auditing of company compliance with training requirements.

The pharmaceutical industry is also making efforts to reduce the opioid abuse problem. Most opioid abusers chew, crush or snort the drugs to maximize psychological effects. Pharmaceutical manufacturers are developing and marketing products that are tamper resistant [40,41]. One approach offers extended release morphine with sequestered naltrexone. Chewing or crushing of the tablet will cause release of the opioid antagonist naltrexone. Another product offers controlled release oxycodone in a crush resistant formulation and another in a high viscosity hard gelatin capsule; it is impossible to extract its contents with a needle. The impact of this approach to deterring prescription opioid abuse is still unknown but there is evidence of reduced street value of and opioid poisonings from the reformulated crush resistant long-acting oxycodone that has replaced the older formulation.

CONCLUSIONS

The United States has let opioid prescribing for chronic noncancer pain outpace both the growth of evidence about the long-range benefits and harms of opioid pharmacotherapy for chronic noncancer pain and also necessary clinician education and systems strategies that can reduce opioid-related morbidity and mortality. To date, the long-range benefits of opioid pharmacotherapy, its effectiveness, remains poorly defined while evidence on the negative effects of opioid pharmacotherapy accumulates at a greater rate. A number of unanticipated adverse drug effects have emerged. The long-range incidences and harms of these are also unknown. Initial concerns about addiction have largely given way to concerns about drug diversion and misuse, and these concerns include fatal accidental drug overdose. Moreover, the presence of opioid medications in large supply in the community has led to significant social problems.

Although the White House, other federal agencies and state medical boards and others have developed well-reasoned strategies for coping with the immediate problems of medication misuse, diversion and accidental opioid-related poisoning deaths, there is no national strategic plan

for accruing a knowledge base on the effectiveness of opioid pharmacotherapy for chronic noncancer pain patients. Unless and until an adequate body of evidence on medication effectiveness becomes available, and all prescribers are knowledgeable about safe practices, the steps taken by federal and state governments and by industry will at best contain the problem, but they will not resolve it. The solution lies in reconciling practice patterns with a meaningful best practice evidence base.

The American crisis of opioid pharmacotherapy for chronic pain was at least partly foreseeable and preventable. Evidence suggests that similar problems are emerging in parts of Europe and Australia. Developed countries are at the greatest risk for repeating the American experience. Knowledge of the processes that led to the present crisis in the United States may help other nations avoid similar problems as they seek to improve their management of chronic noncancer pain.

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Abusive Prescribing of Controlled Substances — A Pharmacy View

Mitch Betses, R.Ph., and Troyen Brennan, M.D., M.P.H

Public health advocates are increasingly focused on pillness and deaths caused by inappropriate use of controlled substances — in particular, opioid analgesics. Opioid prescriptions have increased

dramatically, by more than 300% between 1999 and 2010.¹ This increase has led to substantial iatrogenic disease. Most strikingly, the number of deaths due to overdose in the United States increased from 4000 in 1999 to 16,600 in 2010.² Indeed, overdose is now the second-leading cause of accidental death in this country, where more than 2.4 million people were considered opioid abusers in 2010.³

The causes of increases in prescriptions and the prevalence of abuse are manifold. In the mid-1990s, advocates for treatment of chronic pain began arguing that pain was largely undertreated and appropriately exhorted clinicians

to be more liberal in their treatment. In addition, a number of new formulations of opioid agents became available, with purported advantages in analgesia.

But perhaps just as important, inappropriate prescribing has grown. The worst form of such prescribing occurs in so-called pill mills, wherein fully licensed physicians with valid Drug Enforcement Administration (DEA) numbers write prescriptions that provide large quantities of powerful analgesics to individual patients. Such bogus pain clinics cater to younger patients, operate on a cash basis, and draw clients from a broad geographic area. States and the DEA have attempt-

ed to curb pill-mill activities — the best example being Florida's closure of 254 "pain clinics" — but the efficacy of such regulation is unclear.⁴

Pharmacies have a role to play in the oversight of prescriptions for controlled substances, and opioid analgesics in particular. Under the Controlled Substances Act, pharmacists must evaluate patients to ensure the appropriateness of any controlled-substance prescription. In addition, state boards of pharmacy regulate the distribution of opioid analgesics and other controlled substances through the discretion of pharmacists. Yet in the majority of cases of potential abuse, pharmacists face a patient who has a legal prescription from a licensed physician, and they have access to very little other background information. That makes it difficult for individual pharma-

Prescribing Habits of Outlier Prescribers.

Specialty or Type of Clinician	Average Monthly Doses of High-Risk Drugs Prescribed		No. of Outlier Prescribers
	42 Outlier Prescribers	Nonoutlier Prescribers	
Internal medicine	11,314	422	12
Physical medicine	5,599	916	1
Family practice	12,903	575	8
General practice	24,502	462	2
Psychiatry	18,757	213	3
Nurse practitioner	10,715	160	2
Obstetrics and gynecology	11,096	110	3
Physician assistant	5,211	116	1
Pain medicine	8,811	3813	1
Sports medicine	7,025	387	1
Pediatrics	5,524	31	2
Anesthesiology	8,128	1749	1
Geriatric medicine	15,544	493	1
Endocrinology	6,142	116	1
Emergency medicine	7,935	203	2
Preventive medicine	44,397	662	1

cists to use their own partially informed judgment to identify prescriptions that have come from a pill-mill doctor.

Chain pharmacies, however, have the advantage of aggregated information on all prescriptions filled at the chain. At CVS, we recently instituted a program of analysis and actions to limit inappropriate prescribing. Our program was intended to identify and take action against physicians and other prescribers who exhibited extreme patterns of use of "high-risk drugs" relative to other prescribers. We aimed to minimize the potential for falsely identifying legitimate prescribers (false positives), accepting that doing so might result in a failure to identify some suspicious prescribers.

We identified high-risk prescribers by benchmarking them against others on several param-

eters. We used data from submitted prescriptions from March 2010 through January 2012 for hydrocodone, oxycodone, alprazolam, methadone, and carisoprodol. Prescribers were compared with others in the same geographic region who had the same listed specialty. The first parameters were the volume of prescriptions for high-risk drugs and the proportion of the prescriber's prescriptions that were for such drugs, as compared with the volume and proportion for others in the same specialty and region; the thresholds for suspicion were set at the 98th percentile for volume and the 95th percentile for proportion. Next, prescribers were evaluated with regard to the number of their patients who paid cash for high-risk-drug prescriptions and the percentage of their patients receiving high-risk drugs who were

18 to 35 years of age. In both cases, the thresholds for suspicion were set at the 90th percentile among clinicians in the same region and specialty. Finally, we compared the prescriptions for noncontrolled substances with the prescriptions for controlled substances within the prescriber's practice on the same parameters. To minimize the possibility that we would suspend dispensing privileges for clinicians who were appropriately treating patients, we attempted to interview physicians whom we'd identified as outliers to ascertain the nature of their practice and their use of controlled substances.

We initially identified 42 outliers (see table) from our database of nearly 1 million prescribers; 17 of the 42 failed to respond to our three letters requesting an interview, despite our indication in the second and third letters that we would stop filling the clinician's controlled-substance prescriptions if he or she would not speak with us. Eight prescribers sent a written response, and one response was sufficiently detailed to convince us that the prescribing was appropriate. The other seven responses were inadequate, and the prescribers refused to engage in a telephone discussion. Two prescribers retained an attorney, and future conversation occurred through legal channels. We considered these 26 clinicians nonresponsive.

The remaining 15 were contacted by phone, and 5 gave us legitimate reasons why their practice had the identified characteristics — in particular, that each was the only practitioner in a given geographic area caring for patients with chronic pain. The remaining 10 either maintained that their approach was legitimate

but that they didn't have to explain why or averred that they planned to curb their prescribing of narcotics. For all 10 of these clinicians, we decided not to fill their controlled-substance prescriptions through our pharmacy. The same approach was taken for the 26 nonresponsive clinicians. Surprisingly, now 9 months after we stopped filling controlled-substance prescriptions for these clinicians' patients, we've had contact from only 3 of them requesting reinstatement in our pharmacy chain. The table provides details on the 42 outliers' practices, as compared with those of the average prescriber in our database. There was no clear regional concentration of outliers.

Our program is certainly not a comprehensive solution, but it provides some sense of the kind of inappropriate prescribing that is going on in our health care system. We believe that some of these clinicians may be part of pill mills, doing cursory examinations in high volumes of patients, all of whom then receive opioid analgesics. People seeking to abuse these medications will travel long distances to obtain them and often deal in cash only. These patients are generally younger than the average patient with chronic disease. A comprehensive solution would involve the use of a national prescription-

drug-monitoring database that would be used by clinicians at the point of prescribing and by all pharmacies at the point of dispensing. This enhanced view of a patient's controlled-substance history and behaviors would support both prescribers and pharmacists in applying their professional judgment regarding the appropriateness of dispensing a controlled substance.

As we noted, pharmacists have an ethical duty, backed by both federal and state law, to ensure that a prescription for a controlled substance is appropriate. A young person traveling a good distance to fill a prescription and paying cash should raise some concerns for a pharmacist. If the prescription is valid, the pharmacist might have limited grounds on which to deny medication to someone who might be in pain. Yet the DEA has now identified both pharmaceutical distributors and chain pharmacies as part of the problem,⁵ encouraging our industry to develop new programs to reduce inappropriate use.

Our findings provide a lens into the problem we face as a country. Programs providing greater transparency regarding controlled-substance prescribing, such as mandatory use of e-prescribing for all controlled substances and a national, uniform program of prescription-drug monitoring, would

help pharmacists and clinicians target interventions more accurately to help patients who are abusing medications. Some state solutions, such as the Massachusetts database that allows clinicians to look up their own patients' prescriptions, also have merit. Analyses of aggregated data like ours can also target patterns of abuse by both prescribers and patients. Given the growing use of controlled substances and the resulting illness and deaths, more innovative use of transparent data is only prudent.

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Transforming Academic Health Centers for an Uncertain Future

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Academic health centers (AHCs) have long led the advancement of science and medicine by pursuing missions of clinical care, research, and education. AHCs

have been places where important fundamental and translational research is performed and medical innovations are created and tested. Given the dramatic changes

ahead in health care and deteriorating research funding, can this record of achievement continue, or do AHCs in the United States face a growing risk of extinction?

Health Policy

e Opioid Epidemic in the United States

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Over the past two decades, as the prevalence of chronic pain and health care costs have exploded, an opioid epidemic with adverse consequences has escalated. Efforts to increase opioid use and a campaign touting the alleged undertreatment of pain continue to be significant factors in the escalation. Many arguments in favor of opioids are based solely on traditions, expert opinion, practical experience and uncontrolled anecdotal observations. Over the past 20 years, the liberalization of laws governing the prescribing of opioids for the treatment of chronic non-cancer pain by the state medical boards has led to dramatic increases in opioid use. This has evolved into the present stage, with the introduction of new pain management standards by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) in 2000, an increased awareness of the right to pain relief, the support of various organizations supporting the use of opioids in large doses, and finally, aggressive marketing by the pharmaceutical industry. These positions are based on unsound science and blatant misinformation, and accompanied by the dangerous assumptions that opioids are highly effective and safe, and devoid of adverse events when prescribed by physicians.

Results of the 2010 National Survey on Drug Use and Health (NSDUH) showed that an estimated 22.6 million, or 8.9% of Americans, aged 12 or older, were current or past month illicit drug users. The survey showed that just behind the 7 million people who had used marijuana, 5.1 million had used pain relievers. It has also been shown that only one in 6 or 17.3% of users of non-therapeutic opioids indicated that they received the drugs through a prescription from one doctor.

The escalating use of therapeutic opioids shows hydrocodone topping all prescriptions with 136.7 million prescriptions in 2011, with all narcotic analgesics exceeding 238 million prescriptions. It has also been illustrated that opioid analgesics are now responsible for more deaths than the number of deaths from both suicide and motor vehicle crashes, or deaths from cocaine and heroin combined. A significant relationship exists between sales of opioid pain relievers and deaths. The majority of deaths (60%) occur in patients when they are given prescriptions based on prescribing guidelines by medical boards, with 20% of deaths in low dose opioid therapy of 100 mg of morphine equivalent dose or less per day and 40% in those receiving morphine of over 100 mg per day. In comparison, 40% of deaths occur in individuals abusing the drugs obtained through multiple prescriptions, doctor shopping, and drug diversion.

The purpose of this comprehensive review is to describe various aspects of crisis of opioid use in the United States. The obstacles that must be surmounted are primarily inappropriate prescribing patterns, which are largely based on a lack of knowledge, perceived safety, and inaccurate belief of undertreatment of pain.

Key words: Opioid abuse, opioid misuse, nonmedical use of psychotherapeutic drugs, nonmedical use of opioids, National Survey on Drug Use and Health, opioid guidelines.

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The Institute of Medicine (IOM) recently published a report on relieving pain in America (1,2). The report identified multiple facts, including that there are more than 116 million Americans with pain persisting from weeks to years, with financial costs ranging from \$560 billion to \$635 billion per year. The report alluded to the serious problem of the diversion and abuse of opioid drugs, questioning their long-term usefulness. The IOM committee reported that when opioids are used as prescribed; they can be safe and effective for acute postoperative pain, procedural pain, and patients nearing the end of life who desire more pain relief. While the IOM committee does promote pain treatment, including opioids, they do acknowledge a serious crisis in the diversion and abuse of opioids and a lack of evidence for the long-term usefulness of opioids in treating chronic pain. Along with increases in the prevalence of chronic pain, health care costs, and adverse consequences due to opioid use, the opioid crisis is escalating (1-49). Despite mounting evidence, efforts to increase opioid use based on the alleged undertreatment of pain continue (50-63). In fact, Stein (64) summarized the evidence succinctly, noting that "many arguments in favor of opioids are solely based on traditions, expert opinion, practical experience, and uncontrolled anecdotal observations."

Starting in the late 1990's, state medical boards curtailed restrictions on laws governing the prescribing of opioids for the treatment of chronic non-cancer pain, resulting in a dramatic increase in the number of prescriptions (65). This development gathered momentum with the introduction of new pain management standards for in-patient and out-patient medical care implemented by the Joint Commission on the Accreditation of Health Care Organizations (JCAHO) in 2000 (66) and an increased awareness of the right to pain relief, both of which provided justification for physicians. (67-70). Other factors fueling an increase in prescriptions included aggressive marketing by the pharmaceutical industry, the promotion of opioids by numerous physicians and a call for the increased use of opioids in the treatment of chronic non-cancer pain by myriad organizations. These positions, alongside continued assertions that pain is undertreated, were largely based on untenable science and misinformation, and contended that opioids are highly effective and safe without adverse effects when prescribed by physicians (31,60,66,71-90). Moreover, a recent examination of model guidelines for curtailing controlled substance abuse revealed that the guidelines appeared instead

to condone an increase in prescribing (50,91-93). This is illustrated by the language in the model guidelines, which state (65), "no disciplinary action will be taken against a practitioner based solely on the quantity and/or frequency of opioids prescribed." Thus, the use of opioids in general, including long-acting and potent forms of opioids, have dramatically increased due to a shift in regulations largely driven by published, albeit extremely weak, evidence suggesting that opioids are not only highly effective, but also safe in selected persons with chronic non-cancer pain, even though this selection criteria are extremely weak and these guidelines have only facilitated overuse of opioids (31,71,94-98). Nearly 2 decades later, the scientific evidence for the effectiveness of opioids for chronic non-cancer pain remains unclear (35,71,96,99-119). In addition to ongoing concerns with regard to the lack of effectiveness of opioids in chronic non-cancer pain (31-38,96,99-119), there is growing evidence of multiple physiologic and non-physiologic adverse effects, such as opioid hyperalgesia (32,95,96,107,112-124), misuse and abuse (31-39,71,95,96,102,103,110-115,125-140), the inability of providers to identify and monitor misuse and overuse (31,32,36,95,96,126,127,130,138-151), and a steady increase in opioid-related fatalities (32,34,37,129,130,152-163). In fact, in 2008 drug poisoning in the United States has been reported to contribute to one death every 15 minutes (160). Furthermore, opioids have been shown to contribute to one death every 36 minutes in the United States in 2008. Correlating with these fatalities, sales and substance abuse treatment admissions have increased substantially (125-127,159,160,164-168).

With the above background highlighting a steady increase in fatalities with opioid use and very little evidence of effectiveness, it remains to be seen who will ultimately bear the responsibility for the premature adoption of opioids as a treatment standard (116). It has been speculated that in the coming years, there will likely be an extensive "postmortem" on the massive opioid treatment movement and the escalating social crisis that has accompanied it (116). It is universally accepted that this massive treatment movement has led to huge collateral damage in terms of diversion, misuse, and abuse of opioids. The widespread use of opioids for chronic non-cancer pain is in direct violation of the established cardinal principles of medical intervention – that there be compelling evidence of the benefit of a therapy prior to its large-scale use (116).

A cautious approach has been advocated in recent years by many (17,33,35,49,110-115,117-119,169). This

manuscript is undertaken to evaluate the escalating opioid crisis which although heavily regulated, continues to be uncontrolled.

1.0 Non-Medical Use of Psychotherapeutic Drugs

1.1 Current Non-Medical Use

Results of the 2010 National Survey on Drug Use and Health (NSDUH) (170), an annual survey sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), showed that an estimated 22.6 million, or 8.9% of Americans, age 12 or older, were current (past month) illicit drug users. Illicit drugs include marijuana, cocaine, heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics (defined in this survey as prescription-type pain relievers, tranquilizers, stimulants, and sedatives) used non-medically. Marijuana was the most commonly used illicit drug with 17.4 million current (past month) users, or 6.9% of the US

population. Cocaine was used by 1.5 million, whereas hallucinogens were used in the past month by 1.2 million persons (Fig. 1 and Table 1). Next to marijuana, 7.0 million (27%) persons age 12 or older had used prescription-type psychotherapeutic drugs non-medically in the past month (current use). Of these, 5.1 million had used pain relievers. The category of psychotherapeutics used in the tables and figures includes the nonmedical use of any prescription-type pain relievers, tranquilizers, stimulants, or sedatives. However, over-the-counter substances are not included in these studies. The categories of nonmedical use of psychotherapeutics and pain relievers were well ahead of the illicit use of cocaine, hallucinogens, inhalants, methamphetamine, heroin, and lysergic acid diethylamide (LSD).

Overall, there has been an increase in the current use of all illicit drugs and marijuana, without any change for psychotherapeutics and hallucinogens and a decrease for cocaine from 2002 to 2010, as shown in Fig. 2.

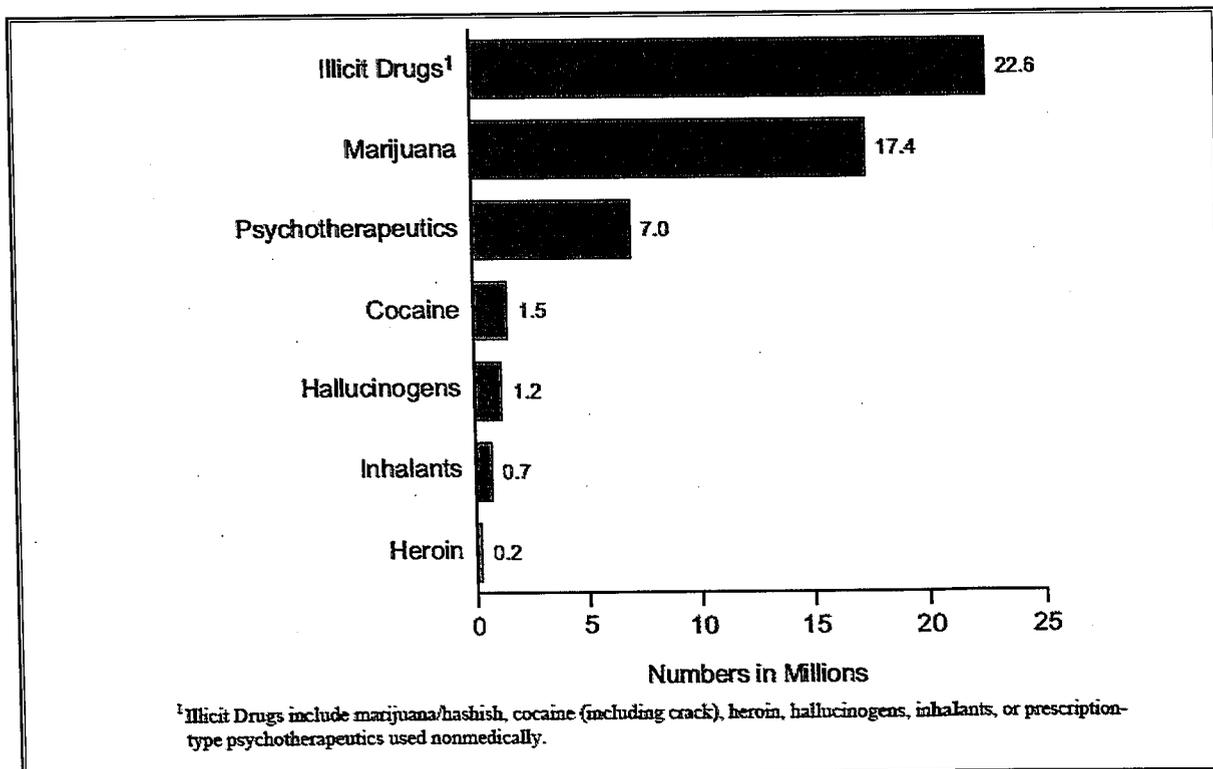


Fig. 1. Past month illicit drug use among persons aged 12 or older: 2010.

Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012.

Table 1. Types of illicit drug use in the past month among persons aged 12 or older. Numbers in thousands, from 1998 to 2010.

Drugs	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	12-Year % change from 1998 to 2010
Nonmedical Use of Psychotherapeutics ^{2,3}	2,477 (1.1%)	3,952 (1.8%)	3,849 (1.7%)	4,811 (2.1%)	6,287 (2.7%)	6,451 (2.7%)	6,110 (2.5%)	6,491 (2.7%)	7,095 ^b (2.9% ^b)	6,895 ^a (2.8% ^a)	6,224 (2.5%)	6,953 (2.8%)	6,967 (2.7%)	181%
Pain Relievers	--	2,621 (1.2%)	2,782 (1.2%)	3,497 (1.6%)	4,377 (1.9%)	4,693 (2.0%)	4,404 (1.8%)	4,658 (1.9%)	5,220 (2.1%)	5,174 (2.1%)	4,747 (1.9%)	5,257 (2.1%)	5,100 (2.0%)	NA
OxyContin*	--	--	--	--	--	--	325 (0.1%)	334 (0.1%)	276 (0.1% ^a)	369 (0.1%)	435 (0.2%)	510 (0.2%)	564 (0.2%)	NA
Tranquilizers	655 (0.3%)	1,097 (0.5%)	1,000 (0.4%)	1,358 (0.6%)	1,804 (0.8%)	1,830 (0.8%)	1,616 (0.7%)	1,817 (0.7%)	1,766 (0.7%)	1,835 (0.7%)	1,800 (0.7%)	2,010 (0.8%)	2,160 (0.9%)	230%
Stimulants	633 (0.3%)	950 (0.4%)	788 (0.4%)	1,018 (0.5%)	1,303 ^b (0.6% ^b)	1,310 ^b (0.6% ^b)	1,312 ^b (0.5% ^b)	1,188 ^b (0.5% ^b)	1,385 ^b (0.6% ^b)	1,053 (0.4%)	904 (0.4%)	1,290 (0.5%)	1,077 (0.4%)	70%
Sedatives ³	210 (0.1%)	229 (0.1%)	175 (0.1%)	306 (0.1%)	436 ^b (0.2% ^b)	294 (0.1%)	265 (0.1%)	272 (0.1%)	385 (0.2% ^a)	346 (0.1%)	234 (0.1%)	370 (0.1%)	374 (0.1%)	78%
Marijuana and Hashish	11,016 (5.0%)	10,458 (4.7%)	10,714 (4.8%)	12,122 (5.4%)	14,584 (6.2%)	14,638 (6.2%)	14,576 (6.1%)	14,626 (6.0%)	14,813 (6.0%)	14,448 (5.8%)	15,203 (6.1%)	16,718 (6.6%)	17,373 (6.9%)	58%
Cocaine	1,750 (0.8%)	1,552 (0.7%)	1,213 (0.5%)	1,667 (0.7%)	2,020 (0.9%)	2,281 (1.0%)	2,021 (0.8%)	2,397 (1.0%)	2,421 (1.0%)	2,075	1,855	1,637 (0.7%)	1,466 (0.6%)	-16%
TOTAL ILLICIT DRUGS	13,615 (6.2%)	13,829 (6.3%)	14,027 (6.3%)	15,910 (7.1%)	19,522 (8.3%)	19,470 (8.2%)	19,071 (7.9%)	19,720 (8.1%)	20,357 (8.1%)	19,847 (8.0%)	20,077 (8.0%)	21,813 (8.7%)	22,622 (8.9%)	61%

-- Not available.
 Note: 2002 to 2008 data is based on 2008 National Survey on Drug Use and Health Survey Report.
 a Difference between estimate and 2008 estimate is statistically significant at the 0.05 level. b Difference between estimate and 2008 estimate is statistically significant at the 0.01 level.
 1 Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. Illicit Drugs Other Than Marijuana include cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. The estimates for Nonmedical Use of Psychotherapeutics, Stimulants, and Methamphetamine incorporated in these summary estimates do not include data from the methamphetamine items added in 2005 and 2006.
 2 Nonmedical use of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives and does not include over-the-counter drugs.
 3 Estimates of Nonmedical Use of Psychotherapeutics, Stimulants, and Methamphetamine in the designated rows include data from methamphetamine items added in 2005 and 2006 and are not comparable with estimates presented in NSDUH reports prior to the 2007 National Findings report. For the 2002 through 2005 survey years, a Bernoulli stochastic imputation procedure was used to generate adjusted estimates comparable with estimates for survey years 2006 and later.
 Source: SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 1998 - 2010.
www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10results.pdf (170) Access date 2/22/2012

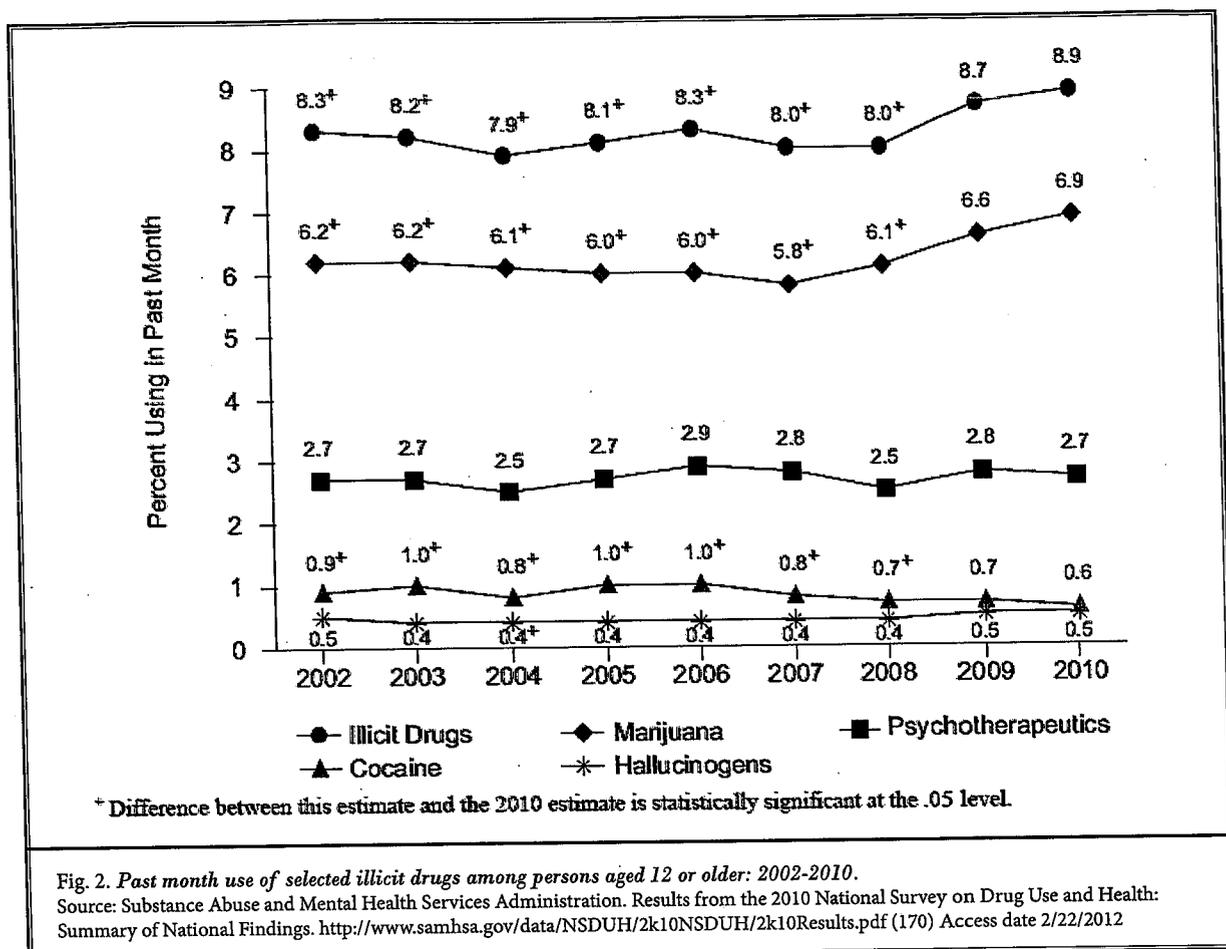


Fig. 2. Past month use of selected illicit drugs among persons aged 12 or older: 2002-2010. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

1.2 Past Year Initiates

In 2010, there were 2.4 million persons age 12 or older who used psychotherapeutics non-medically for the first time within the past year. Numbers of new users for specific psychotherapeutics in 2010 were 2.0 million for pain relievers, 1.2 million for tranquilizers, 624,000 for stimulants, and 252,000 for sedatives (Table 2 and Fig. 3). The specific drug categories with the largest number of recent initiatives among persons age 12 or older were nonmedical use of pain relievers (2,004 million) and marijuana (2,426 million), followed by nonmedical use of tranquilizers (1,238 million), ecstasy (0.937 million), inhalants (0.793 million), cocaine (0.637 million), and stimulants (0.624 million) (Fig. 3). More strikingly, in 2010, the number of new nonmedical users of OxyContin (oxycodone) age 12 or older was 598,000 with an average age at first use of 22.8 years among those age 12 to 49 (170).

1.3 Past Year Use

The analysis of long-term statistics based on yearly use of illicit drugs is disturbing. The past year use of illicit drugs in 2010 was 38.806 million, or 15.3% of the population (Table 3). Nonmedical use of psychotherapeutics for the past year in the 2010 survey was 16.031 million or 6.3% population age 12 or older, compared to 2.6% of the population in 1998. Of importance is the fact that nonmedical use of psychotherapeutics was just behind marijuana and hashish with use by 11.5% of the population age 12 or older in 2010, increased from 8.6% in 1998. Overall, nonmedical use of psychotherapeutics increased 178% from 1998 to 2010, compared to marijuana 56% and cocaine at 17%.

1.4 Lifetime Use

Lifetime use of illicit drugs (lifetime use indicates use of a specific drug at least once in the respondent's

Table 2. Past year initiates for illicit drugs from 1998 to 2010 (numbers in thousands) for 12 years.

Drugs	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	12-Year % change from 1998 to 2010
Pain Relievers ²	1,548	1,810	2,268	2,400	2,320	2,456	2,422	2,193	2,150	2,147	2,176	2,179	2,004	29%
Tranquilizers	860	916	1,298	1,212	1,184	1,071	1,180	1,286	1,112	1,232	1,127	1,226	1,238	44%
Stimulants ²	648	706	808	853	783	715	793 ^a	647	845 ^b	642	599	702	624	-4%
Sedatives	147	164	191	225	209	194	240	247	267	198	181	186	252	71%
Marijuana	2,498	2,640	2,746	2,793	2,196	1,973	2,142	2,114	2,063	2,090	2,208	2,361	2,426	-3%
Cocaine	868	917	1,002	1,140	1,032 ^b	986 ^b	998 ^b	872 ^a	977 ^b	906 ^b	722	617	637	-27%
Heroin	140	121	114	154	117	92	118	108	91	106	114	180	140	0%

Note: 2002 to 2008 data is based on 2008 National Survey on Drug Use and Health Survey Report.

-- Not available.

a Difference between estimate and 2008 estimate is statistically significant at the 0.05 level.

b Difference between estimate and 2008 estimate is statistically significant at the 0.01 level.

1 Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. Illicit Drugs Other Than Marijuana include cocaine (including crack), heroin, hallucinogens, Stimulants, and Methamphetamine incorporated in these summary estimates do not include data from the methamphetamine items added in 2005 and 2006. See Section B.4.8 in Appendix B of the Results from the 2008 National Survey on Drug Use and Health: National Findings.

2 Nonmedical use of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives and does not include over-the-counter drugs.

3 Estimates of Nonmedical Use of Psychotherapeutics, Stimulants, and Methamphetamine in the designated rows include data from methamphetamine items added in 2005 and 2006 and are not comparable with estimates presented in NSDUH reports prior to the 2007 National Findings report. For the 2002 through 2005 survey years, a Bernoulli stochastic imputation procedure was used to generate adjusted estimates comparable with estimates for survey years 2006 and later.

Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170). Access date 2/22/2012

lifetime), including psychotherapeutics, among persons age 12 or older has been increasing over the years (Table 4). In 2010, the lifetime use of illicit drugs among persons age 12 or older was slightly more than 2009 with 119,508 or 47.1% of the population. Similarly, nonmedical use of psychotherapeutics remained the

same from 2009 with 20.4% in 2010, or almost 51.6 million using prescription psychotherapeutic drugs for nonmedical purposes. Among the subgroups, only OxyContin increased significantly from 1.9 million in 2005 to 6.1 million in 2010, or 0.8% of the population in 2005 to 2.4% in 2010 (171). Lifetime use of illicit drugs in per-

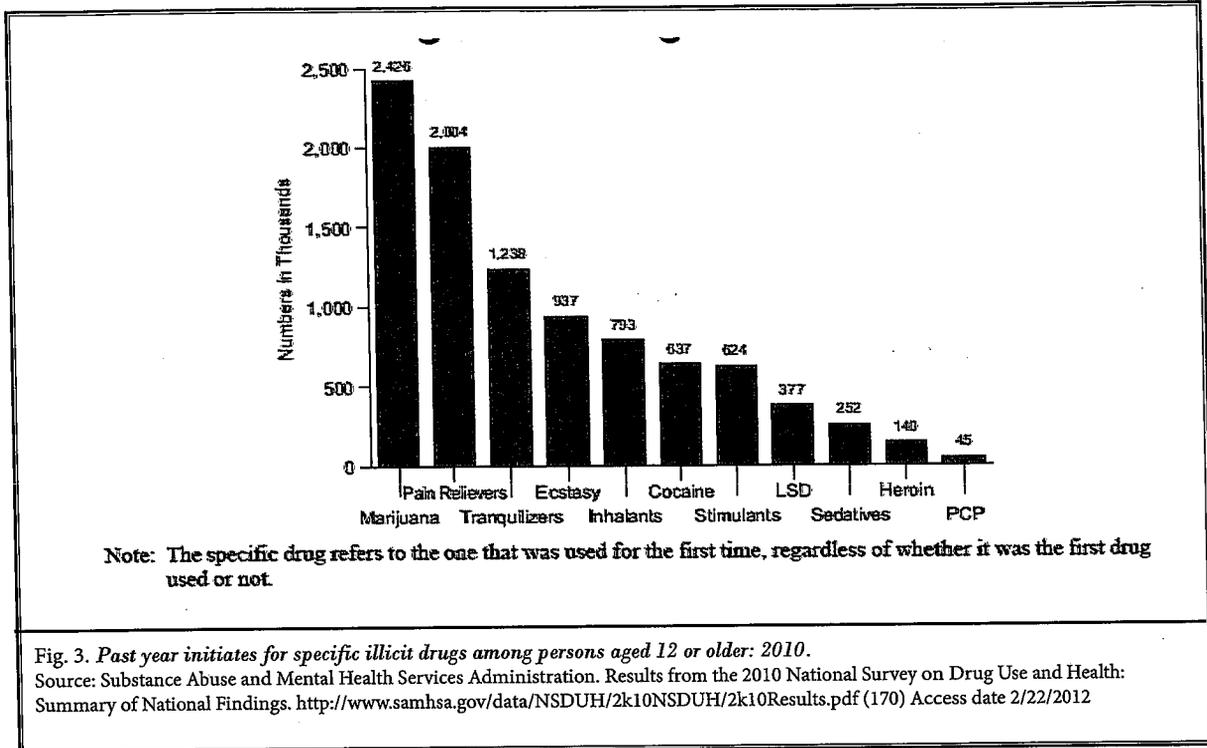


Fig. 3. Past year initiates for specific illicit drugs among persons aged 12 or older: 2010. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

sons age 12 or older was topped by marijuana (41.9% of the population) followed by nonmedical use of psychotherapeutics (20.4% of the population).

1.5 Abuse Based on Age

In 2010, young adults age 18 to 25 demonstrated rates of current use of illicit drugs to be higher (21.5%) than for youths age 12 to 17 (10.1%) and adults age 26 or older (6.6%), with 6.9% using marijuana, 2.7% using psychotherapeutics non-medically, 0.6% using cocaine, and 0.5% using hallucinogens among young adults 18-25 (Fig. 4). Past month nonmedical use of prescription-type drugs among young adults increased from 20.2% in 2002 to 21.5% in 2010. This was primarily due to an increase in the rate of pain reliever use which was 4.1% in 2002 and 4.9% in 2006 (170). As illustrated in Figure 5, overall illicit drug use increased from 8.3% to 8.9% in 2010 in the age group from 18 to 25.

Rates of past month illicit drug use varied with age. Through the adolescent years from 12 to 17, the rates of current illicit drug use in 2010 increased from 4.0% at ages 12 or 13, to 9.3% at ages 14 or 15, to 16.6% at ages 16 or 17 (170). The highest rate of 23.1% was noted among persons age 18 to 20, with the next high-

est rate among 21 to 25 year olds 20.5% (Fig. 6) (144). In 2010, adults age 26 or older were less likely to be current drug users than youths age 12 to 17 or young adults age 18 to 25 (6.6 versus 10.1 and 21.5%, respectively). However, there were more drug users age 26 or older (12.8 million) than users in the 12-to-17-year age group (2.5 million) and 18-to-25-year age group (7.3 million) combined.

1.6 Abuse Based on Gender

In 2010, the survey results were similar to prior years with males being more likely than females to be current illicit drug users (11.2% versus 6.8%). Males were more likely than females to be past month users of marijuana (9.1% versus 4.7%). Rates of past month nonmedical use of psychotherapeutic drugs among males and females was 3% and 2.5%, pain relievers was 2.3% and 1.7%, cocaine was 0.8% and 0.4% and hallucinogens was 0.6% and 0.3% (170).

1.7 Abuse During Pregnancy

Among pregnant woman age 15 to 44 years, a significantly lower proportion of women used illicit drugs in the past month (4.4%) compared to 10.9% of their

Table 3. Types of illicit drug use in the past year among persons aged 12 or older: numbers in thousands from 1998 to 2010 (12 years).

Drugs	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	12-year % change from 1998 to 2010
Nonmedical Use of Psychotherapeutics ^{2,3}	5,759 (2.6%)	9,220 (4.2%)	8,761 (3.9%)	11,102 (4.9%)	14,795 (6.3%)	15,163 (6.4%)	14,849 (6.2%)	15,346 (6.3%)	16,482 ^b (6.7%)	16,280 ^a (6.6%)	15,166 (6.1%)	16,006 (6.4%)	16,031 (6.3%)	178%
Pain Relievers	--	6,582 (3.0%)	6,466 (2.9%)	8,353 (3.7%)	10,992 ^a (4.7%)	11,671 (4.9%)	11,256 (4.7%)	11,815 (4.9%)	12,649 (5.1%)	12,466 (5.0%)	11,885 (4.8%)	12,405 (4.9%)	12,213 (4.8%)	85% From 1999
OxyContin ^a	--	--	--	--	--	--	1,213 ^a (0.5%)	1,226 (0.5%)	1,323 (0.5%)	1,422 (0.6%)	1,459 (0.6%)	1,677 (0.7%)	1,869 (0.7%)	54% From 2004
Tranquilizers	1,940 (0.9%)	2,728 (1.2%)	2,731 (1.2%)	3,673 (1.6%)	4,849 (2.1%)	5,051 (2.1%)	5,068 (2.1%)	5,249 (2.2%)	5,058 (2.1%)	5,282 (2.1%)	5,103 (2.0%)	5,460 (2.2%)	5,581 (2.2%)	188%
Stimulants ³	1,489 (0.7%)	2,291 (1.0%)	2,112 (0.9%)	2,486 (1.1%)	3,380 ^b (1.4%)	3,031 ^a (1.3%)	3,254 ^b (1.4%)	3,088 ^a (1.3%)	3,791 ^b (1.5%)	2,998 (1.2%)	2,639 (1.1%)	3,060 (1.2%)	2,887 (1.1%)	94%
Sedatives	522 (0.2%)	631 (0.3%)	611 (0.3%)	806 (0.4%)	981 ^b (0.4%)	831 ^a (0.3%)	737 (0.3%)	750 (0.3%)	926 ^b (0.4%)	864 ^a (0.3%)	621 (0.2%)	811 (0.3%)	907 (0.4%)	56%
Marijuana and Hashish	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%)	25,375 (10.4%)	25,378 (10.3%)	25,085 (10.1%)	25,768 (10.3%)	28,521 (11.3%)	29,206 (11.5%)	56%
Cocaine	3,811 (1.7%)	3,742 (1.7%)	3,328 (1.5%)	4,186 (1.9%)	5,902 ^a (2.5%)	5,908 ^a (2.5%)	5,658 (2.4%)	5,523 (2.3%)	6,069 ^b (2.5%)	5,738 (2.3%)	5,255 (2.1%)	4,797 (1.9%)	4,449 (1.8%)	17%
TOTAL ILLICIT DRUGS	23,015 (10.6%)	25,409 (11.5%)	24,535 (11.0%)	28,409 (12.6%)	35,139 (14.9%)	34,993 (14.7%)	34,807 (14.5%)	35,091 (14.4%)	35,775 (14.5%)	35,692 (14.4%)	35,935 (14.4%)	37,957 (16.1%)	38,806 (16.5%)	68%

-- Not available.
 Note: 2002 to 2010 data is based on 2010 National Survey on Drug Use and Health Survey Report. a Difference between estimate and 2010 estimate is statistically significant at the 0.05 level. b Difference between estimate and 2010 estimate is statistically significant at the 0.01 level.
 1 Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used non-medically. Illicit drugs other than marijuana include cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used non-medically. The estimates for nonmedical use of psychotherapeutics, stimulants, and methamphetamine incorporated in these summary estimates do not include data from the methamphetamine items added in 2005 and 2006.
 2 Nonmedical use of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives and does not include over-the-counter drugs.
 3 Estimates of nonmedical use of psychotherapeutics, stimulants, and methamphetamine in the designated rows include data from methamphetamine items added in 2005 and 2006 and are not comparable with estimates presented in NSDUH reports prior to the 2007 National Findings report. For the 2002 through 2005 survey years, a Bernoulli stochastic imputation procedure was used to generate adjusted estimates comparable with estimates for survey years 2006 and later.
 Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170). Access date 2/22/2012

Table 4. Types of illicit drugs of lifetime use among persons aged 12 or older: numbers in thousands, 1998–2010.

Drug	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	12-Year % change from 1998 to 2010
Nonmedical Use of Psychotherapeutics ²	20,193 (9.2%)	34,076 (15.4%)	32,443 (14.5%)	36,028 (16.0%)	47,958 ^b (20.4%)	49,001 ^b (20.6%)	49,157 (20.4%)	49,571 ^a (20.4%)	50,965 (20.7%)	50,415 (20.3%)	51,970 (20.8%)	51,771 (20.6%)	51,641 (20.4%)	156%
Pain Relievers	--	19,888 (9.0%)	19,210 (8.6%)	22,133 (9.8%)	29,611 ^b (12.6%)	31,207 ^b (13.1%)	31,768 ^b (13.2%)	32,692 ^b (13.4%)	33,472 (13.6%)	33,060 ^a (13.3%)	34,861 (14.0%)	35,046 (13.9%)	34,776 (13.7%)	75% From 1999
OxyContin ³	--	--	--	--	1,924 ^b (0.8%)	2,832 ^b (1.2%)	3,072 ^b (1.3%)	3,481 ^b (1.4%)	4,098 ^b (1.7%)	4,354 (1.8%)	4,842 (1.9%)	5,829 (2.3%)	6,121 (2.4%)	218% From 2002
Tranquilizers	7,726 (3.5%)	13,860 (6.3%)	13,007 (5.8%)	13,945 (6.2%)	19,267 ^b (8.2%)	20,220 (8.5%)	19,852 ^a (8.3%)	21,041 (8.7%)	21,303 (8.7%)	20,208 (8.2%)	21,476 (8.6%)	21,755 (8.6%)	22,103 (8.7%)	186%
Stimulants	9,614 (4.4%)	15,922 (7.2%)	14,661 (6.6%)	16,007 (7.1%)	23,496 ^b (10.0%)	23,004 ^a (9.7%)	22,297 (9.3%)	20,983 (8.6%)	22,468 (9.1%)	21,654 (8.7%)	21,206 (8.5%)	21,930 (8.7%)	21,660 (8.5%)	125%
Sedatives	4,640 (2.1%)	7,747 (3.5%)	7,142 (3.2%)	7,477 (3.3%)	9,960 ^a (4.2%)	9,510 (4.0%)	9,891 (4.1%)	8,982 (3.7%)	8,822 (3.6%)	8,396 (3.4%)	8,882 (3.6%)	8,605 (3.4%)	7,631 (3.2%)	64%
Marijuana and Hashish	72,070 (33.0%)	76,428 (34.6%)	76,321 (34.2%)	83,272 (36.9%)	94,946 ^b (40.4%)	96,611 ^b (40.6%)	96,772 ^b (40.2%)	97,545 ^b (40.1%)	97,825 ^b (39.8%)	100,518 (40.6%)	102,404 (41.0%)	104,446 (41.5%)	106,232 (41.9%)	47%
Cocaine	23,089 (10.6%)	25,406 (11.5%)	24,896 (11.2%)	27,788 (12.3%)	33,910 ^b (14.4%)	34,891 ^a (14.7%)	34,153 ^b (14.2%)	33,673 ^b (13.8%)	35,298 (14.3%)	35,882 (14.5%)	36,773 (14.7%)	36,599 (14.5%)	37,210 (14.7%)	61%
TOTAL ILLICIT DRUGS	74,125 (33.3%)	87,734 (39.7%)	86,931 (38.9%)	94,140 (41.7%)	108,215^b (46.0%)	110,205^b (46.2%)	110,057^b (45.8%)	112,035^b (46.1%)	111,774^b (45.4%)	114,273^b (46.1%)	117,325 (47.0%)	119,705 (47.1%)	119,518 (47.1%)	58%

-- Not available.
 Note: 2002 to 2010 data is based on 2010 National Survey on Drug Use and Health Survey Report.

^a Difference between estimate and 2010 estimate is statistically significant at the 0.05 level.

^b Difference between estimate and 2010 estimate is statistically significant at the 0.01 level.

¹ Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used non-medically. Illicit drugs other than marijuana include cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used non-medically. The estimates for nonmedical use of psychotherapeutics, stimulants, and methamphetamine incorporated in these summary estimates do not include data from the methamphetamine items added in 2005 and 2006.

² Nonmedical use of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives and does not include over-the-counter drugs.

³ Estimates of nonmedical use of psychotherapeutics, stimulants, and methamphetamine in the designated rows include data from methamphetamine items added in 2005 and 2006 and are not comparable with estimates presented in NSDUH reports prior to the 2007 National Findings report. For the 2002 through 2005 survey years, a Bernoulli stochastic imputation procedure was used to generate adjusted estimates comparable with estimates for survey years 2006 and later.

Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

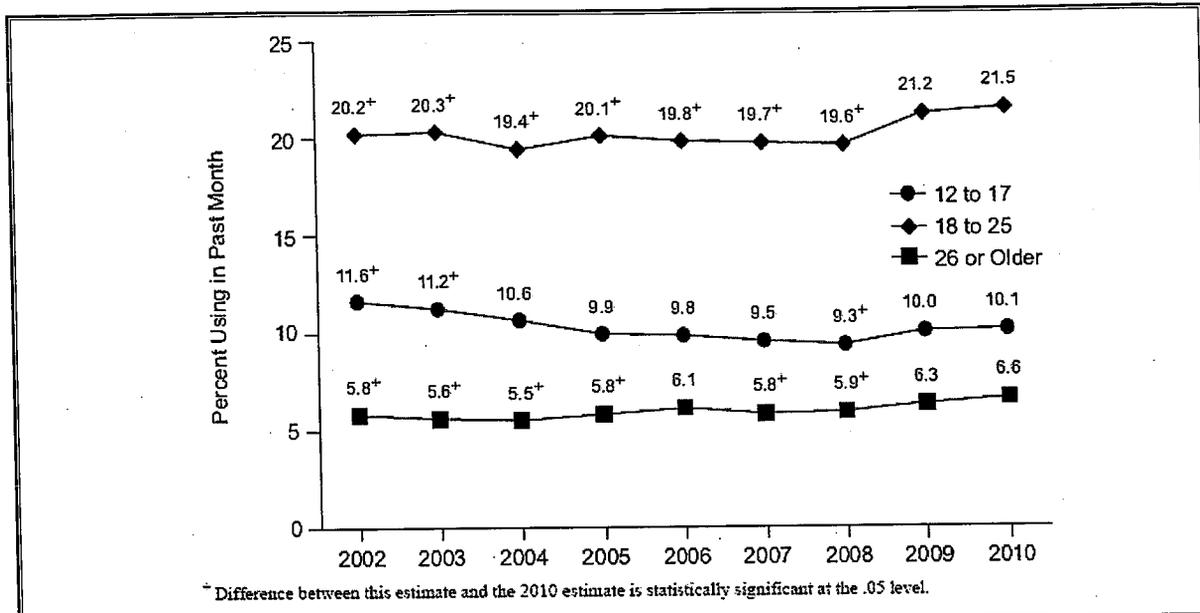


Fig. 4. Comparative analysis of past month use of illicit drugs among various age groups. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

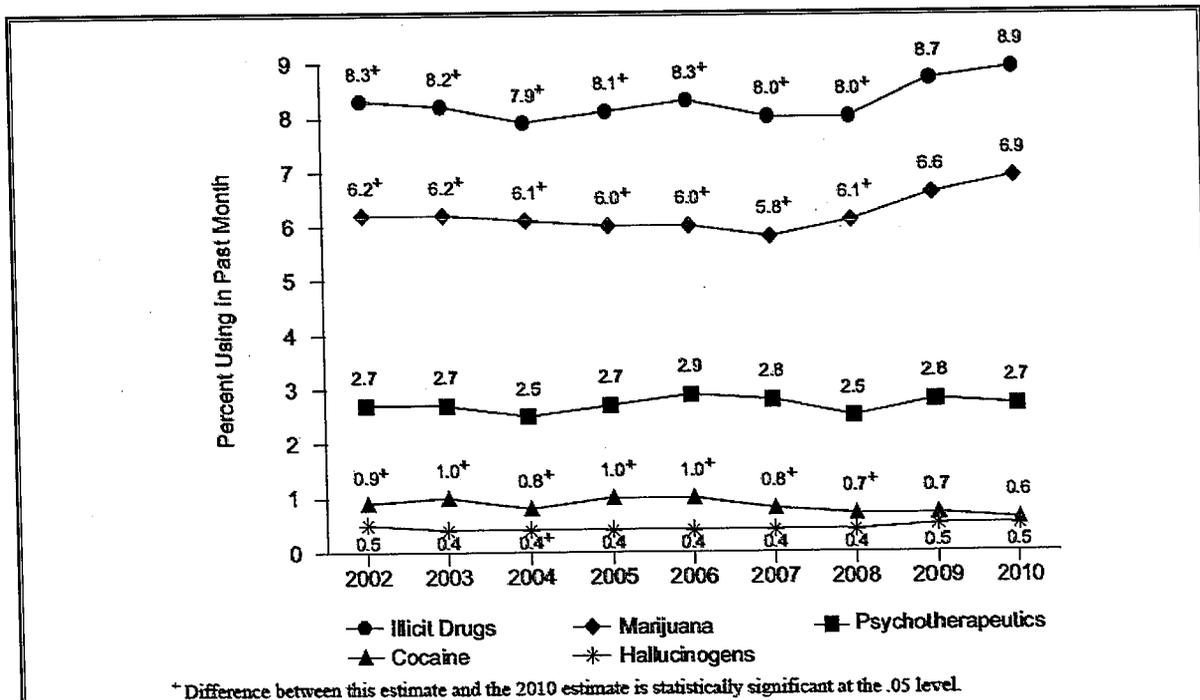


Fig. 5. Past month use of selected illicit drugs among young adults aged 18 to 25: 2002-2010. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

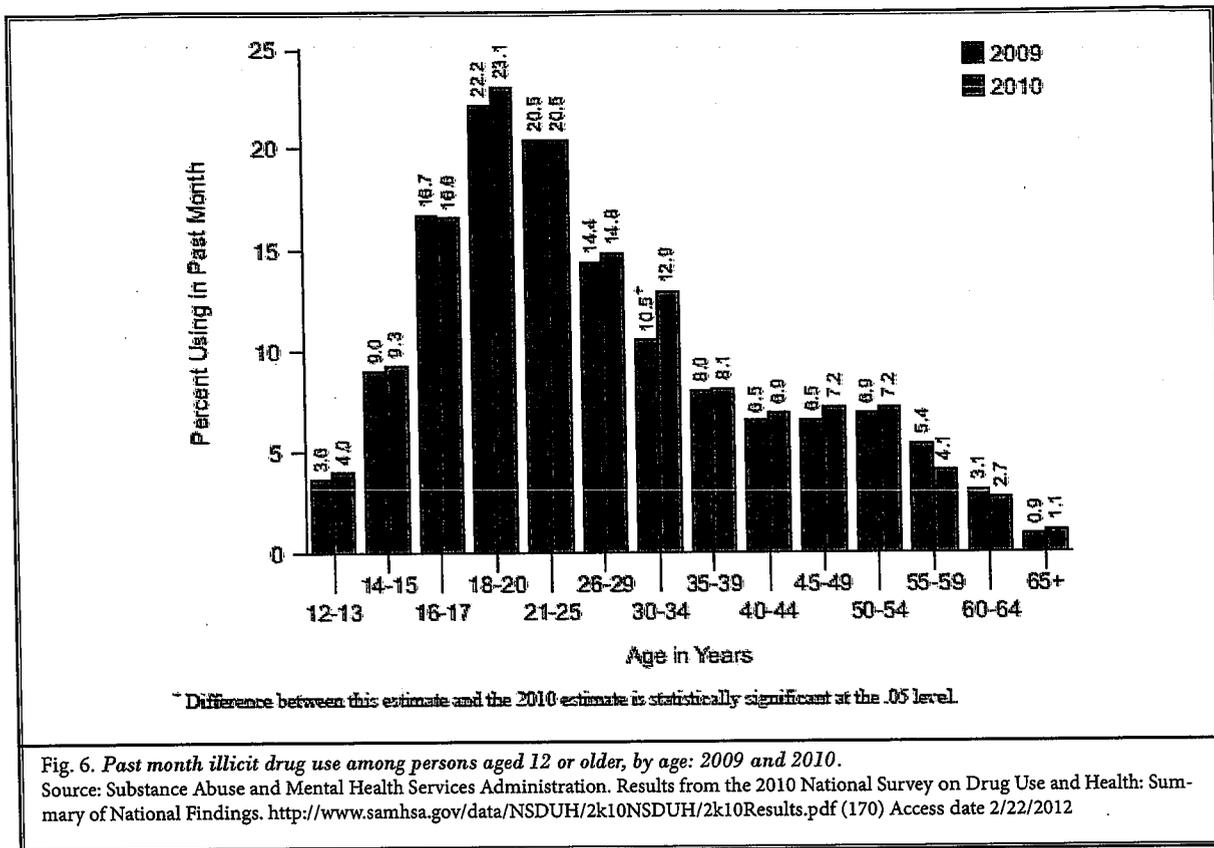


Fig. 6. Past month illicit drug use among persons aged 12 or older, by age: 2009 and 2010. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. <http://www.samhsa.gov/data/NSDUH/2k10NSDUH/2k10Results.pdf> (170) Access date 2/22/2012

nonpregnant counterparts. These figures are based on data averaged for 2009 and 2010 (170).

1.8 Abuse Based on Employment

Employment also seemed to have a significant influence in 2010. Among adults age 18 or older, the rate of illicit drug use was higher for unemployed persons (17.5%) than for those who were employed full time (8.4%) or part time (11.2%) (170).

1.9 Regional Variations

There were also differences based on geographic area among persons age 12 or older in 2010. The rate of current illicit drug use in 2010 was 11.0% in the West, 9.4% in the Northeast, 8.2% in the Midwest, and 7.8% in the South (170). Further, the rate of current illicit drug use in metropolitan areas was higher than the rate in non-metropolitan areas with 9.4% in large metropolitan counties, 8.8% in small metropolitan counties, and 7.5% in non-metropolitan counties as a group (170).

1.10 Drug Abuse Among Criminals

In 2010, an estimated 1.5 million adults age 18 or older who were on parole or supervised release from jail during the past year had higher rates of dependence on or abuse of a substance (27%) than their counterparts who were not on parole or supervised release during the past year (8.7%). In 2010, probation status was associated with substance dependence or abuse. The rate of substance dependence or abuse was 29.9% among adults who were on probation during the past year, which was significantly higher than the rate among adults who were not on probation during the past year was 8.3% (170).

1.11 Driving Under the Influence

Driving under the influence of illicit drugs is a criminal act and dangerous to the public. In 2010, 10.6 million persons, or 4.2% of the population age 12 or older, reported driving under the influence of illicit drugs during the past year. This rate was highest among young adults age 18 to 25 with 12.7% (170).

1.12 Frequency of Abuse

Among past year marijuana users age 12 or older in 2010, the following patterns were revealed (170):

- 15.7% used marijuana on 300 or more days within the past 12 months, translating to 4.6 million using marijuana on a daily or almost daily basis over a 12-month period.
- 39.9%, or 6.9 million, used the drug on 20 or more days in the past month (current use).

2.0 MENTAL HEALTH PROBLEMS AND NONMEDICAL USE OF DRUGS

The NSDUH survey of 2010 evaluated the prevalence and treatment of serious mental illness (SMI), serious psychological distress (SPD), and major depressive episode (MDE) and the association of these problems with substance use and substance dependency or abuse. SPD is an overall indicator of the past 30 days of psychological distress, whereas MDE is defined as a period of at least 2 weeks when a person experienced a depressed mood or loss of interest or pleasure in daily activities and had symptoms that met the criteria for a

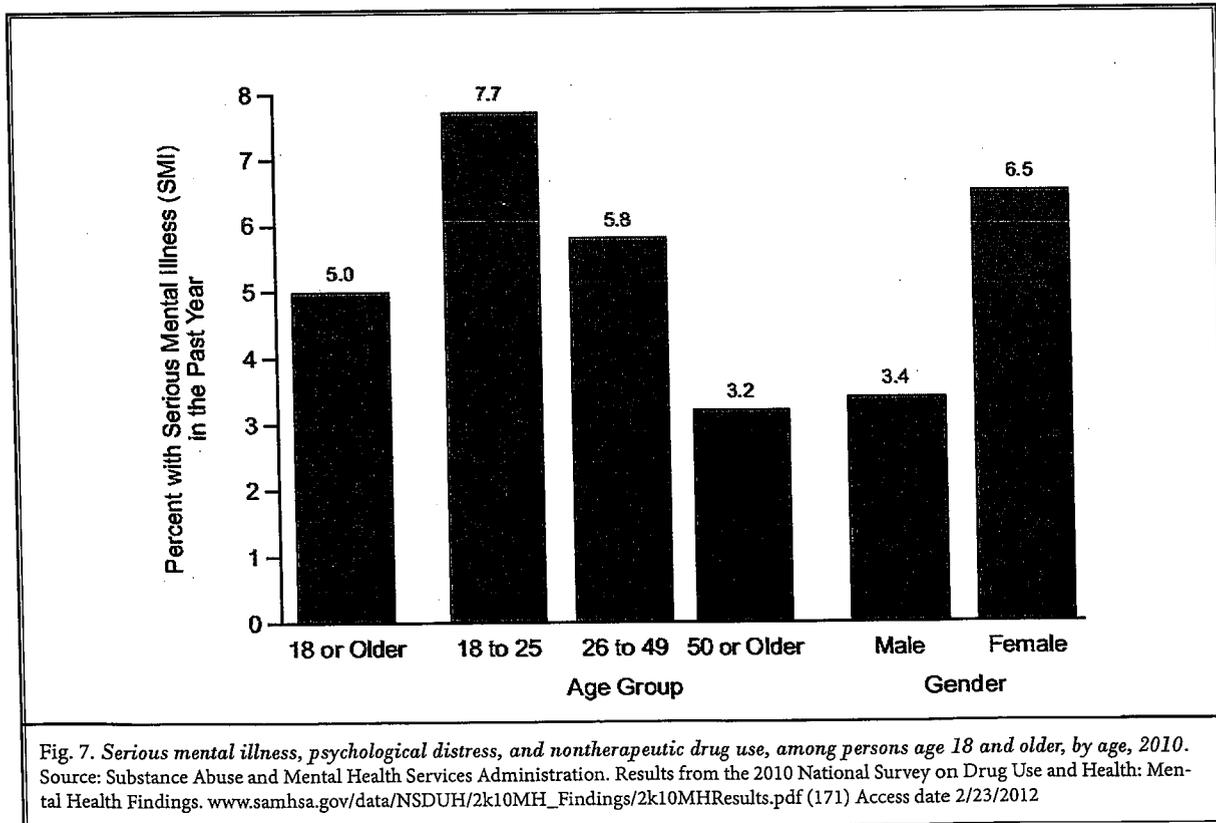
major depressive disorder (171). Further, SPD indicates a respondent recently experienced heightened distress symptomatology that may be affecting health and behavior during the past 30 days. However, this distress may be part of a chronic psychological disturbance (even SMI) or may represent a temporary disturbance that could subside after a brief period of adjustment.

2.1 Serious Medical Illness and Drug Abuse

The prevalence of SMI in 2010 was shown in 11.4 million adults, representing 5.0% of all adults, with the highest rates being in adults age 18 to 25 (7.7%) and lowest for adults age 50 or older (3.2%) as shown in Figure 7 (171). The prevalence of SPD among women age 18 or older was higher (6.5%) than among men (3.4%) in that age group (171).

2.2 Major Depressive Episodes and Drug Abuse

The prevalence of a MDE in 2010 was 6.8% of persons age 18 or older, or 15.5 million adults, with at least one MDE in the past year. The number of adults who had past year MDE was 6.8%. Even then, the past year



prevalence of MDE in 2010 was lower for those age 50 or older (5.6%) compared with rates among persons age 18 to 25 (8.2%) and those age 26 to 49 (7.5%). However, the past year prevalence of MDE was higher among adult females than among adult males, 8.4% versus 5.1%. In addition, among women, past year MDE rates were higher with 11.3% for 18 to 25 year olds, 9.2 for 26 to 49 year olds compared with those of 50 or older with only 6.7%. Further, the prevalence of MDE also varied by race and ethnicity with the highest rate among persons reporting 2 or more races (10.8%), while rates for single race groups were 7.3% among whites, 5.6% among Hispanics, 7.7% among American Indians or Alaska Natives, 5.8% among blacks, and 3.8% among Asians.

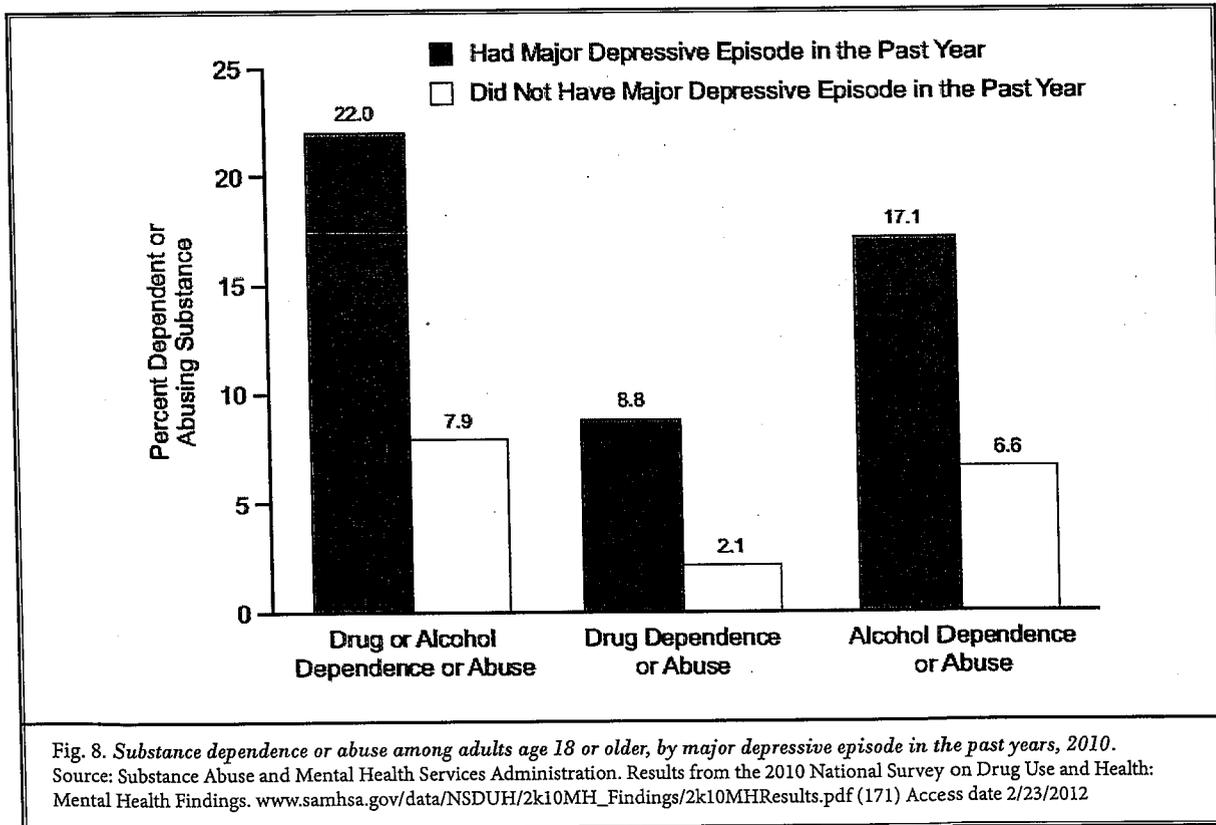
In addition, in 2010 the past prevalence of MDE with severe impairment for adults age 18 or older was higher among unemployed persons (9.3%) than among persons employed full time (5.4%).

In 2010, an adult age 18 or older with a combination of a MDE and substance use and dependence or

abuse in the past year was more likely than those with MDE to have used an illicit drug in the past year (22.0% versus 7.9%) (171). A similar pattern was observed for specific types of past year illicit drug use, such as marijuana and the nonmedical use of prescription-type psychotherapeutics. Figure 8 illustrates substance abuse in adults by MDE.

The prevalence of a MDE in youths age 12 to 17 in 2010 showed that 1.9 million (8.9%) reported at least one MDE during the past year. Among youths age 12 to 17, the past year prevalence of MDE ranged from 3.3% among 12-year-olds to 10.9% among those age 16, and 10.3% among those age 17 (171).

Among youths with MDE age 12 to 17, 37.2% had used illicit drugs in 2010, in contrast to 37.4% in 2008. This was higher than the 17.8% of youths in the past year that did not have a MDE but had used illicit drugs. This pattern, however, was similar to specific types of illicit drug use including marijuana and the nonmedical use of prescription-type psychotherapeutics (171).



3.0 WHERE DO NON-THERAPEUTIC DRUGS COME FROM?

Among persons aged 12 or older in 2009-2010 who used pain relievers nonmedically in the past 12 months, 55% obtained pain relievers from a friend or relative for free (170). Among the remaining 45%, 11.4% bought them from a friend or relative (which was significantly higher than the 8.9% from 2007-2008), and 4.8% essentially stole them from a friend or relative (Fig. 9). However, only one in 6 or 17.3% indicated that they received the drugs through a prescription from one doctor, while only 4.4% received pain relievers from a drug dealer or other stranger, and 0.4% bought them on the Internet, with no significant changes from 2007 to 2008.

Even more striking is the fact that in 2009-2010, 41.5% of past year methamphetamine users reported that they obtained the methamphetamine they used most recently for free from a friend or relative, with an additional 30.7% buying it from a friend or relative (170).

4.0 ESCALATING USE OF THERAPEUTIC OPIOIDS

The escalating use of therapeutic opioids, specifically in high doses over long periods of time or even lifetime use of long-acting drugs, and the combination of long and short-acting drugs continue to have serious consequences for costs of health care and economic stability.

The data overwhelmingly suggest that the increased supply of opioids, high medical users, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of fatalities. The quadrupled sales of opioid analgesics between 1999 and 2010 are a perfect example of the therapeutic opioid explosion. The data on sales and distribution of opioids show an increase from 96 mg morphine equivalents per person in the United States in 1997 to 710 mg per person in 2010 (34,153). This has been estimated to be the equivalent of 7.1 kg of opioid medication per 10,000 persons or enough to supply every adult American with 5 mg of hydrocodone every 6 hours for 45 days. Sales of hy-

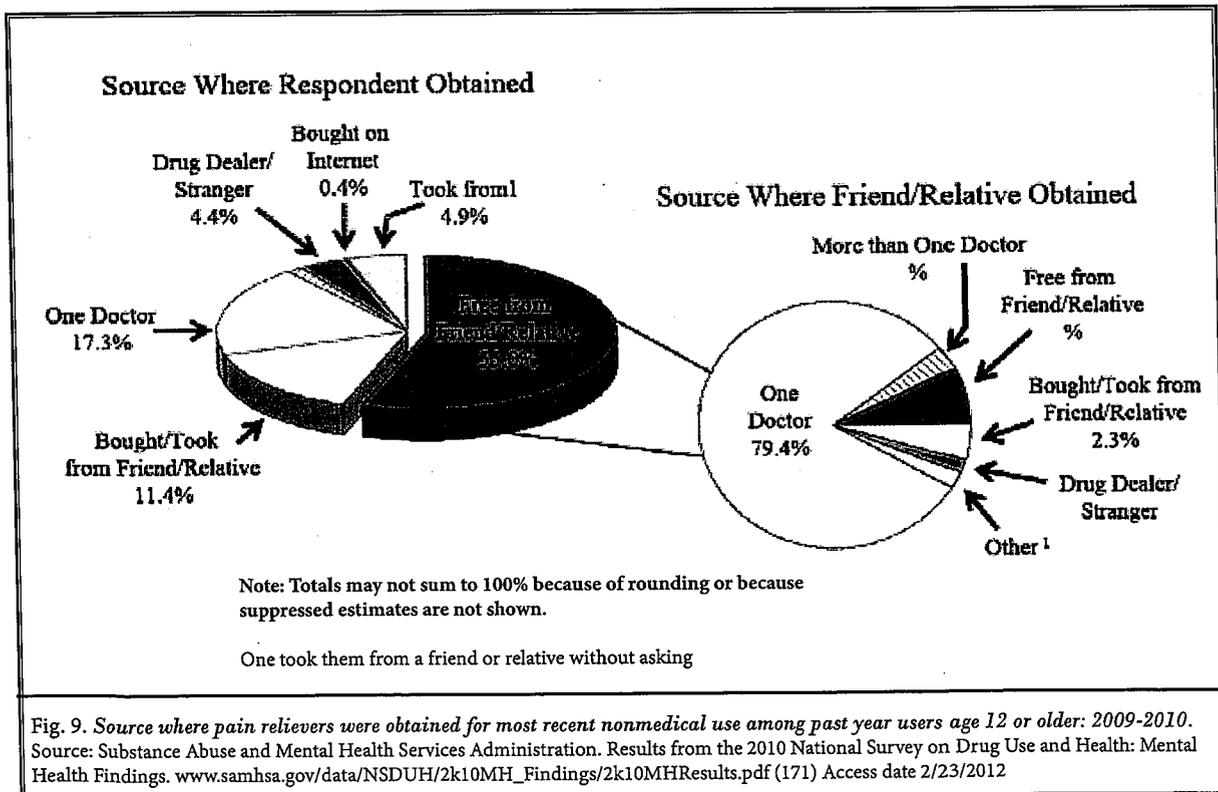


Fig. 9. Source where pain relievers were obtained for most recent nonmedical use among past year users age 12 or older: 2009-2010. Source: Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: Mental Health Findings. www.samhsa.gov/data/NSDUH/2k10MH_Findings/2k10MHResults.pdf (171) Access date 2/23/2012

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drocodone have increased by 280% from 1997 to 2007, whereas methadone usage has increased 1,293% and oxycodone usage by 866%, as illustrated in Table 5 (32). The estimated number of prescriptions filled for opi-

oids exceeded 256 million in the United States in 2009, with 234 million prescriptions for immediate-release (IR) opioids and 22.9 million for extended-release (ER) opioids with significant increases from 21.3 million for

Table 5. Retail sales of opioid medications (grams of medication) from 1997 to 2007.

Drug	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	% of Change from 1997
Methadone	518,737	692,675 (34%)	964,982 (39%)	1,428,840* (48%)	1,892,691 (32%)	2,649,559 (40%)	3,683,881 (39%)	4,730,157 (28%)	5,362,815 (13%)	6,621,687 (23%)	7,228,219 (9%)	1293%
Oxycodone	4,449,562	6,579,719 (48%)	9,717,600 (48%)	15,305,913 (58%)	19,927,286 (30%)	22,376,892 (12%)	26,655,152 (19%)	29,177,530 (9%)	30,628,973 (5%)	37,034,220 (21%)	42,977,043 (16%)	866%
Fentanyl Base	74,086	90,618 (22%)	107,141 (18%)	146,612* (37%)	186,083 (27%)	242,027 (30%)	317,200 (31%)	370,739 (17%)	387,928 (5%)	428,668 (11%)	463,340 (8%)	525%
Hydromorphone	241,078	260,009 (8%)	292,506 (12%)	346,574* (18%)	400,642 (16%)	473,362 (18%)	579,372 (22%)	655,395 (13%)	781,287 (19%)	901,663 (15%)	1,011,028 (12%)	319%
Hydrocodone	8,669,311	10,389,503 (20%)	12,101,621 (16%)	14,118,637 (17%)	15,594,692 (10%)	18,822,619 (21%)	22,342,174 (19%)	24,081,900 (8%)	25,803,543 (7%)	29,856,368 (16%)	32,969,527 (10%)	280%
Morphine	5,922,872	6,408,322 (8%)	6,804,935 (6%)	7,807,511 (15%)	8,810,700 (13%)	10,264,264 (16%)	12,303,956 (20%)	14,319,243 (16%)	15,054,846 (5%)	17,507,148 (16%)	19,051,426 (9%)	222%
Codeine	25,071,410	26,018,054 (4%)	23,917,088 (-8%)	23,474,865* (-2%)	23,032,641 (-2%)	22,633,733 (-2%)	21,865,409 (-3%)	20,264,555 (-7%)	18,960,038 (-6%)	18,762,919 (-1%)	18,840,329 (0.4%)	-25%
Meperidine (Pethidine)	5,765,954	5,834,294 (1%)	5,539,592 (-5%)	5,494,898* (-1%)	5,450,204 (-1%)	5,412,389 (-1%)	5,239,932 (-3%)	4,856,644 (-7%)	4,272,520 (-12%)	4,160,033 (-3%)	3,936,179 (-5%)	-32%
Total	50,713,010	56,273,194 (11%)	59,445,465 (6%)	35,962,089.84 (15%)	75,294,939 (11%)	82,874,845 (10%)	92,987,076 (12%)	98,456,163 (6%)	101,251,950 (6%)	115,272,706 (14%)	126,477,091 (10%)	149%

Number in parenthesis is percentage of change from previous year.

* For year 2000 data is not available, the average of 1999 and 2001 was taken.

Source: www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html Access date: 8/25/2010

Source for 2007 data - www.justice.gov/ndic/pubs33/33775/dlinks.htm

Adapted from: Manchikanti L, et al. Therapeutic use, abuse, and nonmedical use of opioids: A ten-year perspective. *Pain Physician* 2010; 13:401-435 (32).

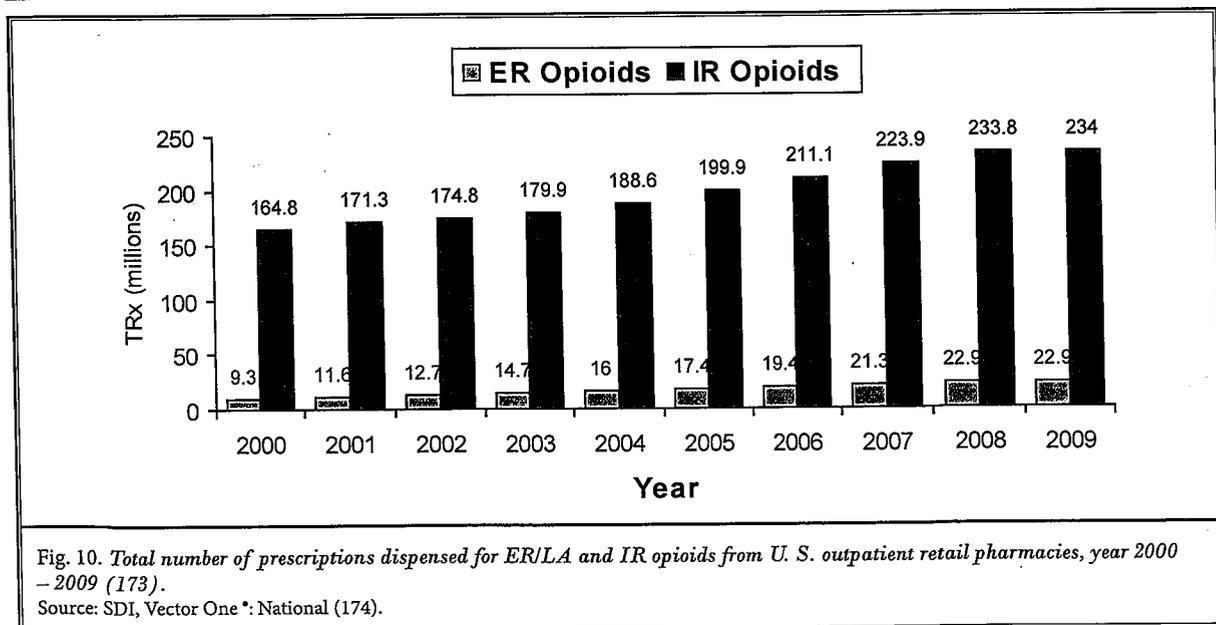


Fig. 10. Total number of prescriptions dispensed for ER/LA and IR opioids from U.S. outpatient retail pharmacies, year 2000 - 2009 (173).

Source: SDI, Vector One*; National (174).

ER opioids and from 223.9 million for IR opioids from 2007 as illustrated in Figure 10 (172-174). The data are even more compelling when compared from 2002 to 2009 with an increase from 9.3 million for ER opioids to 22.9 million, a 146% increase, and from 164.8 million to 234 million for IR opioids, a 42% increase with an annual increase of 21% for ER opioids and 6% for IR opioids. Most prescriptions were for hydrocodone and oxycodone-containing products (84.9%) and issued for short treatment courses, 19.1% for less than 2 weeks, 65.4% for 2-3 weeks. Of these, however, approximately 12% of the prescriptions were issued to those aged 10 to 29 years. This may signal a potential problem for this population, as this is also the population most likely to abuse drugs and develop addictions (172). In addition, the data also illustrates an 8-fold increase in stimulant prescriptions from 1991 to 2009 as illustrated in Fig. 11.

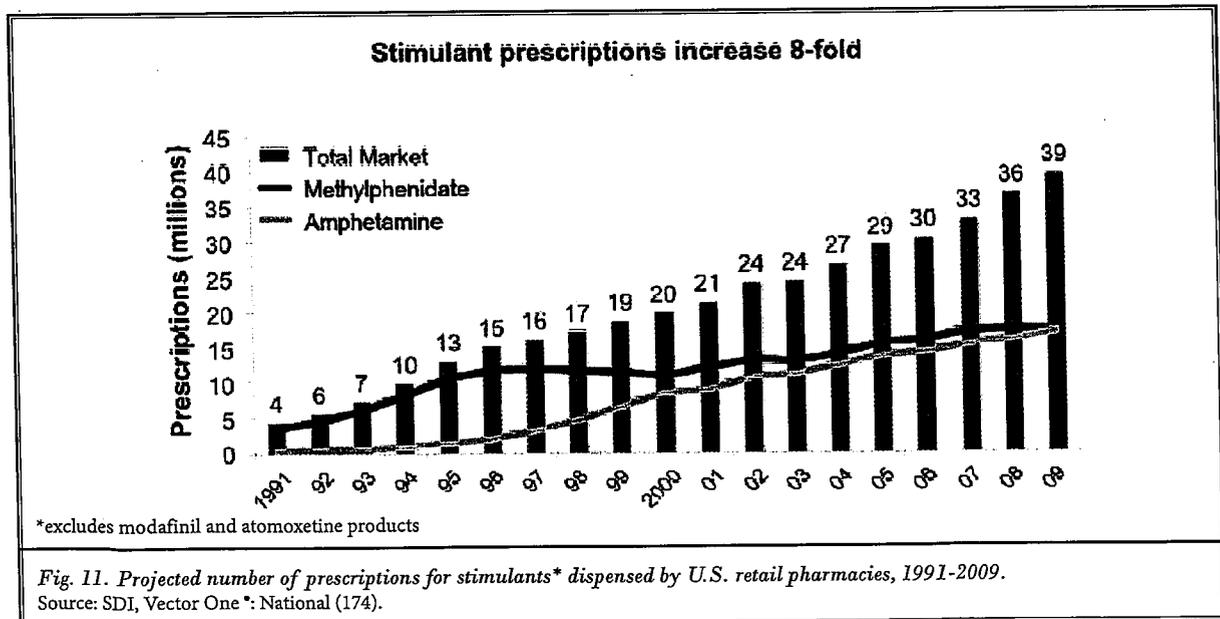
Table 6 illustrates hydrocodone with acetaminophen being the number one prescription from 2006 through 2011 (175). However, narcotic analgesics constitute number 4 in the proportion of patients treated in selected therapies with hypertension, topping at 42.4 million and narcotic analgesics at 15.6 million, constituting number 10 in spending in leading therapy areas with oncologicals constituting 23.2 billion and narcotic analgesics constituting 8.3 billion in 2011 as illustrated in Tables 7 and 8 and Fig. 12 (175).

The United Nations Office on Drugs and Crime, in an evaluation of the world supply of opioid, shows 90%

of the global consumption of morphine, fentanyl, and oxycodone registered in 2009 occurring in Australia, Canada, New Zealand, the United States and several European countries (60,85).

Another World Health Organization (WHO) report (87) showed that based on the statistics from the International Narcotics Control Board (INCB) in 2003, 6 developed countries accounted for 79% of global morphine consumption, whereas developing countries which represent 80% of the world population accounted for only about 6% of global morphine consumption. In addition, the most recent data showed that in 2007, 6 developed countries reported the highest level of morphine consumption and 132 of the 160 signatory countries that require reporting of consumption were below the global mean as illustrated in Fig. 13. This simply illustrates that millions of patients with moderate to severe pain caused by different diseases and conditions may not be getting treatment to alleviate their suffering in some countries, while more of them are receiving it in other countries such as the United States, which uses 99% of the world's supply of hydrocodone and 83% of the world's oxycodone (176-178).

Gram for gram, people in the United States consume more narcotic medication than any other nation worldwide. The International Narcotic Control Board, a division of the United States, estimates global pharmaceutical companies produce more than 75 tons a year of oxycodone, compared with 11.5 tons in 1999,



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Table 6. *Top medicines by prescriptions.*

DISPENSED PRESCRIPTIONS MN		2007	2008	2009	2010	2011
Total US Market		3,825	3,866	3,949	3,993	4,024
1	Hydrocodone/acetaminophen	120.9	125.5	129.4	132.1	136.7
2	Levothyroxine sodium	97.4	98.9	100.2	103.2	104.7
3	Simvastatin	49.0	68.0	84.1	94.4	96.8
4	Lisinopril	71.5	77.2	83.0	87.6	88.8
5	Amlodipine besylate	40.8	46.0	52.1	57.8	62.5
6	Omeprazole (RX)	27.7	35.8	45.6	53.5	59.4
7	Metformin HCL	49.2	51.6	53.8	57.0	59.1
8	Azithromycin	47.1	51.9	54.7	53.6	56.2
9	Amoxicillin	54.0	51.3	52.9	52.4	53.8
10	Alprazolam	41.4	43.3	45.3	47.7	49.1
11	Hydrochlorothiazide	48.5	48.5	47.9	47.8	48.1
12	Zolpidem tartrate	34.5	39.1	42.7	43.7	44.6
13	Atorvastatin	65.8	58.5	51.7	45.3	43.3
14	Furosemide	44.7	44.4	43.8	43.6	42.3
15	Oxycodone/acetaminophen	31.3	33.6	36.7	37.9	38.8
16	Fluticasone	23.9	26.2	30.1	34.8	38.4
17	Citalopram HBR	18.1	22.6	27.3	32.2	37.8
18	Metoprolol tartrate	43.5	38.4	41.1	38.9	37.8
19	Sertraline HCL	33.4	33.7	34.8	36.2	37.6
20	Metoprolol succinate	33.0	41.5	26.9	33.0	34.5
21	Warfarin sodium	34.4	34.9	35.7	35.6	33.9
22	Tramadol HCL	20.6	23.3	25.5	28.0	33.9
23	Potassium	36.7	35.8	35.2	34.7	33.7
24	Prednisone	25.9	27.1	27.8	28.7	33.7
25	Atenolol	45.0	42.0	39.5	36.4	33.4

Source: IMS Health, National Prescription Audit, Dec. 2011 (175).

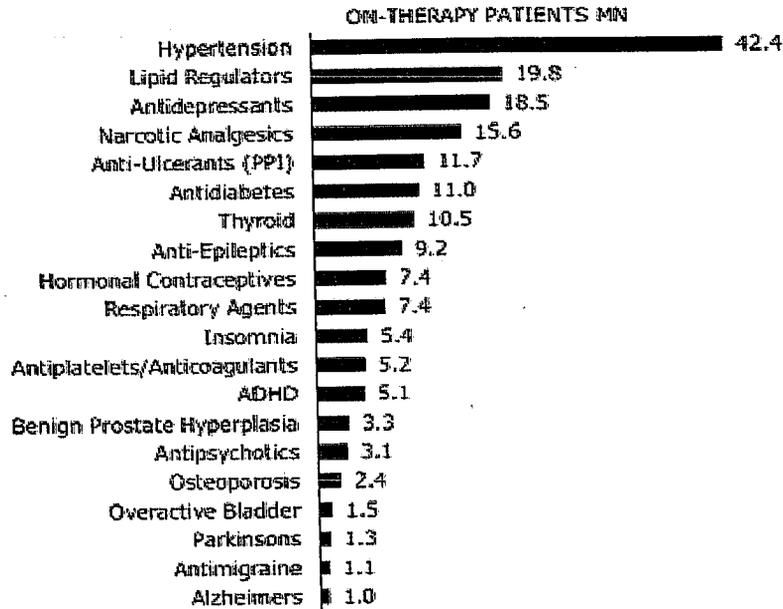
Notes: Report reflects prescription-bound products including insulins and excluding other products such as OTC. Table shows leading active-ingredients or ingredient fixed-combinations, and includes those produced by both branded and generic manufacturers. Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities. Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

Updated February 17, 2012.

of which more than 80% of is consumed in the United States. The International Narcotics Board also reports that U.S. demand for hydrocodone, the most commonly prescribed opioid, is about 27.4 million grams annually compared to 3,237 grams for Britain, France, Germany, and Italy combined (61,177,178).

Caudill-Slosberg et al (165) in one of the earliest evaluations demonstrated that opioid use doubled from 8% in 1980 to 16% in 2000. The data also illus-

trates that from 1999 to 2002, 4.2% of U.S. adults reported the use of opioid analgesics for pain within the past month (179). In a report of opioid use in one of the states in the United States (Utah) (180), the data showed that 20.8% of adults had been prescribed an opioid in the last year and that 29.1% of these prescriptions were for long-term pain. Sullivan et al (181) also showed over a 6 year period that the proportion of enrollees receiving opioids with a diagnosis of chronic



Source: IMS Health, LifeLink, Dec 2011

Fig. 12. Treated patients in selected therapy.

Table 7. Spending based on the therapeutic class.

SPENDING \$BN		2007	2008	2009	2010	2011
Total US Market		280.5	285.7	300.7	308.6	319.9
1	Oncologics	18.1	19.7	21.5	22.3	23.2
2	Respiratory Agents	15.1	16.0	18.1	19.3	21.0
3	Lipid Regulators	19.4	18.1	18.6	18.8	20.1
4	Antidiabetics	12.2	13.6	15.8	17.7	19.6
5	Antipsychotics	12.8	14.3	14.7	16.2	18.2
6	Autoimmune Diseases	7.6	8.6	9.7	10.6	12.0
7	Antidepressant	11.7	11.7	11.5	11.6	11.0
8	HIV Antivirals	6.2	7.1	8.2	9.3	10.3
9	Anti-Ulcerants	14.6	14.2	14.1	11.9	10.1
10	Narcotic Analgesics	6.7	7.3	8.0	8.4	8.3
11	ADHD	4.0	4.7	5.8	6.7	7.9
12	Platelet Aggregation Inhibitors	5.0	5.7	6.5	7.1	7.8
13	Angiotensin II Inhibitors	6.5	7.6	8.6	8.7	7.6
14	Multiple Sclerosis	3.4	4.1	5.0	5.8	7.1
15	Vaccines (Pure, Comb, Other)	5.9	5.0	4.7	5.7	6.3
16	Anti-Epileptics	10.0	11.1	6.9	5.6	5.9
17	Erythropoietins	4.1	4.5	4.7	4.8	5.2
18	Immunostimulating Agents	8.4	6.9	6.3	6.1	5.1
19	Hormonal Contraceptives	4.1	4.1	4.1	4.2	4.5
20	Antivirals, excl. Anti-HIV	3.6	3.9	4.8	3.2	3.7

Source: IMS Health, National Prescription Audit, Dec. 2011 (175).

Notes:

Therapy areas are based on proprietary IMS Health definitions. Report reflects prescription-bound products including insulins and excluding other products such as OTC. Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities. Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

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Table 8. *Top therapeutic classes by prescriptions.*

DISPENSED PRESCRIPTIONS MN		2007	2008	2009	2010	2011
Total US Market		3,825	3,866	3,949	3,993	4,024
1	Antidepressants	237	241	247	254	264
2	Lipid Regulators	233	242	254	260	260
3	Narcotic Analgesics	231	239	241	244	238
4	Antidiabetics	165	166	169	172	173
5	Ace Inhibitors (Plain & Combo)	159	163	166	168	164
6	Beta Blockers (Plain & Combo)	162	164	163	162	161
7	Respiratory Agents	147	147	152	153	153
8	Anti-Ulcerants	134	139	146	147	150
9	Diuretics	137	135	132	131	128
10	Anti-Epileptics	102	110	116	122	128
11	Tranquillizers	98	101	104	108	111
12	Thyroid Preparations	103	104	105	107	110
13	Calcium Antagonists (Plain & Combo)	87	90	93	96	98
14	Antirheumatic Non-Steroid	90	91	92	93	97
15	Hormonal Contraceptives	94	94	93	91	90
16	Angiotensin II Inhibitors	83	86	85	84	86
17	Broad Spectrum Penicillins	77	74	77	76	77
18	Macrolides & Similar Type Antibiotics	63	66	69	67	69
19	Hypnotics & Sedatives	58	60	63	63	63
20	Vitamins & Minerals	60	59	58	58	60

Source: IMS Health, National Prescription Audit, Dec. 2011 (175).

Appendix notes:

Therapy areas are based on proprietary IMS Health definitions. Report reflects prescription-bound products including insulins and excluding other products such as OTC. Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities. Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

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non-cancer pain and opioid prescriptions increase. Opioids are also used commonly in combination with sedative hypnotics. Vogt et al (182) in an evaluation of analgesic usage for low back pain and its impact on health care costs and service use showed that in 2001, a total of \$1.4 million was spent on opioids, which constituted 68% of prescriptions for analgesics.

The data from reports and pain management settings is disconcerting. Over 90% of patients received opioids for chronic pain management (32,169,172,183-188). Even more alarming, however, is the fact that the majority of the prescriptions are from outside pain

management settings. Volkow et al (172) showed that only a small proportion of prescriptions were from pain clinics or specialists from anesthesiology in 2009. Moreover, Deyo et al (31) illustrated that approximately 20% of patients in primary care settings were long-time opioid users with 61% receiving a course of opioids. In young veterans, Wu et al (189) showed that prevalence of chronic opioid use increased from 3% in 2003 to 4.5% in 2007. Patients on average were exposed to 2 different opioids and had 3 different opioid prescribers. Not surprisingly, 80% of the opioid prescriptions during the study were prescribed by pri-

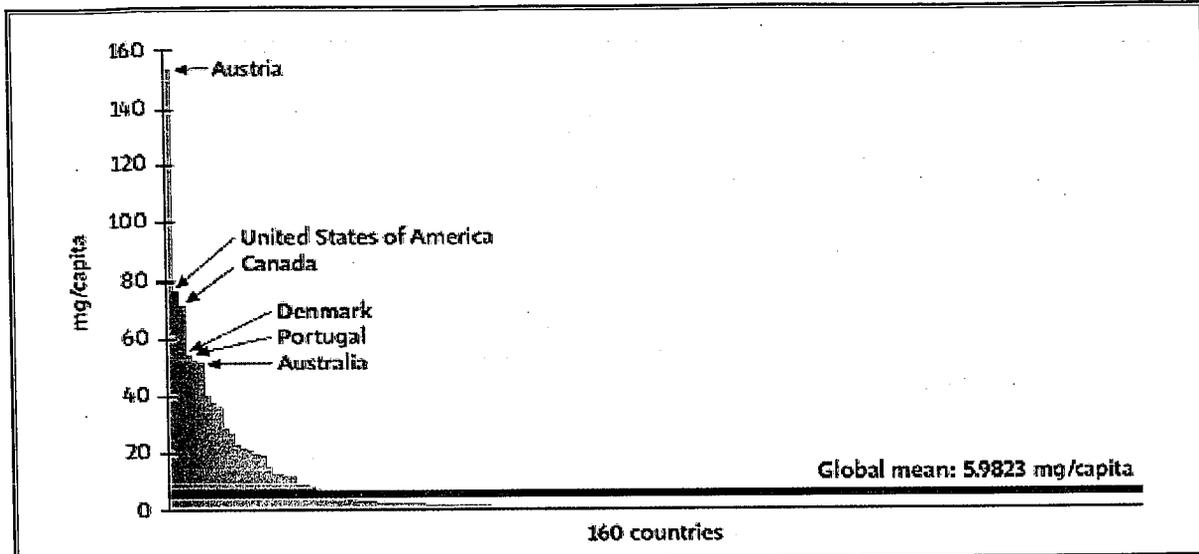


Fig. 13. Global morphine consumption in 2007 (mg/capita). Source: International Narcotics Control Board, United Nations data. Graphic created by the Pain and Policy Study Group, University of Wisconsin/WHO Collaborating Center, 2009.

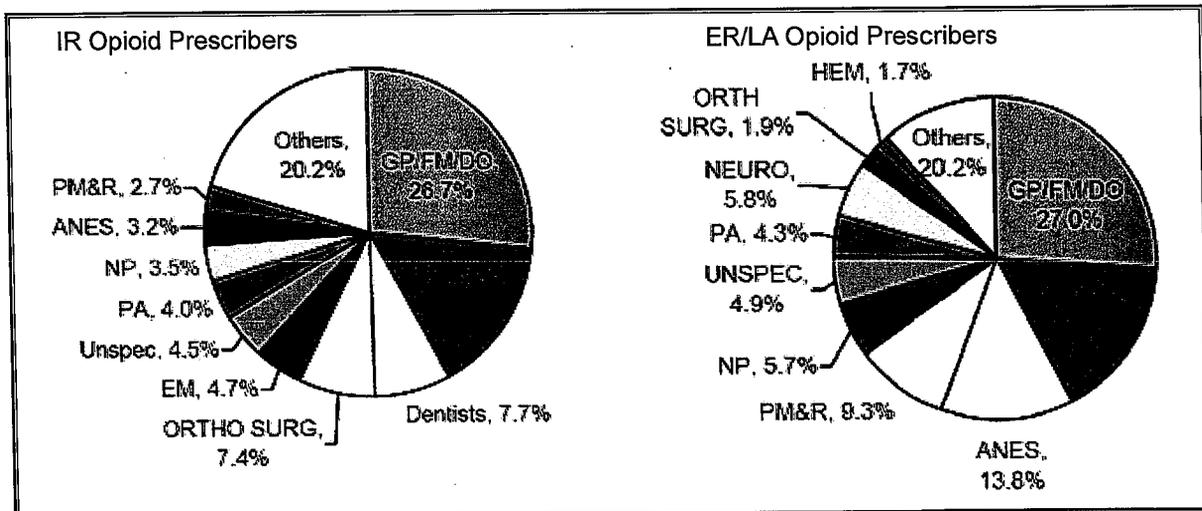


Fig. 14. Total number of prescriptions dispensed in the U.S. by top 10 prescribing specialties for IR and ER/LA opioids, year 2009 (173). Source: SDI, Vector One *: National (174).

many care providers, and less than 1% was from pain specialists.

In fact, the data illustrates that in 2009 (Fig. 14), among the top 10 specialties of those prescribing immediate release opioids were general practitioners/family medicine 26.7%, internal medicine 15.4%, anesthesiologists constituting 3.2%, and physical medicine and rehabilitation spe-

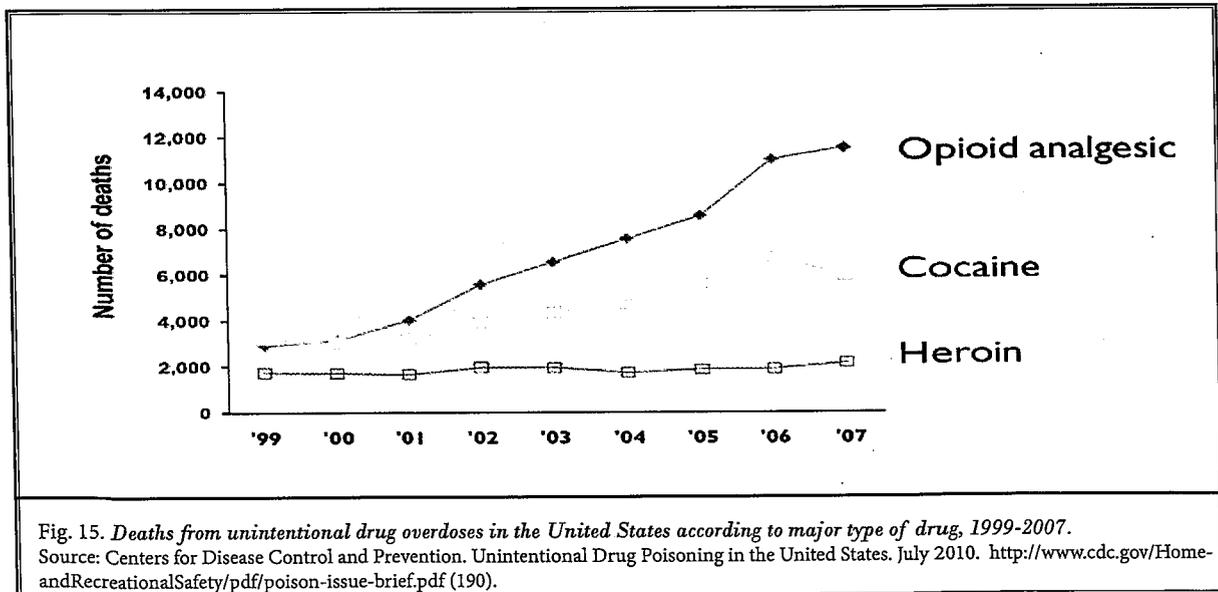
cialists constituting 2.7% (173,174). In contrast, for ER or long-acting opioids in 2009, anesthesiologists constituted 13.8% and physical medicine and rehabilitation constituted 9.3%, with general practitioners, family medical doctors, osteopaths, and internal medicine specialists still dominating the field with 27% and 16.8%, in essence exceeding their prescriptions of immediate release opioids (173,174).

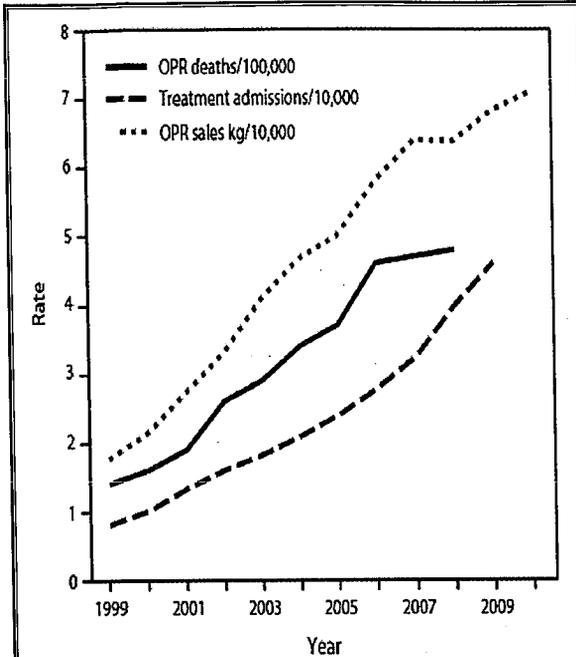
5.0 RELATIONSHIP OF ESCALATING OPIOID USE AND ADVERSE CONSEQUENCES

While numerous adverse effects have been reported, ever increasing opioid related fatalities, including drug poisoning deaths, are crucial. In the United States, in 2008, one or more prescription drugs were involved in 20,044 of the 27,153 deaths with a specified drug. Opioid pain relievers were involved in 14,800 drug overdose deaths, compared to 11,500 of 27,500 fatal unintended drug overdose deaths in 2007 – an increase of 3,300 in just one year (160). Alarmingly, in 2007 there were more opioid analgesic overdose deaths than overdoses involving heroin and cocaine combined (Fig. 15). In addition, during the same time frame, drug-related suicides also increased, with opioid analgesics being involved in roughly 3,000 of the 8,400 overdose deaths in the United States in 2007 that were suicide or of undetermined intent (190). Complicating these grave statistics, for every unintentional overdose death related to an opioid analgesic, 9 are admitted for substance abuse treatment, 35 visit emergency departments, 161 report drug abuse or dependence, and 461 report non-medical uses of opioid analgesics (34). Not surprisingly, in 2007, non-suicidal drug poisoning deaths exceeded both motor vehicle traffic and suicide deaths in 20 states, with data from Ohio illustrating that the number of deaths from unintentional drug poisoning surpassed the numbers of deaths from both suicide and motor vehicle crashes

combined (190-192). Thus, it has been concluded that opioid analgesics contributed to fatalities based on opioid abuse and increasing doses, doctor shopping, and other aspects of drug abuse as illustrated in Fig. 16 (160). The data from emergency department visits sadly illustrate that opioids, sedatives, and non-prescription sleep aides are often taken more than prescribed or solely for the feeling they cause, and that this trend is steadily increasing (170).

The Centers for Disease Control and Prevention (CDC) (34) also reported the percentage of prescription drug overdoses by risk group in the United States. This report showed that approximately 80% of prescribed low-doses (less than 100 mg of morphine equivalent dose per day – considered as high dose by many) were by a single practitioner, accounting for an estimated 20% of all prescription overdoses (Fig. 17). In contrast, among the remaining 20% of patients, 10% of prescribed high doses (greater than 100 mg morphine equivalent dose per day) (193-195) per day of opioids by single prescribers account for an estimated 40% of the prescription opioid overdoses (131,195). The remaining 10% of patients seeing multiple doctors and typically involved in drug diversion contribute to 40% of overdoses (152). Furthermore, among persons who died of opioid overdoses, a significant proportion did not have a prescription in their records for the opioid that killed them; in West Virginia, Utah, and Ohio, 25% to 66% of those who died of pharmaceutical overdose used opioids originally prescribed to someone





* Age-adjusted rates per 100,000 population for OPR deaths, crude rates per 10,000 population for OPR abuse treatment admissions, and crude rates per 10,000 population for kilograms of OPR sold.

Fig. 16. Rates of opioid pain reliever overdose death, opioid pain relief treatment admissions, and kilograms of opioid pain relievers sold – United States, 1999-2010.

Source: Centers for Disease Control and Prevention. Vital signs: Overdoses of prescription opioid pain relievers – United States, 1999-2008. MMWR. Morb. Mortal Wkly. Rep. 60, 1487-1492 (2011) (160).

else (152,192,196).

The responsible opioid prescription community considers that the adverse consequences of appropriately prescribed and used opioids are least considered, as the blame is placed predominantly on abuses and overuses (49,71,116-119). Consequently, it is coupled with a lack of evidence regarding long-term benefits and ample evidence that the increased prescription of opioids is fueling an epidemic of addiction and overdose deaths. This crisis is rooted in a lack of education and misinformation, leading to overprescribing and a tendency to focus on ineffective strategies (49,71,197-199). In fact, the majority of cases involving injury and death occur in people using opioids exactly as prescribed, not just those misusing or abusing them (71). Even more importantly, most studies indicate that patients on long-term opioid therapy are unlikely to stop even if analgesia and function are poor and safety issues arise. Frequently, despite good relief and improvement in function with modalities other than opioids including interventional techniques and surgery, patients continue on opioids (200-215).

Even though there is no evidence to support the previous teaching that long-acting opioids can provide better analgesia, and less risk for abuse than immediate release products (32,71,96,100,103,107,116-119,216), the use of higher doses, with a combination of short-acting and long-acting opioids, continues to escalate. Thus, it is believed that commencing long-acting opioid therapy is often the starting point for high dose opi-

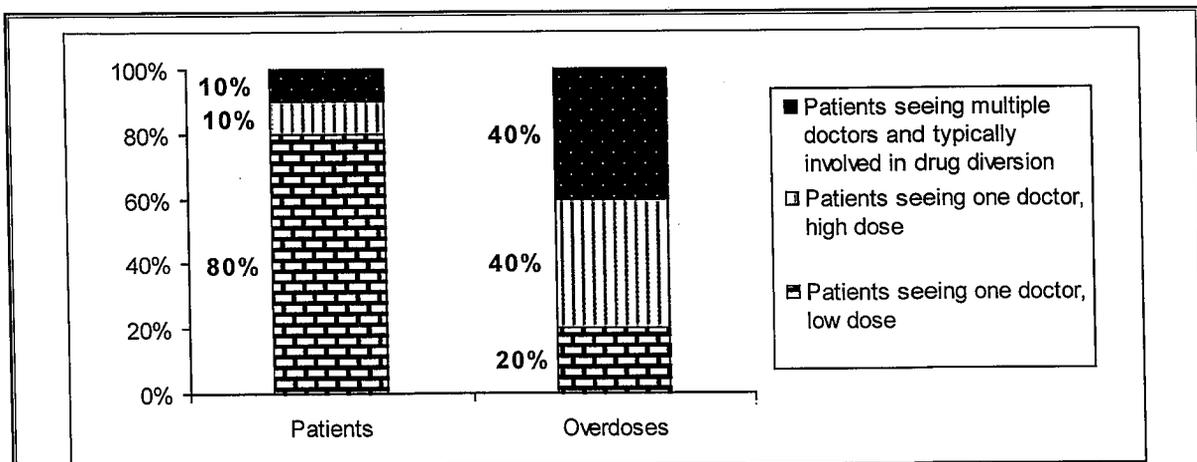


Fig. 17. Percentage of patients and prescription drug overdoses, by risk group – United States.

Source: Centers for Disease Control and Prevention. CDC grand rounds: Prescription drug overdoses – a U.S. epidemic. MMWR. Morb. Mortal Wkly. Rep. 61, 10-13 (2012) (34).

oid therapy, a practice that growing evidence suggests is harmful to patients and increases the black market availability of opioids through diversion (71,217-222).

Multiple studies in the literature (23,32,37,46-49,223-236) have reported an association between opioid prescribing and overall health status, with increased disability, medical costs, subsequent surgery, and continued or late opioid use. Overall, the epidemiologic studies are less positive with regards to improvement in function and quality of life with opioids in chronic pain patients (110,116-119,170,232,237). In fact, in an epidemiologic study from Denmark (23) where opioids are prescribed liberally for chronic pain, it was demonstrated that in patients receiving opioids, pain was worse, health care utilization was higher, and activity levels were lower compared to a matched cohort of chronic pain patients not using opioids. This study suggested that when opioids are prescribed liberally, even if some patients benefit, the overall population does not. Another study (33) also reported worse pain, higher health care utilization, and lower activity levels in opioid-treated patients compared to matched cohort of chronic pain patients not using opioids. Sjøgren et al (49) in a population-based cohort study on chronic pain and the role of opioids, showed that the odds of recovery from chronic pain were almost 4 times higher among individuals not using opioids compared with individuals using opioids. In addition, they also showed that use of strong opioids was associated with poor health-related quality of life, and higher risk of death. In addition,

opioid abuse in chronic pain has been highly prevalent, along with illicit drug usage in addition to misuse or abuse of therapeutic opioids (32,143-152,183-188).

CONCLUSION

What emerges from the available data utilized in this review is the conclusion that over the past 20 years there has been an escalation of the therapeutic use of opioids and other psychotherapeutics as well as their abuse and nonmedical use. As a consequence of the fact that hydrocodone has become the number one prescribed medication in America, it is not difficult to see the significant impact that this has had on the overall patterns of abuse and nonmedical use, particularly since the illicit use of prescribed psychotherapeutics (including opioids, which are currently at the top of that list) now overshadows the use of nonprescription illicit drugs. Drug dealers are no longer the primary source of illicit drugs. Our greatest enemy is now inappropriate prescribing patterns, based on a lack of knowledge, perceived safety, and undertreatment of pain.

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Medication Reconciliation for Controlled Substances — An "Ideal" Prescription-Drug Monitoring Program

Jeanmarie Perrone, M.D., and Lewis S. Nelson, M.D.

The United States is in the midst of an epidemic of misuse of prescription opioids and related deaths. Between 1997 and 2007, the use of prescription opioids more than quadrupled,¹ and it has become clear that the risk of opioid overdose is correlated with the quantity of these drugs being prescribed.² This liberalization of opioid prescribing can be attributed to a heightened focus on pain management, reflected in such developments as a Joint Commission mandate that pain be assessed as a "vital sign," the use of pain scores to measure patient satisfaction, and an extension of the indications for long-term opioid treatment to include chronic non-cancer-related pain. In this new model, physicians, dentists, and nurse practitioners — rather than drug cartels and street dealers — play prominent roles in escalating drug use. Paradoxically, there are simultaneous pressures to increase opioid prescribing for the benefit of individual patients and to reduce it for the sake of public health. As health care providers attempting to balance these mandates, we must advocate for more informed prescribing.

Since 1993, federal legislation has supported the formation of state-based prescription-drug monitoring programs (PDMPs) to track prescribing of controlled substances. In the pre-Internet era, such programs had limited effects, owing to the lag time inherent in reporting with paper documentation, the absence of off-hours access to the programs,

and the voluntary nature of reporting. Now, these programs are benefiting from renewed interest and increased funding; 42 states currently have operational PDMPs, and 6 have enacted legislation to develop programs.³

The White House Office of National Drug Control Policy, the Centers for Disease Control and Prevention, and the Food and Drug Administration suggest that state-based PDMPs should be expanded.⁴ Yet many clinicians are unaware of these programs, and their use varies among states and specialties.⁵ Research examining the effect of these monitoring systems has been limited by the variations and evolution of states' PDMP designs. As states develop, expand, or retool their PDMPs, it is worthwhile to analyze the current thinking regarding the usefulness and successful characteristics of the existing programs so as to enhance their future impact (see table).

Clinical evaluation of a new patient with chronic pain can be difficult without a comprehensive pain-management record. Although relying solely on the patient's history is generally acceptable and well intentioned, it may lead to dangerous misprescribing. Furthermore, primary care providers who embrace the mandate to treat patients' chronic pain are faced with guidelines suggesting the use of patient-provider agreements ("pain contracts") and urine drug screening. Some physicians may feel uncomfortable with the mistrust implied by such confrontational

approaches and may find that a highly functional PDMP readily alerts its users to signs of aberrant drug-procurement behavior. A benefit for clinicians and patients is the opportunity to intervene immediately when aberrant behavior is first noted and while the patient is in the medical setting. In addition, a PDMP may identify patients who are receiving multiple legitimate prescriptions for opioids or benzodiazepines and are at risk for complications from polypharmacy.

Web-based PDMPs solve many of the problems that limited earlier, fax-based systems, but they also raise new concerns. In a recent survey of prescribers, respondents cited barriers to use of PDMPs that included "time" and "access issues" but not computer availability (see graph). To facilitate access, a simple log-on with user-specified passwords may improve utilization. As an added benefit, prescribers may monitor use of their own Drug Enforcement Administration (DEA) number to detect forged or stolen prescriptions. In addition, PDMPs should allow access by certain non-prescribers, especially medical examiners, researchers, and law-enforcement officials. Other hurdles to provider verification, including complicated application and notarization procedures, limit prescriber access and should be reduced. Ultimately, prescribers will have to be educated about PDMPs if voluntary compliance is to be improved and routine use encouraged.

The collection and provision

Characteristics of an Ideal Prescription-Drug Monitoring Program.*

Ease of access
 Standardized content
 Real-time updates
 Mandatory pharmacy reporting
 Monitoring of prescribing of drugs in DEA Schedules 2–5 and “drugs of concern”
 Interstate accessibility
 Confidentiality and security
 Support for public health initiatives and research
 Capability for strictly monitored access by nonprescribers

* DEA denotes Drug Enforcement Administration.

of consistent information at all stages of the prescribing process would unify reporting expectations and simplify communication. Each PDMP should include contact information of the prescriber, recipient, and pharmacy; the standardized generic name of the drug, the dose prescribed, and the number of units dispensed; the dates of both prescribing and dispensing; and other relevant information (e.g., DEA number).

Some states have considered logging prescriptions at the time of prescribing, but most require entry at the dispensing pharmacy. Unfortunately, pharmacy data entry is time-consuming, and data are uploaded to the prescription database at variable intervals — from immediately or once daily to weekly or monthly. For a PDMP to be most valuable in clinical practice, it must be current, which would require pharmacists to promptly upload information. It's easier to do so in states that use serialized, bar-coded prescription paper, and it would be even easier with an e-prescribing system that allowed pharmacies direct access to prescriptions. By eliminating paper, e-prescribing

could greatly reduce prescription fraud and “doctor shopping” by nonmedical drug users.

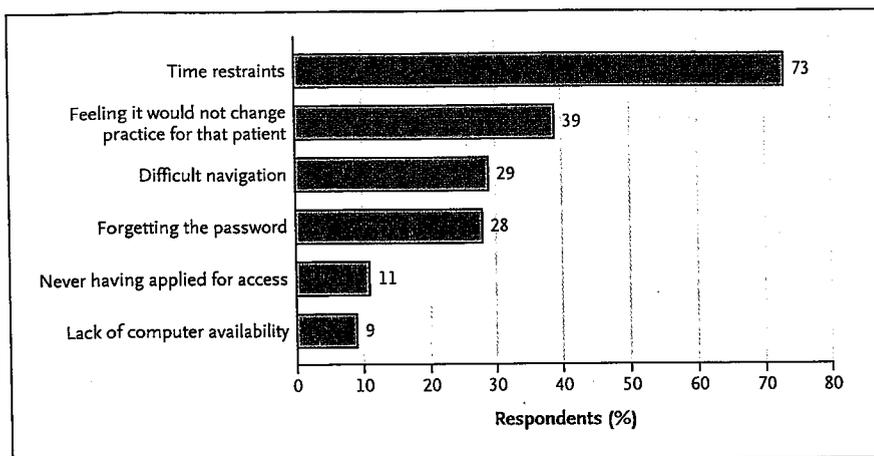
A PDMP should monitor all controlled substances that fall within DEA Schedule 2 (e.g., oxycodone), Schedule 3 (e.g., hydrocodone), Schedule 4 (e.g., benzodiazepines), and Schedule 5 (e.g., low-dose codeine cough suppressants), and including nonopioids such as stimulants (e.g., methylphenidate), since there is misuse in all these categories. In addition, monitoring of certain unscheduled medications, such as the muscle relaxant carisoprodol, may assist in determining the need for enhanced surveillance or stricter control.

In urban areas that straddle state borders, interstate collaboration regarding PDMP access is essential. A network that was recently implemented by 20 states, funded by the pharmaceutical industry and organized by state pharmacy boards, allows interstate sharing of PDMPs (www.nabp.net/programs/pmp-interconnect/nabp-pmp-interconnect/index.php). The perspective provided by insurance carriers and the military and veterans' health systems may complement the overall strategy for

improving pain care and mitigate the risk of prescription-drug abuse.

As plans are optimized, barriers to implementation must be addressed. There are realistic concerns that a PDMP is burdensome for prescribers and dispensers and may inappropriately reduce the amount of opioid analgesic prescribed. Given the required balance between optimizing pain management and the excessive accessibility of opioids, the effect of any unintended consequence remains unclear. Internet database-security and patient-confidentiality measures are needed, particularly when programs span state lines, to address potential issues of compliance with the Health Insurance Portability and Accountability Act. Lingering concerns about punitive action for perceived misprescribing may lead to reluctance among physicians and medical boards to adopt PDMPs. The costs of implementing such programs will probably be borne by taxpayers, the insurance and pharmaceutical industries, and individual patients, prescribers, and dispensers. In addition to the infrastructural costs, the time and effort required to use the PDMP, particularly if its use is mandated, must be considered.

Clinicians are facing the challenges of caring for an increasing number of patients with chronic pain. Safety measures, including the expanded use of well-designed PDMPs, must be instituted to address the issues of opioid prescribing in this growing population. PDMPs are no panacea; a multimodal approach is required. Cultural change related to the expectations of patients and providers, new medications and formulations, and extensive



Reasons That Prescribers Are Not Using a PDMP if Available.

Data are from the Prescription Opioid Misuse Academy, American College of Medical Toxicology, 2012. PDMP denotes prescription-drug monitoring program.

education at many levels can contribute to a reduction in opioid misuse, even as appropriate access to this pharmacotherapy is maintained. As the number of deaths associated with prescription-drug use surpasses the number of fatalities from motor vehicle crashes in many states, we can

learn from the success of auto-safety innovations that have mitigated mortality despite increased automobile use over the past three decades. We should initiate active safety measures to address the growing rates of illness and death associated with the pharmaceuticalization of the 21st century.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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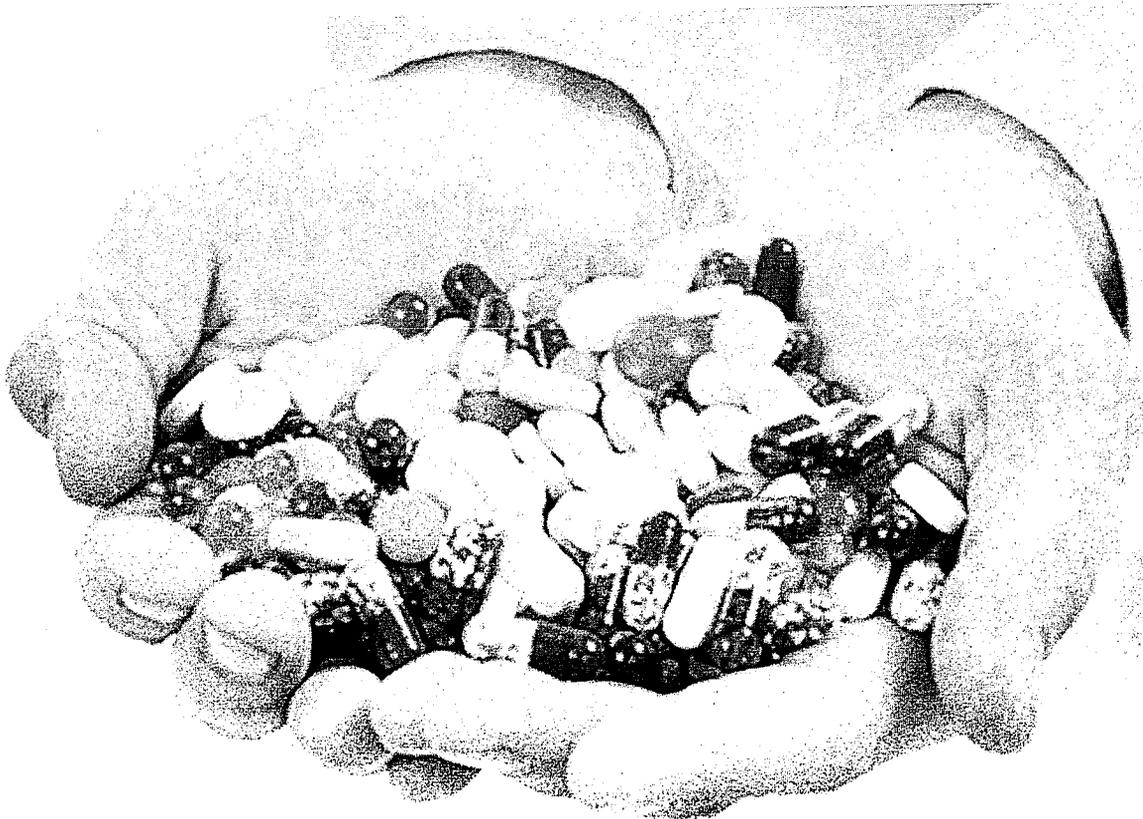


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WASHINGTON, June 24, 2013 — A study released in June 2013 by the Department of Health and Human Services reveals alarming, although not surprising, problems of prescription medication practices among doctors and pharmacies servicing Medicare patients. According to the study, the problems include over-prescribing, over-billing, and over-medicating. Medicare part D, Medicaid, and ultimately the tax-payer pays for these problems.

There were a total of 1.1 million prescribers who ordered Part D drugs for Medicare beneficiaries in 2009. These prescribers included many specialties, such as general-care physicians, dentists, and nurse practitioners. These individuals ordered over one billion prescriptions during the year. In total, Medicare paid \$70.7 billion for these prescriptions. On average, these 1.1 million prescribers each ordered Part D prescriptions costing \$64,102. On average, each prescriber ordered prescriptions for 80 beneficiaries and averaged six prescriptions per beneficiary.

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"The review found more than 2,200 doctors whose records stood out in one of five areas: prescriptions per patient, brand name drugs, painkillers and other addictive drugs or the number of pharmacies that dispensed their orders," wrote ProPublica reporters in a press release.

More than half of 736 physicians studied wrote prescriptions for extremely high amounts of controlled substances that have the potential for addiction and abuse. The most commonly prescribed drugs, the report found, include antibiotics, antidepressants and opioid painkillers. The most commonly abused painkillers are oxycodone, morphine, and hydrocodone. Overdoses of these prescription painkillers—called opioids—are among the leading causes of accidental death in the United States. These are dangerous medications, prescriptions written mostly for the elderly and disabled.

Jennifer St. Sauver, Ph.D., the study author said, "Often when people talk about health conditions they're talking about chronic conditions such as heart disease or diabetes. However, the second most common prescription was for antidepressants — that suggests mental health is a huge issue and is something we should focus on. And the third most common drugs were opioids, which is a bit concerning considering their addicting nature."

The finding also showed women and the elderly receive more prescriptions overall than other patients

The Centers for Medicare & Medicaid Services (CMS) contracts with private insurance companies and provides drug coverage to beneficiaries who choose to enroll. In 2011, 36 million beneficiaries were enrolled. The Centers for Disease Control and Prevention (CDC) has characterized prescription drug abuse as an epidemic.

The study showed one doctor in California with what CMS calls 'extreme outliers' with regard to prescriptions cost Medicare \$9.7 million. According to the study, extreme outliers are physicians whose patters raise questions about whether their prescriptions are "legitimate or necessary."

The total cost of prescriptions written by 'extreme outliers' totaled \$352 million, according to the report.

While the study specifically highlighted Medicare patients, it is likely this same pattern of abuse replicates in other patients.

Until the Center for Medicare Services provides more oversight to prescription drugs, you could be at risk.

Patients should educate themselves on their medications, and can take advantage of pharmacist counseling to glean information. They can also ask pharmacist for black box warnings or contraindications to their medications. Pharmacists often offer drug reviews and many times will communicate with physicians when there are concerns about certain drugs.

—

Dr Peter Lind practices metabolic and neurologic chiropractic in his wellness clinic in Salem, Oregon. USA. He is the author of three books on health, one novel, and hundreds of wellness articles. His clinical specialty is in physical, nutritional, and emotional stress.

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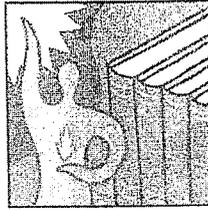


Prescription drugs: Over prescribed, over billed and over medicated



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The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy

Art Van Zee, MD

I focus on issues surrounding the promotion and marketing of controlled drugs and their regulatory oversight. Compared with noncontrolled drugs, controlled drugs, with their potential for abuse and diversion, pose different public health risks when they are overpromoted and highly prescribed. An in-depth analysis of the promotion and marketing of OxyContin illustrates some of the associated issues.

Modifications of the promotion and marketing of controlled drugs by the pharmaceutical industry and an enhanced capacity of the Food and Drug Administration to regulate and monitor such promotion can have a positive impact on the public health. (*Am J Public Health*. 2009;99:221–227. doi: 10.2105/AJPH.2007.131714)

CONTROLLED DRUGS, WITH their potential for abuse and diversion, can pose public health risks that are different from—and more problematic than—those of uncontrolled drugs when they are overpromoted and highly

prescribed. An in-depth analysis of the promotion and marketing of OxyContin (Purdue Pharma, Stamford, CT), a sustained-release oxycodone preparation, illustrates some of the key issues. When Purdue Pharma introduced OxyContin in 1996, it was aggressively marketed and highly promoted. Sales grew from \$48 million in 1996 to almost \$1.1 billion in 2000.¹ The high availability of OxyContin correlated with increased abuse, diversion, and addiction, and by 2004 OxyContin had become a leading drug of abuse in the United States.²

Under current regulations, the Food and Drug Administration (FDA) is limited in its oversight of the marketing and promotion of controlled drugs. However, fundamental changes in the promotion and marketing of controlled drugs by the pharmaceutical industry, and an enhanced capacity of the FDA to regulate and monitor such promotion, can positively affect public health.

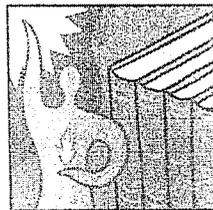
OxyContin's commercial success did not depend on the merits

of the drug compared with other available opioid preparations. The *Medical Letter on Drugs and Therapeutics* concluded in 2001 that oxycodone offered no advantage over appropriate doses of other potent opioids.³ Randomized double-blind studies comparing OxyContin given every 12 hours with immediate-release oxycodone given 4 times daily showed comparable efficacy and safety for use with chronic back pain⁴ and cancer-related pain.^{5,6} Randomized double-blind studies that compared OxyContin with controlled-release morphine for cancer-related pain also found comparable efficacy and safety.^{7–9} The FDA's medical review officer, in evaluating the efficacy of OxyContin in Purdue's 1995 new drug application, concluded that OxyContin had not been shown to have a significant advantage over conventional, immediate-release oxycodone taken 4 times daily other than a reduction in frequency of dosing.¹⁰ In a review of the medical literature, Chou et al. made similar conclusions.¹¹

The promotion and marketing of OxyContin occurred during a recent trend in the liberalization of the use of opioids in the treatment of pain, particularly for chronic non-cancer-related pain. Purdue pursued an “aggressive” campaign to promote the use of opioids in general and OxyContin in particular.^{12–17} In 2001 alone, the company spent \$200 million¹⁸ in an array of approaches to market and promote OxyContin.

PROMOTION OF OXYCONTIN

From 1996 to 2001, Purdue conducted more than 40 national pain-management and speaker-training conferences at resorts in Florida, Arizona, and California. More than 5000 physicians, pharmacists, and nurses attended these all-expenses-paid symposia, where they were recruited and trained for Purdue's national speaker bureau.^{19(p22)} It is well documented that this type of pharmaceutical company symposium influences physicians' prescribing,



even though the physicians who attend such symposia believe that such enticements do not alter their prescribing patterns.²⁰

One of the cornerstones of Purdue's marketing plan was the use of sophisticated marketing data to influence physicians' prescribing. Drug companies compile prescriber profiles on individual physicians—detailing the prescribing patterns of physicians nationwide—in an effort to influence doctors' prescribing habits. Through these profiles, a drug company can identify the highest and lowest prescribers of particular drugs in a single zip code, county, state, or the entire country.²¹ One of the critical foundations of Purdue's marketing plan for OxyContin was to target the physicians who were the highest prescribers for opioids across the country.^{11,12-17,22} The resulting database would help identify physicians with large numbers of chronic-pain patients. Unfortunately, this same database would also identify which physicians were simply the most frequent prescribers of opioids and, in some cases, the least discriminate prescribers.

A lucrative bonus system encouraged sales representatives to increase sales of OxyContin in their territories, resulting in a large number of visits to physicians with high rates of opioid prescriptions, as well as a multifaceted information campaign aimed at them. In 2001, in addition to the average sales representative's annual salary of \$55 000, annual bonuses averaged \$71 500, with a range of \$15 000 to nearly \$240 000. Purdue paid \$40 million in sales

incentive bonuses to its sales representatives that year.¹⁹

From 1996 to 2000, Purdue increased its internal sales force from 318 sales representatives to 671, and its total physician call list from approximately 33 400 to 44 500 to approximately 70 500 to 94 000 physicians.¹⁹ Through the sales representatives, Purdue used a patient starter coupon program for OxyContin that provided patients with a free limited-time prescription for a 7- to 30-day supply. By 2001, when the program was ended, approximately 34 000 coupons had been redeemed nationally.¹⁹

The distribution to health care professionals of branded promotional items such as OxyContin fishing hats, stuffed plush toys, and music compact discs ("Get in the Swing With OxyContin") was unprecedented for a schedule II opioid, according to the Drug Enforcement Administration.¹⁹

Purdue promoted among primary care physicians a more liberal use of opioids, particularly sustained-release opioids. Primary care physicians began to use more of the increasingly popular OxyContin; by 2003, nearly half of all physicians prescribing OxyContin were primary care physicians.¹⁹ Some experts were concerned that primary care physicians were not sufficiently trained in pain management or addiction issues.²³ Primary care physicians, particularly in a managed care environment of time constraints, also had the least amount of time for evaluation and follow-up of patients with complicated chronic pain.

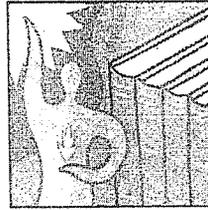
Purdue "aggressively" promoted the use of opioids for use in

TABLE 1—Distribution of OxyContin, Oxycodone (Excluding OxyContin), and Hydrocodone per 100 000 Population: Virginia, West Virginia, and Kentucky, 2000

State and County	Distribution in Grams per 100 000 Population		
	OxyContin	Oxycodone (Excluding OxyContin)	Hydrocodone
Virginia			
Dickenson	25 801	2 777	16 692
Lee	23 398	6 232	8 445
Buchanan	19 138	3 235	15 996
Scott	18 328	4 946	12 274
Roanoke City	17 856	2 808	7 201
Tazewell	17 135	3 482	27 714
Winchester City	15 242	6 764	14 057
Manassas City	14 735	5 920	5 511
Fauquier	14 396	6 935	4 434
Wythe	14 236	3 165	8 812
Kentucky			
Cumberland	22 113	1 486	8 148
Perry	20 996	6 145	27 413
Harlan	19 359	3 121	10 141
Leslie	18 221	4 017	16 925
Whitley	13 438	3 410	19 532
Greenup	13 222	5 151	44 872
McCreary	12 573	3 026	12 996
Clinton	12 517	2 911	14 892
Bell	11 739	3 118	26 037
Clay	11 563	3 260	21 093
West Virginia			
Pocahontas	17 318	3 605	17 651
Raleigh	16 813	5 959	8 718
Berkeley	16 299	5 254	5 009
Logan	16 153	2 224	22 950
McDowell	15 770	3 200	24 235
Greenbrier	15 752	2 539	12 380
Mercer	15 040	3 306	21 175
Hancock	13 465	4 327	8 831
Harrison	12 409	3 407	12 658
Cabell	11 665	3 608	13 018
US average	3 750	1 761	5 083

Source. Office of Diversion Control, Drug Enforcement Administration.⁶⁷

Note. Data are for the counties or independent cities with the highest quantities of opioids (in grams) prescribed in each of the 3 states.



the “non-malignant pain market.”^{15(p187)} A much larger market than that for cancer-related pain, the non-cancer-related pain market constituted 86% of the total opioid market in 1999.¹⁷ Purdue’s promotion of OxyContin for the treatment of non-cancer-related pain contributed to a nearly tenfold increase in OxyContin prescriptions for this type of pain, from about 670 000 in 1997 to about 6.2 million in 2002, whereas prescriptions for cancer-related pain increased about fourfold during that same period.¹⁹ Although the science and consensus for the use of opioids in the treatment of acute pain or pain associated with cancer are robust, there is still much controversy in medicine about the use of opioids for chronic non-cancer-related pain, where their risks and benefits are much less clear. Prospective, randomized, controlled trials lasting at least 4 weeks that evaluated the use of opioids for chronic, non-cancer-related pain showed statistically significant but small to modest improvement in pain relief, with no consistent improvement in physical functioning.^{24–38} A recent review of the use of opioids in chronic back pain concluded that opioids may be efficacious for short-term pain relief, but longer-term efficacy (>16 weeks) is unclear.³⁹

In the long-term use of opioids for chronic non-cancer-related pain, the proven analgesic efficacy must be weighed against the following potential problems and risks: well-known opioid side effects, including respiratory depression, sedation, constipation, and nausea; inconsistent improvement in functioning; opioid-induced hyperalgesia; adverse

hormonal and immune effects of long-term opioid treatment; a high incidence of prescription opioid abuse behaviors; and an ill-defined and unclarified risk of iatrogenic addiction.⁴⁰

MISREPRESENTING THE RISK OF ADDICTION

A consistent feature in the promotion and marketing of OxyContin was a systematic effort to minimize the risk of addiction in the use of opioids for the treatment of chronic non-cancer-related pain. One of the most critical issues regarding the use of opioids in the treatment of chronic non-cancer-related pain is the potential of iatrogenic addiction. The lifetime prevalence of addictive disorders has been estimated at 3% to 16% of the general population.⁴¹ However, we lack any large, methodically rigorous prospective study addressing the issue of iatrogenic addiction during long-term opioid use for chronic nonmalignant pain.⁴²

In much of its promotional campaign—in literature and audiotapes for physicians, brochures and videotapes for patients, and its “Partners Against Pain” Web site—Purdue claimed that the risk of addiction from OxyContin was extremely small.^{43–49}

Purdue trained its sales representatives to carry the message that the risk of addiction was “less than one percent.”^{50(p99)} The company cited studies by Porter and Jick,⁵¹ who found iatrogenic addiction in only 4 of 11 882 patients using opioids and by Perry and Heidrich,⁵² who found no addiction among 10 000 burn patients

treated with opioids. Both of these studies, although shedding some light on the risk of addiction for acute pain, do not help establish the risk of iatrogenic addiction when opioids are used daily for a prolonged time in treating chronic pain. There are a number of studies, however, that demonstrate that in the treatment of chronic non-cancer-related pain with opioids, there is a high incidence of prescription drug abuse. Prescription drug abuse in a substantial minority of chronic-pain patients has been demonstrated in studies by Fishbain et al. (3%–18% of patients),⁵³ Hoffman et al. (23%),⁵⁴ Kouyanou et al. (12%),⁵⁵ Chabal et al. (34%),⁵⁶ Katz et al. (43%),⁵⁷ Reid et al. (24%–31%),⁵⁸ and Michna et al. (45%).⁵⁹ A recent literature review showed that the prevalence of addiction in patients with long-term opioid treatment for chronic non-cancer-related pain varied from 0% to 50%, depending on the criteria used and the subpopulation studied.⁶⁰

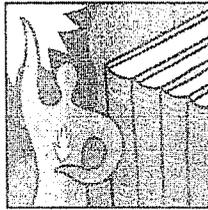
Misrepresenting the risk of addiction proved costly for Purdue. On May 10, 2007, Purdue Frederick Company Inc, an affiliate of Purdue Pharma, along with 3 company executives, pled guilty to criminal charges of misbranding OxyContin by claiming that it was less addictive and less subject to abuse and diversion than other opioids, and will pay \$634 million in fines.⁶¹

Although research demonstrated that OxyContin was comparable in efficacy and safety to other available opioids,^{11,63} marketing catapulted OxyContin to blockbuster drug status. Sales escalated from \$44 million (316 000

prescriptions dispensed) in 1996 to a 2001 and 2002 combined sales of nearly \$3 billion (over 14 million prescriptions).¹⁹

The remarkable commercial success of OxyContin, however, was stained by increasing rates of abuse and addiction. Drug abusers learned how to simply crush the controlled-release tablet and swallow, inhale, or inject the high-potency opioid for an intense morphinelike high.⁶⁴ There had been some precedence for the diversion and abuse of controlled-release opioid preparations. Purdue’s own MS Contin had been abused in the late 1980s in a fashion similar to how OxyContin was later to be; by 1990, MS Contin had become the most abused prescription opioid in one major metropolitan area.⁶⁵ Purdue’s own testing in 1995 had demonstrated that 68% of the oxycodone could be extracted from an OxyContin tablet when crushed.⁶⁶

Opioid prescribing has had significant geographical variations. In some areas, such as Maine, West Virginia, eastern Kentucky, southwestern Virginia, and Alabama, from 1998 through 2000, hydrocodone and (non-OxyContin) oxycodone were being prescribed 2.5 to 5.0 times more than the national average. By 2000, these same areas had become high OxyContin-prescribing areas—up to 5 to 6 times higher than the national average in some counties (Table 1).⁶⁷ These areas, in which OxyContin was highly available, were the first in the nation to witness increasing OxyContin abuse and diversion, which began surfacing in 1999 and 2000.²³



From 1995 to 2001, the number of patients treated for opioid abuse in Maine increased 460%, and from 1997 to 1999 the state had a 400% increase in the number of chronic hepatitis C cases reported.⁶⁸ In eastern Kentucky from 1995 to 2001, there was a 500% increase in the number of patients entering methadone maintenance treatment programs, about 75% of whom were OxyContin dependent (Mac Bell, administrator, Narcotics Treatment Programs, Kentucky Division of Substance Abuse, written communication, March 2002). In West Virginia, the first methadone maintenance treatment program opened in August 2000, largely in response to the increasing number of people with OxyContin dependence. By October 2003, West Virginia had 7 methadone maintenance treatment clinics with 3040 patients in treatment (M. Moore, Office of Behavioral Health Services, Office of Alcoholism and Drug Abuse, West Virginia, written communication, March 16, 2004). In southwestern Virginia, the first methadone maintenance treatment program opened in March 2000, and within 3 years it had 1400 admissions (E. Jennings, Life Center of Galax, Galax, Virginia, written communication, March 12, 2004).

With increasing diversion and abuse, opioid-related overdoses escalated. In southwest Virginia, the number of deaths related to opioid prescriptions increased 830%, from 23 in 1997 to 215 in 2003 (William Massello III, MD, assistant chief medical examiner, Office of Chief Medical Examiner, Western District, Virginia Department of Health, written

communication, January 12, 2007). The high availability of OxyContin in these 5 regions seemed to be a simple correlate of its abuse, diversion, and addiction.

With the growing availability of OxyContin prescriptions, the once-regional problem began to spread nationally. By 2002, OxyContin accounted for 68% of oxycodone sales.⁶⁹ Lifetime nonmedical use of OxyContin increased from 1.9 million to 3.1 million people between 2002 and 2004, and in 2004 there were 615 000 new nonmedical users of OxyContin.⁷⁰ By 2004, OxyContin had become the most prevalent prescription opioid abused in the United States.²

The increasing OxyContin abuse problem was an integral part of the escalating national prescription opioid abuse problem. Liberalization of the use of opioids, particularly for the treatment of chronic non-cancer-related pain, increased the availability of all opioids as well as their abuse. Nationwide, from 1997 to 2002, there was a 226%, 73%, and 402% increase in fentanyl, morphine, and oxycodone prescribing, respectively (in grams per 100 000 population). During that same period, the Drug Abuse Warning Network reported that hospital emergency department mentions for fentanyl, morphine, and oxycodone increased 641%, 113%, and 346%, respectively.⁷¹ Among new initiates to illicit drug use in 2005, a total of 2.1 million reported prescription opioids as the first drug they had tried, more than for marijuana and almost equal to the number of new cigarette smokers (2.3 million).⁷² Most

abusers of prescription opioids get their diverted drugs directly from a doctor's prescription or from the prescriptions of friends and family.⁷³

In terms of illicit drug abuse, prescription opioids are now ahead of cocaine and heroin and second only to marijuana.⁷² Mortality rates from drug overdose have climbed dramatically; by 2002, unintentional overdose deaths from prescription opioids surpassed those from heroin and cocaine nationwide.⁷⁴ Nationally, as well as regionally, the high availability of OxyContin and all prescription opioids was correlated with high rates of abuse and diversion.

THE FOOD AND DRUG ADMINISTRATION

Under the Food, Drug, and Cosmetics Act and implementing regulations, the FDA regulates the advertising and promotion of prescription drugs and is responsible for ensuring that prescription drug advertising and promotion are truthful, balanced, and accurately communicated. There is no distinction in the act between controlled and noncontrolled drugs regarding the oversight of promotional activities. Although regulations require that all promotional materials for prescription drugs be submitted to the FDA for review when the materials are initially disseminated or used, it is generally not required that these materials be approved by the FDA prior to their use. The FDA has a limited number of staff for overseeing the enormous amount of promotional materials. In 2002,

for example, 39 FDA staff members were responsible for reviewing roughly 34 000 pieces of promotional materials.¹⁹ This limited staffing significantly diminishes the FDA's ability to ensure that the promotion is truthful, balanced, and accurately communicated.

In 1998, Purdue distributed 15 000 copies of an OxyContin video to physicians without submitting it to the FDA for review, an oversight later acknowledged by Purdue. In 2001, Purdue submitted to the FDA a second version of the video, which the FDA did not review until October 2002—after the General Accounting Office inquired about its content. After its review, the FDA concluded that the video minimized the risks from OxyContin and made unsubstantiated claims regarding its benefits to patients.¹⁹

When OxyContin entered the market in 1996, the FDA approved its original label, which stated that iatrogenic addiction was "very rare" if opioids were legitimately used in the management of pain. In July 2001, to reflect the available scientific evidence, the label was modified to state that data were not available for establishing the true incidence of addiction in chronic-pain patients. The 2001 labeling also deleted the original statement that the delayed absorption of OxyContin was believed to reduce the abuse liability of the drug.¹⁹ A more thorough review of the available scientific evidence prior to the original labeling might have prevented some of the need for the 2001 label revision.



CONCLUSIONS

OxyContin appears to be as efficacious and safe as other available opioids and as oxycodone taken 4 times daily.^{11,63} Its commercial success, fueled by an unprecedented promotion and marketing campaign, was stained by escalating OxyContin abuse and diversion that spread throughout the country.^{2,75} The regions of the country that had the earliest and highest availability of prescribed OxyContin had the greatest initial abuse and diversion.^{23,67} Nationally, the increasing availability of OxyContin was associated with higher rates of abuse, and it became the most prevalent abused prescription opioid by 2004.²

Compared with noncontrolled drugs, controlled drugs, with their potential for abuse and diversion, pose different public health risks when overpromoted and highly prescribed. Several marketing practices appear to be especially questionable.

The extraordinary amount of money spent in promoting a sustained-release opioid was unprecedented. During OxyContin's first 6 years on the market, Purdue spent approximately 6 to 12 times more on promoting it than the company had spent on promoting MS Contin, or than Janssen Pharmaceutical Products LP had spent on Duragesic, one of OxyContin's competitors.¹⁹ Although OxyContin has not been shown to be superior to other available potent opioid preparations,^{11,63} by 2001 it had become the most frequently prescribed brand-name opioid in the United States for treating moderate to severe pain.¹⁹ Carefully

crafted limits on the marketing and promotion of controlled drugs would help to realign their actual use with the principles of evidence-based medicine.

Physicians' interactions with pharmaceutical sales representatives have been found to influence the prescribing practices of residents and physicians in terms of decreased prescribing of generic drugs, prescribing cost, nonrational prescribing, and rapid prescribing of new drugs.⁷⁶ Carefully crafted limits on the promotion of controlled drugs by the pharmaceutical sales force and enhanced FDA oversight of the training and performance of sales representatives would also reduce over- and misprescribing.

Although there are no available data for evaluating the promotional effect of free starter coupons for controlled drugs, it seems likely that the over- and misprescribing of a controlled drug are encouraged by such promotional programs and the public health would be well served by eliminating them.

The use of prescriber profiling data to influence prescribing and improve sales is imbedded in pharmaceutical detailing. Very little data are publicly available for understanding to what extent this marketing practice boosts sales. One market research report indicated that profiling improved profit margins by as much as 3 percentage points and the initial uptake of new drugs by 30%.⁷⁷ The use of prescriber profiling data to target high-opioid prescribers—coupled with very lucrative incentives for sales representatives—would seem to fuel increased

prescribing by some physicians—perhaps the most liberal prescribers of opioids and, in some cases, the least discriminate. Regulations eliminating this marketing tool might decrease some potential overprescribing of controlled drugs.

The public health would be better protected if the FDA reviewed all advertising and promotional materials as well as associated educational materials—for their truthfulness, accuracy, balance, and scientific validity—before dissemination. Such a change would require a considerable increase in FDA support, staffing, and funding from what is currently available. Public monies spent on the front end of the problem could prevent another such tragedy.

The pharmaceutical industry's role and influence in medical education is problematic. From 1996 through July 2002, Purdue funded more than 20 000 pain-related educational programs through direct sponsorship or financial grants,¹⁹ providing a venue that had enormous influence on physicians' prescribing throughout the country. Particularly with controlled drugs, the potential for blurring marketing and education carries a much higher public health risk than with uncontrolled drugs. At least in the area of controlled drugs, with their high potential for abuse and diversion, public health would best be served by severing the pharmaceutical industry's direct role and influence in medical education.

Marketing and promotion by the pharmaceutical industry have considerably amplified the prescription sales and availability of opioids. A number of factors have

contributed to the marked growth of opioid abuse in the United States, but one factor is certainly the much increased availability of prescription opioids.⁷⁸ The public interest and public health would be better served by a redefinition of acceptable and allowable marketing practices for opioids and other controlled drugs. ■

About the Author

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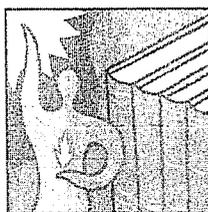
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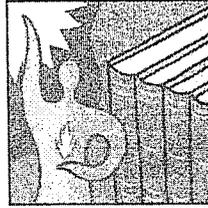
I thank Michael McNeer, MD, for his thoughtful review of the essay and helpful suggestions.

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Attachment 3



MEDICAL BOARD OF CALIFORNIA
PRESCRIBING TASK FORCE
MEETING AGENDA



**MEMBERS OF THE
TASK FORCE**

Michael Bishop, M.D., Chair
Barbara Yaroslavsky, Chair

California Bureau of Real Estate
 First Floor Conference Room
 1651 Exposition Boulevard
 Sacramento, CA 95815

Monday, September 23, 2013
9:30 a.m. – 4:00 p.m.
 (or until completion of business)

ALL TIMES ARE APPROXIMATE AND SUBJECT TO CHANGE
*If a quorum of the Board is present, members of the Board who are not members
 of the Committee may attend only as observers.*

1. Call to Order / Introductions
2. Prescribing History/Physician Responsibility Presentation – Laura Sweet
3. Board of Pharmacy Precedential Decision regarding Pacifica Pharmacy/Pharmacist
 Corresponding Responsibility – Joshua Room
4. Work Group Activity
5. Reports from Work Group Activity
6. Summary of Information to be Shared Between Physicians and Pharmacists
7. Adjournment

The mission of the Medical Board of California is to protect health care consumers through the proper licensing and regulation of physicians and surgeons and certain allied health care professions and through the vigorous, objective enforcement of the Medical Practice Act, and to promote access to quality medical care through the Board's licensing and regulatory functions.

Meetings of the Medical Board of California are open to the public except when specifically noticed otherwise in accordance with the Open Meetings Act. The audience will be given appropriate opportunities to comment on any issue presented in open session before the Board, however, the Chair may apportion available time among those who wish to speak. For additional information call (916) 263-2389.

NOTICE: *The meeting is accessible to the physically disabled. A person who needs disability-related accommodations or modifications in order to participate in the meeting may make a request by contacting Lisa Toof at (916) 263-2389 or Lisa.Toof@mbc.ca.gov or sending a written request to Lisa Toof. Providing your request at least five (5) business days before the meeting will help ensure availability of the requested accommodation.*

MEDICAL BOARD STAFF REPORT

DATE REPORT ISSUED: July 2, 2013
 ATTENTION: Board Members
 SUBJECT: Prescribing Task Force
 STAFF CONTACT: Renee Threadgill

REQUESTED ACTION:

This report is intended to provide an update to the Members on the activities of the Prescribing Task Force. No action is needed at this time.

BACKGROUND AND ANALYSIS:

At the April 24-25, 2013 Board Meeting the Members approved the establishment of a Prescribing Task Force in order to address the serious problem of prescription drug abuse. Ms. Yaroslavsky and Mike Bishop, M.D. were appointed to the Task Force.

On July 2, 2013, the Task Force Board Members met with Staff to discuss and establish the mission, vision, and objective of the Task Force. The Members adopted a mission and vision statement and developed objectives for the Task Force.

Mission Statement

The Task Force will identify ways to proactively approach and find solutions to the epidemic of prescription drug overdoses through education, prevention, best practices, communication, and outreach by engaging all stakeholders in this endeavor.

Vision

To significantly reduce prescription drug overdoses.

Objectives

- *Identify appropriate patient information that can be shared/discussed between the prescriber and the pharmacist*
- *Identify best practices for prescribing*
 - *Revisit the current Pain Management Guidelines*
 - *Educate prescribers on best practices for prescribing and the public on diversion, disposal and additional information regarding overprescribing and addiction*
 - *Define an outreach plan to provide information to all stakeholders*
- *Review the Board's policy on experts for overprescribing cases*

The first meeting of the Task Force will be an all-day meeting held in September, 2013 in Sacramento. The Task Force meeting will be a working meeting with all invited interested parties providing input toward the objectives of the Task Force based upon their areas of expertise/perspective. The interested parties will include individual prescribers from all specialties and dispensers from all types of facilities/settings, but also representatives from:

- Attorney General's Office
- District Attorney's Offices
- County Sheriff's Offices
- Other Healing Arts Boards (Pharmacy, Registered Nursing, Physician Assistants, Dental, etc.)
- Drug Enforcement Administration
- Consumer and Advocate Groups

All Prescriber Associations (California Medical Association, California Nursing Association, etc.)
California Pharmacist Association
Specialty Boards
Kaiser
California Hospital Association
Media
Schools (including medical, pharmacy, dental, etc.[all prescribers/dispensers])
Teaching physicians/pharmacists
Department of Insurance
Insurance Companies
Senate and Assembly Committees (B&P, Health)

Several meetings may be required in order to meet all of the objectives of the Task Force. The Task Force Board Members have identified the first two objective on the above list as its first priorities. The Task Force will also be asking all interested parties to articulate problems from their perspectives. As these problems are brought forward, they will be added to the objectives list and the working group will establish solutions that can then be shared with the prescribing and dispensing communities.

Prescribing Task Force

First Meeting: After July Board Meeting (possible August) – All day meeting

Mission Statement: The Task Force will identify ways to proactively approach and find solutions to the epidemic of prescription drug overdoses through education, prevention, best practices, communication, and outreach by engaging all stakeholders in this endeavor.

Vision: To significantly reduce prescription drug overdoses.

Objectives:

- Revisit the current Pain Management Guidelines (to be sent out ahead of time)
- Identify best practices for prescribing (including looking at pain agreements, etc.)
- Educate prescribers on best practices for prescribing and the public on diversion, disposal and additional information regarding overprescribing and addiction
- Review the Board's policy on experts for overprescribing cases
- Identify appropriate patient information that can be shared/discussed between the prescriber and the pharmacist (CMA and CPA issue)
- Define an outreach plan to provide information to all stakeholders

Suggested Topics/Discussions for the Task Force:

- Pain Management Presentation – Laura Sweet presentation to ensure everyone is on the same page
- Review the Federation of State Medical Boards policies: *Model Policy on the Appropriate Use of Opioid Analgesics in the Treatment of Pain and Model Policy on Opioid Addiction Treatment in the Medical Office* – does the Board need to revise the Board's based upon the FSMB
- Presentation by Christ Reist, M.D. on a drug analytic program that could help detect problems in overprescribing (best practice – referred by Gerrie Schipske)

Attachment 4



California
LEGISLATIVE INFORMATION

SB-809 Controlled substances: reporting. (2013-2014)

Senate Bill No. 809

CHAPTER 400

An act to add Sections 208, 209, and 2196.8 to the Business and Professions Code, and to amend Sections 11164.1, 11165, and 11165.1 of, and to add Section 11165.5 to, the Health and Safety Code, relating to controlled substances.

[Approved by Governor September 27, 2013. Filed with Secretary of State September 27, 2013.]

LEGISLATIVE COUNSEL'S DIGEST

SB 809, DeSaulnier. Controlled substances: reporting.

(1) Existing law classifies certain controlled substances into designated schedules. Existing law requires the Department of Justice to maintain the Controlled Substance Utilization Review and Evaluation System (CURES) for the electronic monitoring of the prescribing and dispensing of Schedule II, Schedule III, and Schedule IV controlled substances by all practitioners authorized to prescribe or dispense these controlled substances.

Existing law requires dispensing pharmacies and clinics to report, on a weekly basis, specified information for each prescription of Schedule II, Schedule III, or Schedule IV controlled substances, to the department, as specified.

This bill would establish the CURES Fund within the State Treasury to receive funds to be allocated, upon appropriation by the Legislature, to the Department of Justice for the purposes of funding CURES, and would make related findings and declarations.

This bill would, beginning April 1, 2014, require an annual fee of \$6 to be assessed on specified licensees, including licensees authorized to prescribe, order, administer, furnish, or dispense controlled substances, and require the regulating agency of each of those licensees to bill and collect that fee at the time of license renewal. The bill would authorize the Department of Consumer Affairs to reduce, by regulation, that fee to the reasonable cost of operating and maintaining CURES for the purpose of regulating those licensees, if the reasonable regulatory cost is less than \$6 per licensee. The bill would require the proceeds of the fee to be deposited into the CURES Fund for the support of CURES, as specified. The bill would also permit specified insurers, health care service plans, qualified manufacturers, and other donors to voluntarily contribute to the CURES Fund, as described.

(2) Existing law requires the Medical Board of California to periodically develop and disseminate information and educational materials regarding various subjects, including pain management techniques, to each licensed physician and surgeon and to each general acute care hospital in California.

This bill would additionally require the board to periodically develop and disseminate to each licensed physician and surgeon and to each general acute care hospital in California information and educational materials relating to the assessment of a patient's risk of abusing or diverting controlled substances and information relating to CURES.

(3) Existing law permits a licensed health care practitioner, as specified, or a pharmacist to apply to the Department of Justice to obtain approval to access information stored on the Internet regarding the controlled

substance history of a patient under his or her care. Existing law also authorizes the Department of Justice to provide the history of controlled substances dispensed to an individual to licensed health care practitioners, pharmacists, or both, providing care or services to the individual.

This bill would require, by January 1, 2016, or upon receipt of a federal Drug Enforcement Administration registration, whichever occurs later, health care practitioners authorized to prescribe, order, administer, furnish, or dispense controlled substances, as specified, and pharmacists to apply to the Department of Justice to obtain approval to access information stored on the Internet regarding the controlled substance history of a patient under their care. The bill would require the Department of Justice, in conjunction with the Department of Consumer Affairs and certain licensing boards, to, among other things, develop a streamlined application and approval process to provide access to the CURES database for licensed health care practitioners and pharmacists. The bill would make other related and conforming changes.

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: no

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. The Legislature finds and declares all of the following:

(a) The Controlled Substance Utilization Review and Evaluation System (CURES) is a valuable preventive, investigative, and educational tool for health care providers, regulatory agencies, educational researchers, and law enforcement. Recent budget cuts to the Attorney General's Division of Law Enforcement have resulted in insufficient funding to support CURES and its Prescription Drug Monitoring Program (PDMP). The CURES PDMP is necessary to ensure health care professionals have the necessary data to make informed treatment decisions and to allow law enforcement to investigate diversion of prescription drugs. Without a dedicated funding source, the CURES PDMP is not sustainable.

(b) Each year CURES responds to more than 800,000 requests from practitioners and pharmacists regarding all of the following:

(1) Helping identify and deter drug abuse and diversion of prescription drugs through accurate and rapid tracking of Schedule II, Schedule III, and Schedule IV controlled substances.

(2) Helping practitioners make prescribing decisions.

(3) Helping reduce misuse, abuse, and trafficking of those drugs.

(c) Schedule II, Schedule III, and Schedule IV controlled substances have had deleterious effects on private and public interests, including the misuse, abuse, and trafficking in dangerous prescription medications resulting in injury and death. It is the intent of the Legislature to work with stakeholders to fully fund the operation of CURES which seeks to mitigate those deleterious effects and serve as a tool for ensuring safe patient care, and which has proven to be a cost-effective tool to help reduce the misuse, abuse, and trafficking of those drugs.

(d) The following goals are critical to increase the effectiveness and functionality of CURES:

(1) Upgrading the CURES PDMP so that it is capable of accepting real-time updates and is accessible in real-time, 24 hours a day, seven days a week.

(2) Upgrading the CURES PDMP in California so that it is capable of operating in conjunction with all national prescription drug monitoring programs.

(3) Providing subscribers to prescription drug monitoring programs access to information relating to controlled substances dispensed in California, including those dispensed through the United States Department of Veterans Affairs, the Indian Health Service, the Department of Defense, and any other entity with authority to dispense controlled substances in California.

(4) Upgrading the CURES PDMP so that it is capable of accepting the reporting of electronic prescription data, thereby enabling more reliable, complete, and timely prescription monitoring.

SEC. 2. Section 208 is added to the Business and Professions Code, to read:

208. (a) Beginning April 1, 2014, a CURES fee of six dollars (\$6) shall be assessed annually on each of the licensees specified in subdivision (b) to pay the reasonable costs associated with operating and maintaining CURES for the purpose of regulating those licensees. The fee assessed pursuant to this subdivision shall be

billed and collected by the regulating agency of each licensee at the time of the licensee's license renewal. If the reasonable regulatory cost of operating and maintaining CURES is less than six dollars (\$6) per licensee, the Department of Consumer Affairs may, by regulation, reduce the fee established by this section to the reasonable regulatory cost.

(b) (1) Licensees authorized pursuant to Section 11150 of the Health and Safety Code to prescribe, order, administer, furnish, or dispense Schedule II, Schedule III, or Schedule IV controlled substances or pharmacists licensed pursuant to Chapter 9 (commencing with Section 4000) of Division 2.

(2) Wholesalers and nonresident wholesalers of dangerous drugs licensed pursuant to Article 11 (commencing with Section 4160) of Chapter 9 of Division 2.

(3) Nongovernmental clinics licensed pursuant to Article 13 (commencing with Section 4180) and Article 14 (commencing with Section 4190) of Chapter 9 of Division 2.

(4) Nongovernmental pharmacies licensed pursuant to Article 7 (commencing with Section 4110) of Chapter 9 of Division 2.

(c) The funds collected pursuant to subdivision (a) shall be deposited in the CURES Fund, which is hereby created within the State Treasury. Moneys in the CURES Fund shall, upon appropriation by the Legislature, be available to the Department of Consumer Affairs to reimburse the Department of Justice for costs to operate and maintain CURES for the purposes of regulating the licensees specified in subdivision (b).

(d) The Department of Consumer Affairs shall contract with the Department of Justice on behalf of the Medical Board of California, the Dental Board of California, the California State Board of Pharmacy, the Veterinary Medical Board, the Board of Registered Nursing, the Physician Assistant Board of the Medical Board of California, the Osteopathic Medical Board of California, the Naturopathic Medicine Committee of the Osteopathic Medical Board, the State Board of Optometry, and the California Board of Podiatric Medicine to operate and maintain CURES for the purposes of regulating the licensees specified in subdivision (b).

SEC. 3. Section 209 is added to the Business and Professions Code, to read:

209. The Department of Justice, in conjunction with the Department of Consumer Affairs and the boards and committees identified in subdivision (d) of Section 208, shall do all of the following:

(a) Identify and implement a streamlined application and approval process to provide access to the CURES Prescription Drug Monitoring Program (PDMP) database for licensed health care practitioners eligible to prescribe, order, administer, furnish, or dispense Schedule II, Schedule III, or Schedule IV controlled substances and for pharmacists. Every reasonable effort shall be made to implement a streamlined application and approval process that a licensed health care practitioner or pharmacist can complete at the time that he or she is applying for licensure or renewing his or her license.

(b) Identify necessary procedures to enable licensed health care practitioners and pharmacists with access to the CURES PDMP to delegate their authority to order reports from the CURES PDMP.

(c) Develop a procedure to enable health care practitioners who do not have a federal Drug Enforcement Administration (DEA) number to opt out of applying for access to the CURES PDMP.

SEC. 4. Section 2196.8 is added to the Business and Professions Code, to read:

2196.8. The board shall periodically develop and disseminate information and educational material regarding assessing a patient's risk of abusing or diverting controlled substances and information relating to the Controlled Substance Utilization Review and Evaluation System (CURES), described in Section 11165 of the Health and Safety Code, to each licensed physician and surgeon and to each general acute care hospital in this state. The board shall consult with the State Department of Public Health, the boards and committees specified in subdivision (d) of Section 208, and the Department of Justice in developing the materials to be distributed pursuant to this section.

SEC. 5. Section 11164.1 of the Health and Safety Code is amended to read:

11164.1. (a) (1) Notwithstanding any other provision of law, a prescription for a controlled substance issued by a prescriber in another state for delivery to a patient in another state may be dispensed by a California pharmacy,

if the prescription conforms with the requirements for controlled substance prescriptions in the state in which the controlled substance was prescribed.

(2) All prescriptions for Schedule II, Schedule III, and Schedule IV controlled substances dispensed pursuant to this subdivision shall be reported by the dispensing pharmacy to the Department of Justice in the manner prescribed by subdivision (d) of Section 11165.

(b) Pharmacies may dispense prescriptions for Schedule III, Schedule IV, and Schedule V controlled substances from out-of-state prescribers pursuant to Section 4005 of the Business and Professions Code and Section 1717 of Title 16 of the California Code of Regulations.

SEC. 6. Section 11165 of the Health and Safety Code is amended to read:

11165. (a) To assist health care practitioners in their efforts to ensure appropriate prescribing, ordering, administering, furnishing, and dispensing of controlled substances, law enforcement and regulatory agencies in their efforts to control the diversion and resultant abuse of Schedule II, Schedule III, and Schedule IV controlled substances, and for statistical analysis, education, and research, the Department of Justice shall, contingent upon the availability of adequate funds in the CURES Fund, maintain the Controlled Substance Utilization Review and Evaluation System (CURES) for the electronic monitoring of, and Internet access to information regarding, the prescribing and dispensing of Schedule II, Schedule III, and Schedule IV controlled substances by all practitioners authorized to prescribe, order, administer, furnish, or dispense these controlled substances.

(b) The Department of Justice may seek and use grant funds to pay the costs incurred by the operation and maintenance of CURES. The department shall annually report to the Legislature and make available to the public the amount and source of funds it receives for support of CURES.

(c) (1) The operation of CURES shall comply with all applicable federal and state privacy and security laws and regulations.

(2) CURES shall operate under existing provisions of law to safeguard the privacy and confidentiality of patients. Data obtained from CURES shall only be provided to appropriate state, local, and federal public agencies for disciplinary, civil, or criminal purposes and to other agencies or entities, as determined by the Department of Justice, for the purpose of educating practitioners and others in lieu of disciplinary, civil, or criminal actions. Data may be provided to public or private entities, as approved by the Department of Justice, for educational, peer review, statistical, or research purposes, provided that patient information, including any information that may identify the patient, is not compromised. Further, data disclosed to any individual or agency as described in this subdivision shall not be disclosed, sold, or transferred to any third party. The Department of Justice shall establish policies, procedures, and regulations regarding the use, access, evaluation, management, implementation, operation, storage, disclosure, and security of the information within CURES, consistent with this subdivision.

(d) For each prescription for a Schedule II, Schedule III, or Schedule IV controlled substance, as defined in the controlled substances schedules in federal law and regulations, specifically Sections 1308.12, 1308.13, and 1308.14, respectively, of Title 21 of the Code of Federal Regulations, the dispensing pharmacy, clinic, or other dispenser shall report the following information to the Department of Justice as soon as reasonably possible, but not more than seven days after the date a controlled substance is dispensed, in a format specified by the Department of Justice:

(1) Full name, address, and, if available, telephone number of the ultimate user or research subject, or contact information as determined by the Secretary of the United States Department of Health and Human Services, and the gender, and date of birth of the ultimate user.

(2) The prescriber's category of licensure, license number, national provider identifier (NPI) number, if applicable, the federal controlled substance registration number, and the state medical license number of any prescriber using the federal controlled substance registration number of a government-exempt facility.

(3) Pharmacy prescription number, license number, NPI number, and federal controlled substance registration number.

(4) National Drug Code (NDC) number of the controlled substance dispensed.

(5) Quantity of the controlled substance dispensed.

(6) International Statistical Classification of Diseases, 9th revision (ICD-9) or 10th revision (ICD-10) Code, if available.

(7) Number of refills ordered.

(8) Whether the drug was dispensed as a refill of a prescription or as a first-time request.

(9) Date of origin of the prescription.

(10) Date of dispensing of the prescription.

(e) The Department of Justice may invite stakeholders to assist, advise, and make recommendations on the establishment of rules and regulations necessary to ensure the proper administration and enforcement of the CURES database. All prescriber and dispenser invitees shall be licensed by one of the boards or committees identified in subdivision (d) of Section 208 of the Business and Professions Code, in active practice in California, and a regular user of CURES.

(f) The Department of Justice shall, prior to upgrading CURES, consult with prescribers licensed by one of the boards or committees identified in subdivision (d) of Section 208 of the Business and Professions Code, one or more of the boards or committees identified in subdivision (d) of Section 208 of the Business and Professions Code, and any other stakeholder identified by the department, for the purpose of identifying desirable capabilities and upgrades to the CURES Prescription Drug Monitoring Program (PDMP).

(g) The Department of Justice may establish a process to educate authorized subscribers of the CURES PDMP on how to access and use the CURES PDMP.

SEC. 7. Section 11165.1 of the Health and Safety Code is amended to read:

11165.1. (a) (1) (A) (i) A health care practitioner authorized to prescribe, order, administer, furnish, or dispense Schedule II, Schedule III, or Schedule IV controlled substances pursuant to Section 11150 shall, before January 1, 2016, or upon receipt of a federal Drug Enforcement Administration (DEA) registration, whichever occurs later, submit an application developed by the Department of Justice to obtain approval to access information online regarding the controlled substance history of a patient that is stored on the Internet and maintained within the Department of Justice, and, upon approval, the department shall release to that practitioner the electronic history of controlled substances dispensed to an individual under his or her care based on data contained in the CURES Prescription Drug Monitoring Program (PDMP).

(ii) A pharmacist shall, before January 1, 2016, or upon licensure, whichever occurs later, submit an application developed by the Department of Justice to obtain approval to access information online regarding the controlled substance history of a patient that is stored on the Internet and maintained within the Department of Justice, and, upon approval, the department shall release to that pharmacist the electronic history of controlled substances dispensed to an individual under his or her care based on data contained in the CURES PDMP.

(B) An application may be denied, or a subscriber may be suspended, for reasons which include, but are not limited to, the following:

(i) Materially falsifying an application for a subscriber.

(ii) Failure to maintain effective controls for access to the patient activity report.

(iii) Suspended or revoked federal DEA registration.

(iv) Any subscriber who is arrested for a violation of law governing controlled substances or any other law for which the possession or use of a controlled substance is an element of the crime.

(v) Any subscriber accessing information for any other reason than caring for his or her patients.

(C) Any authorized subscriber shall notify the Department of Justice within 30 days of any changes to the subscriber account.

(2) A health care practitioner authorized to prescribe, order, administer, furnish, or dispense Schedule II, Schedule III, or Schedule IV controlled substances pursuant to Section 11150 or a pharmacist shall be deemed to have complied with paragraph (1) if the licensed health care practitioner or pharmacist has been approved to access the CURES database through the process developed pursuant to subdivision (a) of Section 209 of the Business and Professions Code.

(b) Any request for, or release of, a controlled substance history pursuant to this section shall be made in accordance with guidelines developed by the Department of Justice.

(c) In order to prevent the inappropriate, improper, or illegal use of Schedule II, Schedule III, or Schedule IV controlled substances, the Department of Justice may initiate the referral of the history of controlled substances dispensed to an individual based on data contained in CURES to licensed health care practitioners, pharmacists, or both, providing care or services to the individual.

(d) The history of controlled substances dispensed to an individual based on data contained in CURES that is received by a practitioner or pharmacist from the Department of Justice pursuant to this section shall be considered medical information subject to the provisions of the Confidentiality of Medical Information Act contained in Part 2.6 (commencing with Section 56) of Division 1 of the Civil Code.

(e) Information concerning a patient's controlled substance history provided to a prescriber or pharmacist pursuant to this section shall include prescriptions for controlled substances listed in Sections 1308.12, 1308.13, and 1308.14 of Title 21 of the Code of Federal Regulations.

SEC. 8. Section 11165.5 is added to the Health and Safety Code, to read:

11165.5. (a) The Department of Justice may seek voluntarily contributed private funds from insurers, health care service plans, qualified manufacturers, and other donors for the purpose of supporting CURES. Insurers, health care service plans, qualified manufacturers, and other donors may contribute by submitting their payment to the Controller for deposit into the CURES Fund established pursuant to subdivision (c) of Section 208 of the Business and Professions Code. The department shall make information about the amount and the source of all private funds it receives for support of CURES available to the public. Contributions to the CURES Fund pursuant to this subdivision shall be nondeductible for state tax purposes.

(b) For purposes of this section, the following definitions apply:

(1) "Controlled substance" means a drug, substance, or immediate precursor listed in any schedule in Section 11055, 11056, or 11057 of the Health and Safety Code.

(2) "Health care service plan" means an entity licensed pursuant to the Knox-Keene Health Care Service Plan Act of 1975 (Chapter 2.2 (commencing with Section 1340) of Division 2 of the Health and Safety Code).

(3) "Insurer" means an admitted insurer writing health insurance, as defined in Section 106 of the Insurance Code, and an admitted insurer writing workers' compensation insurance, as defined in Section 109 of the Insurance Code.

(4) "Qualified manufacturer" means a manufacturer of a controlled substance, but does not mean a wholesaler or nonresident wholesaler of dangerous drugs, regulated pursuant to Article 11 (commencing with Section 4160) of Chapter 9 of Division 2 of the Business and Professions Code, a veterinary food-animal drug retailer, regulated pursuant to Article 15 (commencing with Section 4196) of Chapter 9 of Division 2 of the Business and Professions Code, or an individual regulated by the Medical Board of California, the Dental Board of California, the California State Board of Pharmacy, the Veterinary Medical Board, the Board of Registered Nursing, the Physician Assistant Committee of the Medical Board of California, the Osteopathic Medical Board of California, the State Board of Optometry, or the California Board of Podiatric Medicine.

Attachment 5

CASE SUMMARY

In the Matter of the Accusation Against Pacifica Pharmacy; Thang Tran
Board of Pharmacy Case No. 3802; OAH No. 2011010644; Precedential Decision No. 2013-01
Made precedential by the Board of Pharmacy effective August 9, 2013

Available at <http://www.pharmacy.ca.gov/enforcement/precedential.shtml>

BRIEF SYNOPSIS: In a Decision and Order initially effective June 3, 2012 (after the lapse of a 30-day stay from its initial effective date of May 4, 2012), and made a precedential decision of the Board effective August 9, 2013, the Board of Pharmacy revoked the licenses issued by the Board to Pacifica Pharmacy, PHY 46715, a pharmacy licensee, and Thang Q. Tran, RPH 41172, a pharmacist licensee, based on allegations and proof that respondents engaged in unprofessional conduct including failures to exercise the "corresponding responsibility" a pharmacy/pharmacist owes under California law to determine the legitimate medical purpose of controlled substance prescriptions before dispensing, under Health and Safety Code section 11153, subdivision (a).

PROCEDURAL HISTORY: A Second Amended Accusation (operative pleading) was filed before the Board of Pharmacy on January 3, 2012. The case proceeded to a hearing conducted by Administrative Law Judge James Ahler of the Office of Administrative Hearings (OAH), San Diego, on January 23, 24, 25, and 31, and February 1, 2012. The Proposed Decision was issued on February 29, 2012. The Board adopted the Proposed Decision by Decision and Order issued April 4, 2012, made effective May 4, 2012. On April 10, 2012, the Board received a request for a 30-day stay to file a petition for reconsideration from respondents, and granted same, staying the effective date of the Decision and Order to June 3, 2012. On May 31, 2012, the Board issued an Order Denying Reconsideration, denying respondents' petition. That order confirmed that the Decision and Order of the Board would be effective and final as of June 3, 2012. On August 5, 2013, the Board designated the Decision as precedential, in its entirety, effective August 9, 2013.

DISCIPLINARY ORDER: On the basis of the factual findings and legal conclusions made in the 40-page Proposed Decision made the Decision and Order of the Board, the decision ordered:

- that Original Permit No. PHY 46715 issued to Pacifica Pharmacy Corp. is revoked;
- that Original Pharmacist License No. RPH 4117 issued to Thang Q. Tran is revoked; and
- that Pacifica Pharmacy Corp. and Thang Q. Tran shall pay to the Board of Pharmacy costs of investigation and enforcement in the total amount of \$39,666.00.

FINDINGS AND CONCLUSIONS: The Second Amended Accusation filed January 3, 2012 included a total of eight causes for discipline, two alleged against both respondents, three alleged only against Pacifica Pharmacy, and three alleged only against Thang Q. Tran. All eight of the causes for discipline were sustained. Of these, the cause for discipline receiving the most legal analysis and argument in the decision was the first, for failure to comply with the "corresponding responsibility" placed on pharmacies and pharmacists by Health and Safety Code section 11153. The Decision and Order identifies a series of "red flags" surrounding prescriptions for controlled substances (OxyContin, Opana, Dilaudid, and Alprazolam) by Dr. T, an osteopath with an office located some distance from Pacific Pharmacy, and concludes that Pacifica Pharmacy and Thang Q. Tran failed to make the inquiries necessary to exercise their "corresponding responsibility."

CASE DETAILS: The investigation was prompted by a complaint from a neighbor of the pharmacy, who observed what he believed was unusual traffic in and out of the pharmacy by young patrons, who spread cash across the dashboard of a vehicle on one occasion, and appeared to be exchanging cash for prescriptions in the parking lot of the pharmacy. A CURES report for the pharmacy showed a high number of controlled substance prescriptions (1,844 from January 1, 2009 to January 5, 2010) written by Dr. T. and dispensed by Pacifica Pharmacy.

Inspections of the pharmacy revealed other issues, including expired drugs in active inventory, pre-filled containers with inadequate labels, and inventory discrepancies. But the primary focus of the investigation was controlled substance dispensing practices. During an interview, Thang Q. Tran revealed, among other things, that he had never spoken to Dr. T about the prescriptions received in the pharmacy, that he did not routinely verify prescriptions with prescribers or ask about their prescribing practices, that he considered his role in verifying the legitimacy of the prescription to be limited to verifying the prescription with the prescriber, where appropriate, that he did not ask his patients about their diagnosis or other medical information, that he did not know about the use of CURES reports for evaluating patient therapy, and that he did not have an issue with filling prescriptions for prescribers or patients located far away from the pharmacy.

Expert testimony established that a pharmacist must exercise professional judgment with regard to dispensing controlled substances, a duty that entails more than filling the prescription. After a pharmacist evaluates the prescription to make certain it is valid and legitimate on its face, there is also a duty to evaluate the patient, the prescriber, and the medication therapy. The Decision and Order includes a fairly detailed description of the pharmacist's standard of care / duty of inquiry.

The Decision and Order identified several "red flags" that should give a pharmacy / pharmacist the inkling of a potential problem with prescriptions, and invoke in them a duty of inquiry:

- Irregularities on the face of the prescription itself;
- Nervous patient demeanor;
- Age or presentation of patient (e.g., youthful patients seeking chronic pain medications);
- Multiple patients at the same address(es);
- Cash payments;
- Requests for early refills of prescriptions;
- Prescriptions written for an unusually large quantity of drugs;
- Prescriptions written for potentially duplicative drugs;
- The same combinations of drugs prescribed for multiple patients;
- Initial prescriptions written for stronger opiates (e.g., OxyContin 80mg);
- Long distances traveled from the patient's home to the prescriber's office or pharmacy;
- Irregularities in the prescriber's qualifications in relation to the medication(s) prescribed;
- Prescriptions that are written outside of the prescriber's medical specialty; and
- Prescriptions for medications with no logical connection to diagnosis or treatment;

The Decision and Order concluded that whenever a pharmacist believes that a prescription may not have been written for a legitimate medical purpose, the pharmacist must inquire; when the results of a reasonable inquiry do not overcome the pharmacist's concern about a prescription being written for a legitimate medical purpose, the pharmacist must not fill the prescription.

Attachment 6

Excerpt of the Minutes of the April 12, 2013 Communication and Public Education Committee

Committee Discussion and Action:

The committee discussed the forum, its success, and ideas for future activities and collaborations. There appears to be strong demand for such public and licensee education.

Dr. Castellblanch referenced the positive program evaluations from attendees and offered that follow-up will be extremely important for getting the message out. He suggested that a sub-committee be convened to possibly identify grants that may be available to provide funding for a public awareness campaign.

Board staff has begun working with the Medical Board and their public education committee on outreach to licensees, to other practitioner boards and to the public on prescription drug abuse issues. Additionally, this board is scheduled to co-host four forums with the DEA on controlled substances abuse and dispensing, including a forum on corresponding responsibility to be held in August.

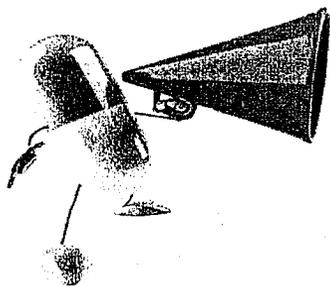
A brochure on corresponding responsibility targeted toward pharmacists has been proposed and will highlight the material provided in the board's forums with the DEA.

Ms. Herold explained that she sits on a high risk medication committee hosted by the California Hospital Association. The committee is researching the ways pain medications are prescribed in emergency rooms and how best practices can be developed to help address a problem with dispensing and prescribing of controlled substances in emergency rooms. She added that the CURES program has pending legislation to address funding needs and that the timing for that is opportune.

Ms. Herold offered that there are many advocacy groups who have initiated public education with respect to prescription drug abuse. DrugAbuse.org and RxAware are two such organizations. She suggested that the Board consider two campaigns, one focused on licensee education and the other on consumer education.

Discussion continued regarding the audience that would benefit most from a public awareness campaign. The problem of prescription drug abuse has increased with teenagers, but has also become a problem for adults. Chair Brooks added that the Board may want to consider producing a curriculum directed at schools to ensure that the message is getting out to school-aged children.

Chair Brooks suggested that a subcommittee be convened to work with the Department of Education on the development of a possible curriculum for students. He added that the Medical Board be involved as well. Mr. Brooks recommended that the suggestion be forwarded to the full Board for discussion and action.



MEDICATION SAFETY



Medication Safety Recommendations for Improving Safety of Opioid use

Opioid use is generally safe but is associated with serious adverse effects such as oversedation (0.5% incidence). The purpose of these recommendations are to reduce the risk of adverse drug events associated with use of opioids in perioperative settings. These recommendations focus on narcotic oversedation in adult patients being treated for acute pain.

Medication Use Step	Actions to Consider to Increase Medication Safety
Prescribing	<p>Recommendation</p> <ul style="list-style-type: none">• Use of acute pain management order set <p>Rationale</p> <ul style="list-style-type: none">• <i>A standardized order set will promote national best practices</i>• <i>Encourages multimodal techniques for pain management (e.g. including round the clock non-opioid therapy if not contraindicated)</i>• <i>Minimize opioid side effects</i><ul style="list-style-type: none">○ <i>Naloxone orders</i>○ <i>Bowel regimen orders</i>○ <i>Antiemetic orders</i>• <i>Reduce variation from best practices</i> <p>Recommendation</p> <p>Increase awareness of patient's history of opioid use and other risk factors for oversedation</p> <p>Rationale</p> <ul style="list-style-type: none">• <i>Opioid naïve patients are at the highest risk for experiencing over sedation.</i>• <i>Screening information (for patients at high risk for oversedation) should be available prescribers and other clinicians.</i>

	<ul style="list-style-type: none"> • <i>Design information support systems to identify patients who are at high risk (Sleep apnea, Morbid obesity, elderly >60 years old)</i> <p>Recommendation</p> <ul style="list-style-type: none"> ± Improve prevalence and use of patient controlled analgesia (PCA) <p>Rationale</p> <ul style="list-style-type: none"> • <i>Patient centered treatment</i> • <i>Minimizes adverse drug events such as oversedation</i> <p>Recommendation</p> <ul style="list-style-type: none"> • Develop and implement an acute pain management service <p>Rationale</p> <ul style="list-style-type: none"> • <i>Minimize adverse opioid events through focused prospective assessment of patients at high risk for respiratory depression/ oversedation</i> • <i>Achieving optimal pain therapy</i> • <i>Maximizing patient satisfaction</i>
<p>Dispensing / Distribution</p>	<p>Recommendation</p> <p>Assess need for current multiple strengths of narcotics</p> <p>Rationale</p> <ul style="list-style-type: none"> • <i>High dose strengths can be mistakenly administered resulting in oversedation</i>
<p>Administration</p>	<p>Recommendation</p> <p>Establish standardized procedure for naloxone administration to ensure availability and consistency in the emergent management of oversedation.</p> <p>Rationale</p> <ul style="list-style-type: none"> • <i>Naloxone is not consistently ordered on patients that are on opioids</i> <p>Recommendation</p> <p>Establish Smart pump "hard maximum" Guardrails® for all continuous opioid infusions</p> <p>Rationale</p> <ul style="list-style-type: none"> • <i>Use of Guardrails® have been shown to prevent harm caused by IV pump programming errors.</i>

<p>Clinical Education</p>	<p>Recommendation Train staff to identify the patients at high risk for oversedation and respiratory depression.</p> <ul style="list-style-type: none"> • No previous use of opioid history • Sleep apnea • Morbid obesity • Elderly >60 years old <p>Recommendation Documentation and communication of risk for oversedation information should be electronically accessible to all clinicians across the continuum of care.</p> <ul style="list-style-type: none"> • Establish standardized handoff process throughout the continuum of care during opioid therapy <p>Recommendation Staff should be educated on equianalgesic potency (prescribers and nurses).</p> <ul style="list-style-type: none"> • Potency reference cards • Talks on pain management therapies and alternatives • Incorporate into order set <p>Recommendation Advise prescribers in the use of multimodal therapies</p> <ul style="list-style-type: none"> • Benefits of multimodal therapy alternatives based on best practices (Tylenol, Motrin, Neurontin) • Around the clock use of non-opioid analgesics therapy unless contraindicated <p>Recommendation Educate clinicians on the recognition of advancing sedation</p> <ul style="list-style-type: none"> • Utilization of sedation scale assessment tools <p>Recommendation Nursing education, pain management</p> <ul style="list-style-type: none"> • Standardized process of pain goal setting • Define frequency of patient/family pain management education • Standardized patient orientation/education to pain scale tool and use
<p>Patient Education</p>	<p>Recommendation</p> <ul style="list-style-type: none"> • Define and educate patients on realistic pain goals and use of pain scale <p>Recommendation Educate patients and families on what adverse effects to watch for and report</p>

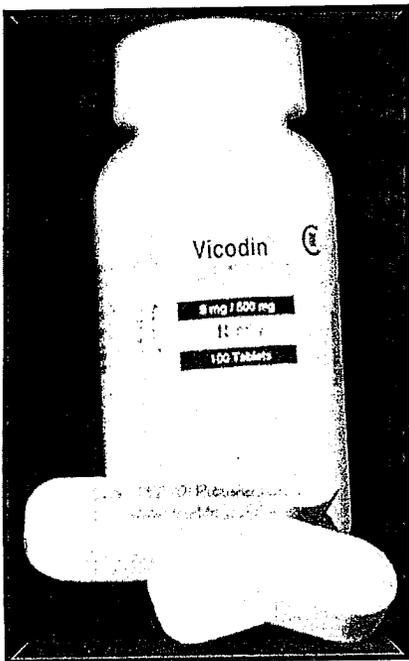
Monitoring	<p>Recommendation: Improve documentation and communication of risk factors for oversedation to all care givers across the continuum of care</p> <ul style="list-style-type: none"> • Pain scale scores • Sedation scale assessment • Pain goals <p>Rationale <i>Complete information should be readily available to prescribers for timely pain treatment care plan adjustments in response to an adverse drug event</i></p> <p>Recommendation</p> <ul style="list-style-type: none"> • Implement best physiologic monitoring practices • Use of capnography to monitor ventilation in identified high risk patients • Continuous pulse oximetry in identified high patients <p>Rationale <i>Enables earlier recognition and intervention in advancing oversedation.</i></p>
Policy and Procedure Documentation Tools	<p>Recommendation Revision of pain assessment and reassessment policy to include</p> <ul style="list-style-type: none"> • Sedation measurement and documentation
Quality Measures	<p>Recommendation</p> <ul style="list-style-type: none"> • Trend naloxone withdrawals • Trend occurrence reported oversedation events • Trend Rapid Response Team calls related to oversedation

Drug Education

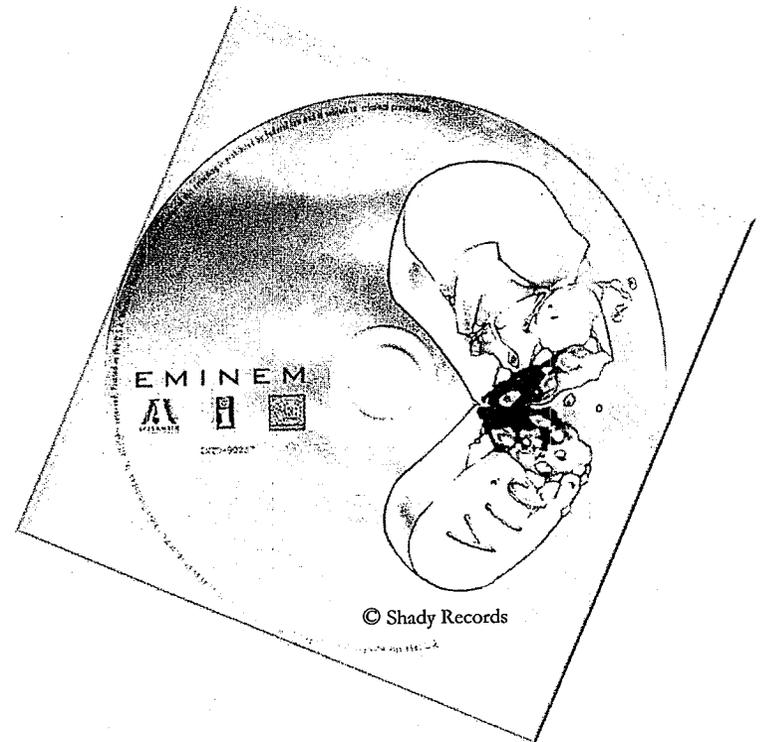
or not

What are kids listening to... Eminem?

- Rap star Eminem has a Vicodin® tattoo on his arm and a picture of a Vicodin® tablet on one of his CDs



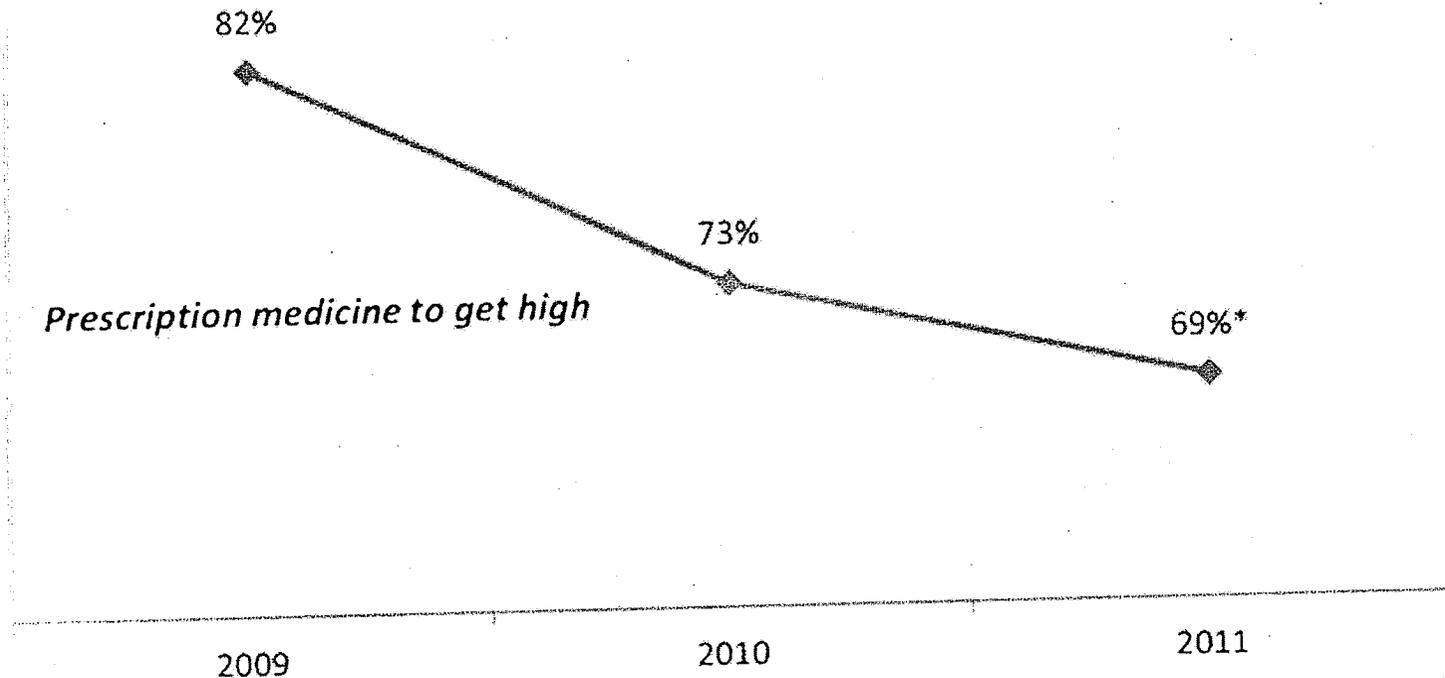
'Vike'



Parents & Their Attitudes

Parents are not discussing the risks of abusing prescription drugs

Parent Discussions with Teens



*Significantly lower than 2009 and 2010 levels

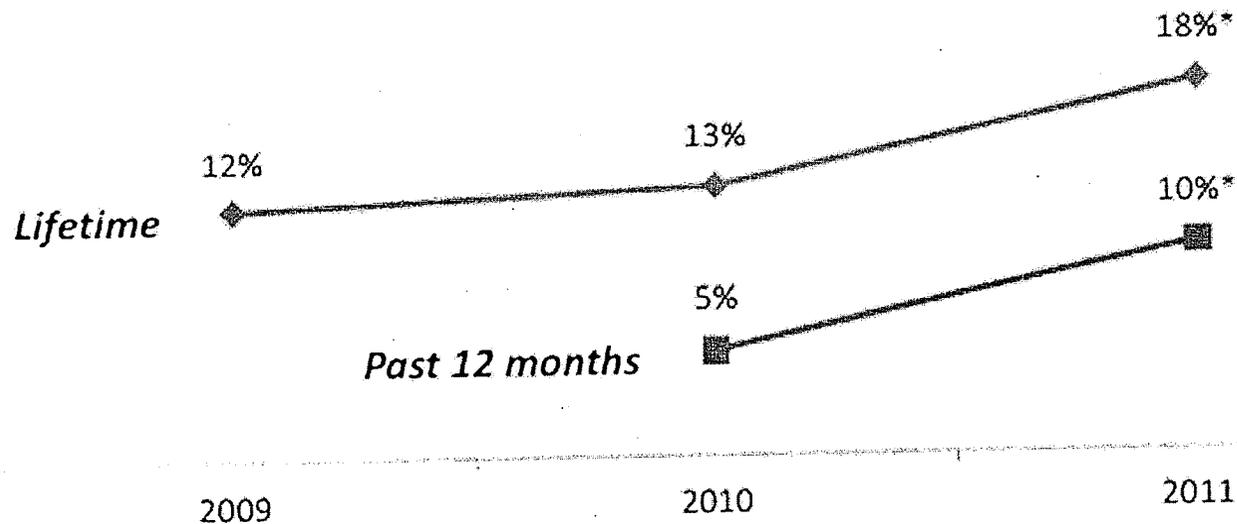
U.S. Drug Enforcement Administration / Operations
Division / Office of Diversion Control

Parents & Their Actions

Parents and their abuse of prescription drugs

Parent Prescription Medicine Use (3 times or more)

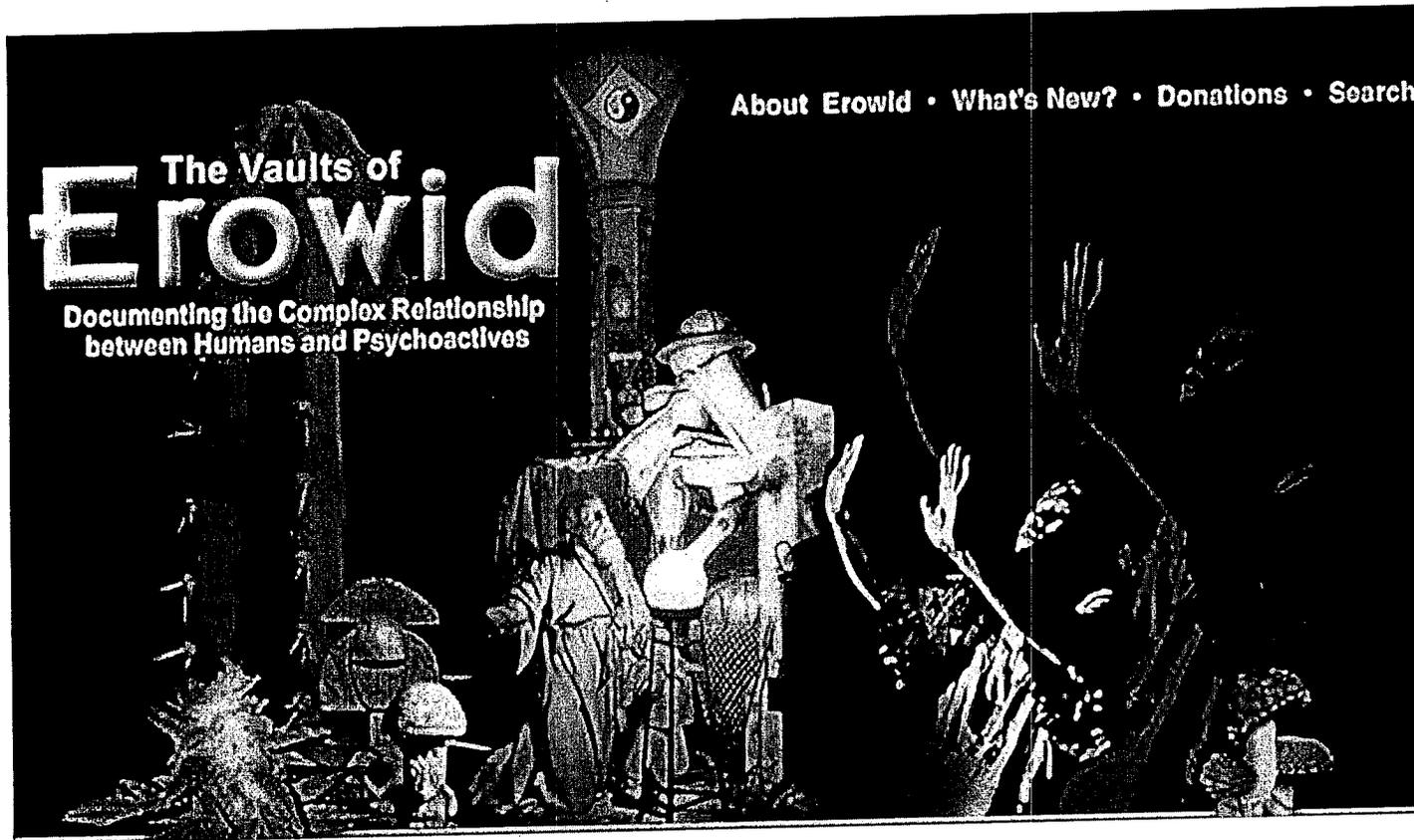
Prescription medicine that was not prescribed specifically for you



**Significantly higher than 2009 and 2010 levels*

U.S. Drug Enforcement Administration / Operations
Division / Office of Diversion Control

Where do kids get their information from?



We will not arrest our way out of this
problem!!!!

- Enforcement is just as important as....
- Prevention/Education
- Treatment
- **TREATMENT!!!!**

**Most Frequent Method of Obtaining a
Pharmaceutical Controlled Substance for
Non Medical Use**

Friends and Family...For Free!!

The Medicine Cabinet
and
the Problem of Pharmaceutical
Controlled Substance Disposal

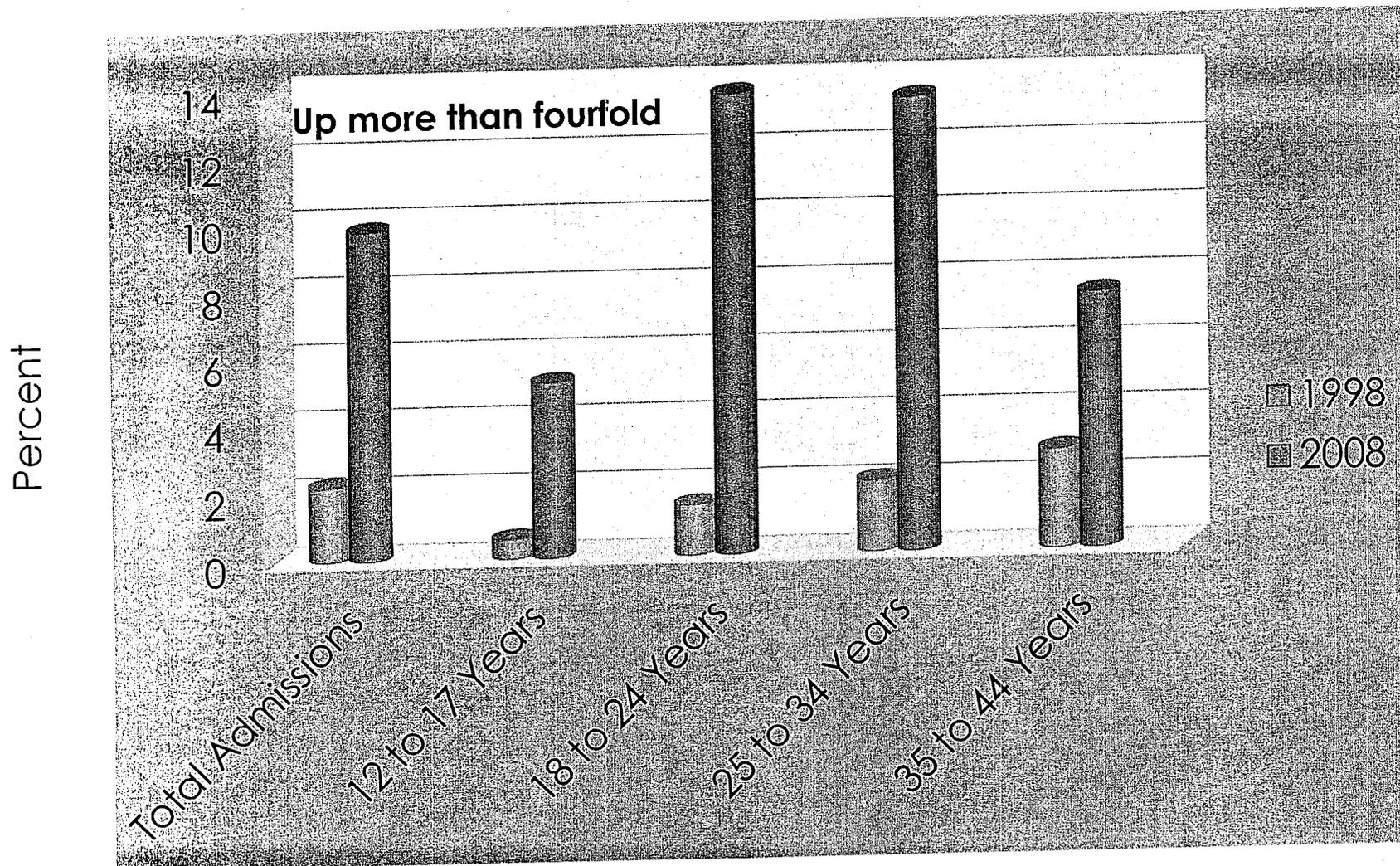
The Problem – Easy Access



So Many Drugs in the Household - Why?

- Unreasonable quantities being prescribed
- Insurance rules

Substance Abuse Treatment Admissions within Specific Age Groups That Reported Any Pain Reliever Abuse: 1998-2008



Source: SAMSHA Treatment Episode Data Set, 1998-2008 released July 15, 2010

Community Impact?

Heroin trafficking organizations relocating to areas where prescription drug abuse is on the rise

Heroin traffickers pave the way for increasing crime and violence

Law enforcement and prosecutors eventually fighting the problem on two fronts (prescription opiate diversion and heroin distribution) further depleting resources

Communities suffer