



U.S. Food and Drug Administration

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# Outpatient Prescription Opioid Utilization in the U.S., Years 2000 – 2009

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# Outline

- Distribution of IR and ER/LA opioids
- Prescription and patient trends and characteristics
- Prescribing specialties
- Diagnoses associated with use
- Limitations
- Summary

# Products Included

- **ER/LA Opioids (Schedule II):** oxycodone, morphine, fentanyl transdermal, hydromorphone, oxymorphone, methadone
- **IR Opioids:**
  - **Single-Ingredient Schedule II:** oxycodone, morphine, fentanyl, hydromorphone, oxymorphone, meperidine, levorphanol
  - **Combination Schedule II:** oxycodone/acetaminophen, oxycodone/aspirin, oxycodone/ibuprofen, meperidine combo
  - **Single-Ingredient Schedule III-IV :** tramadol, propoxyphene, butorphanol, codeine
  - **Combination Schedule III-IV:** propoxyphene combo, codeine combo, tramadol/acetaminophen, dihydrocodeine combo
  - **Hydrocodone (Schedule III):** hydrocodone/acetaminophen, hydrocodone/ibuprofen, hydrocodone other combinations
  - **Buprenorphine (Schedule III):** buprenorphine/naloxone, buprenorphine

# Distribution settings<sup>1</sup>

- ER/LA opioid products
  - outpatient retail pharmacy setting accounted for approximately 76% of sales distribution for year 2009.
- IR single-ingredient and combination opioid products
  - roughly 60% or more of sales distribution was outpatient retail pharmacies
  - single-ingredient morphine and combination codeine products were primarily distributed to non-retail settings of care.

<sup>1</sup> IMS Health, IMS National Sales Perspectives™, Year 2009, Extracted 6/10.



# Prescription and Patient Utilization Trends and Characteristics

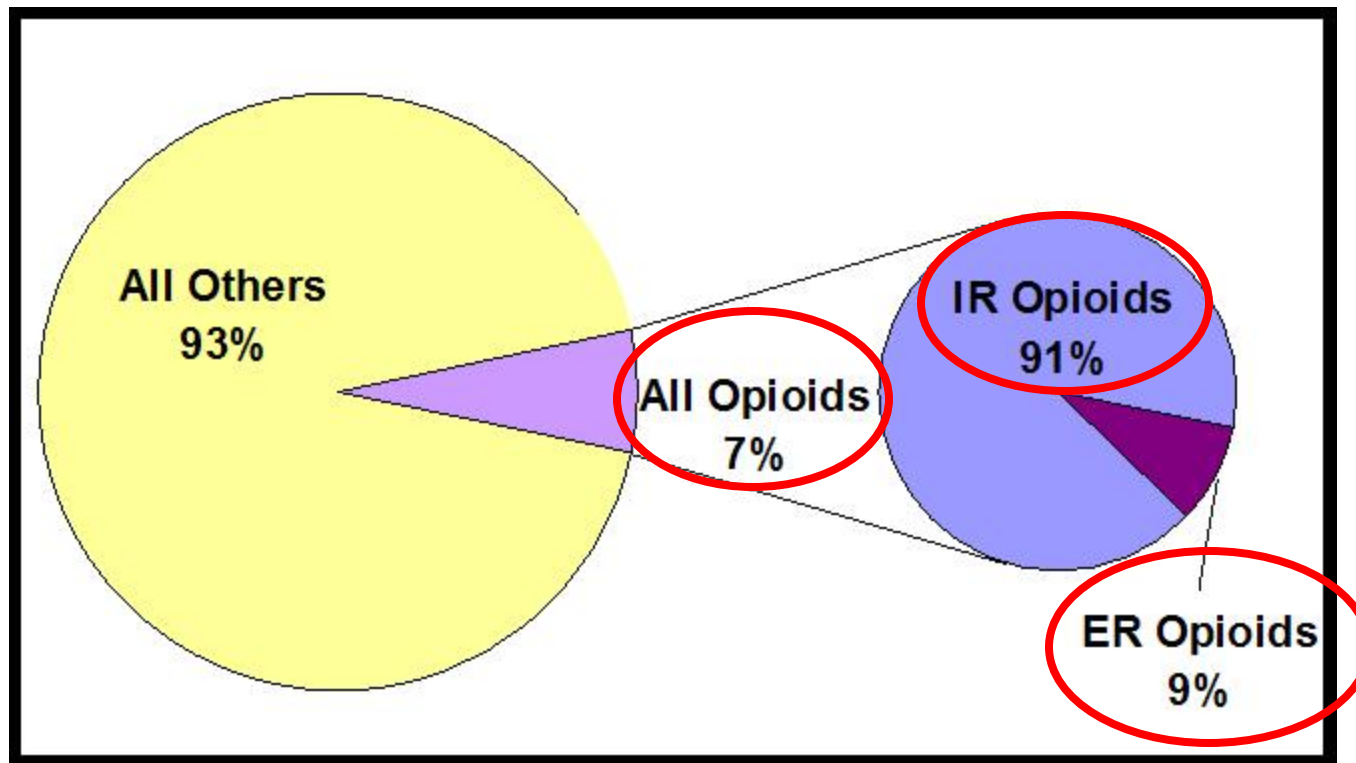
# National dispensed prescription data

## SDI, Vector One<sup>®</sup>: National (VONA)

- SDI's Vector One<sup>®</sup>: National (VONA) is a national-level projected prescription and patient-centric tracking service.
  - Receives over 2.0 billion prescription claims per year, representing over 160 million unique patients
- The number of dispensed prescriptions is obtained from a sample of approximately 59,000 pharmacies throughout the U.S., accounting for nearly all retail pharmacies and representing nearly half of retail prescriptions dispensed nationwide
- Retail pharmacies include: national retail chains, mass merchandisers, pharmacy benefits managers and their data systems, and provider groups

# Share of outpatient opioid prescription market, Year 2009

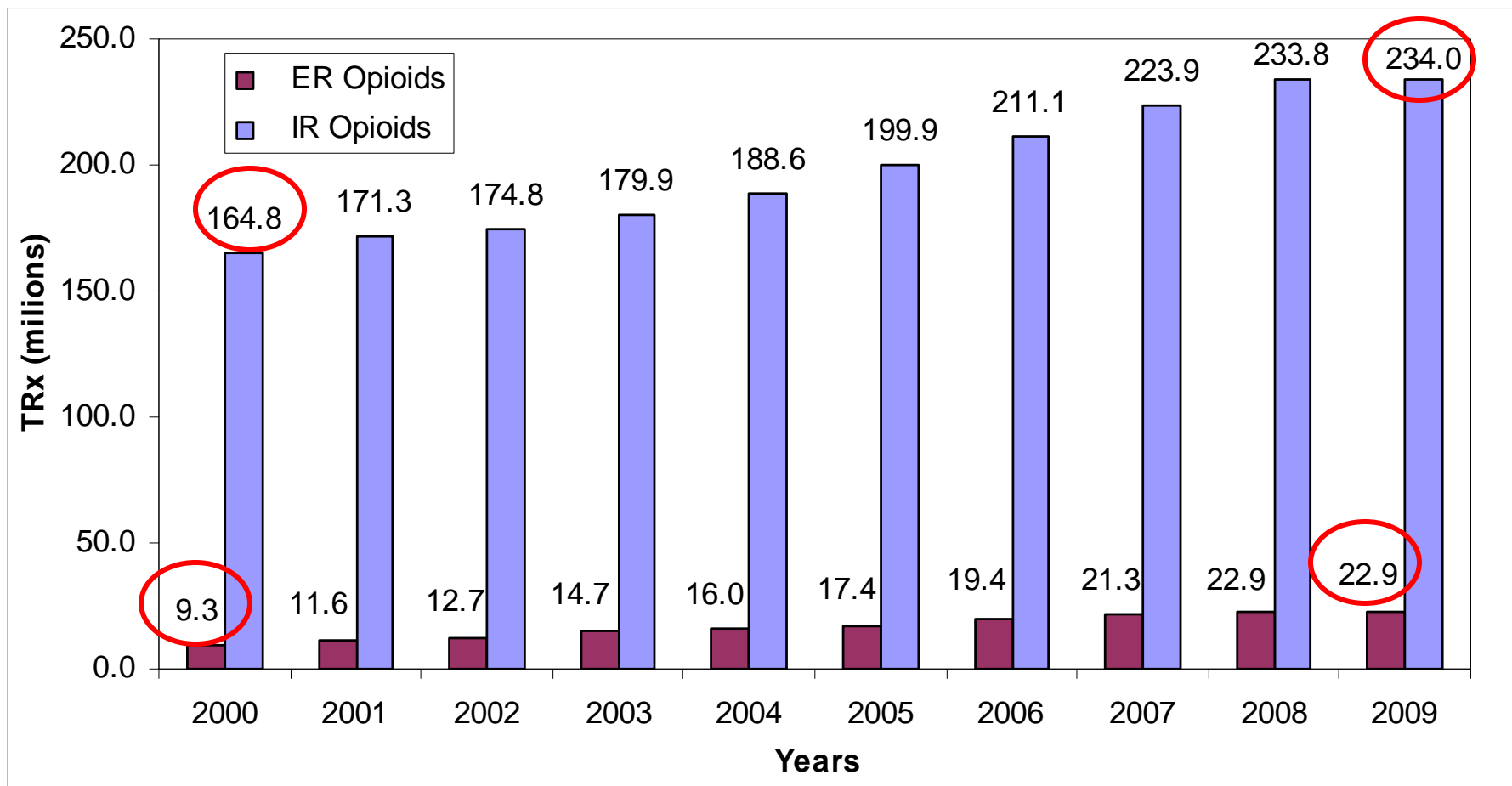
SDI, Vector One®: National. Extracted June 2010.





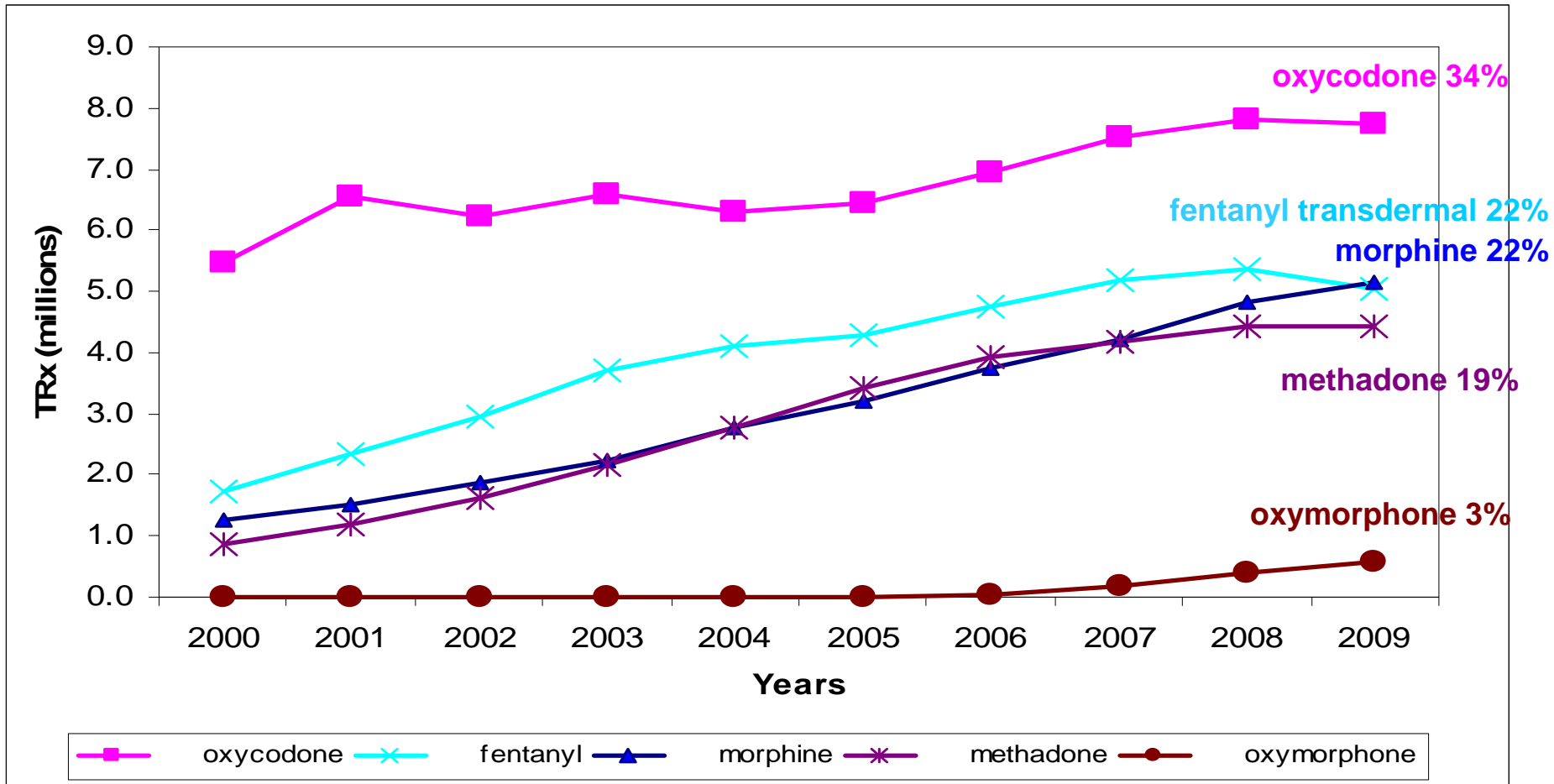
## Total number of prescriptions dispensed for ER/LA and IR opioids from U.S. outpatient retail pharmacies, Year 2000 - 2009

SDI, Vector One®: National. Extracted June 2010.



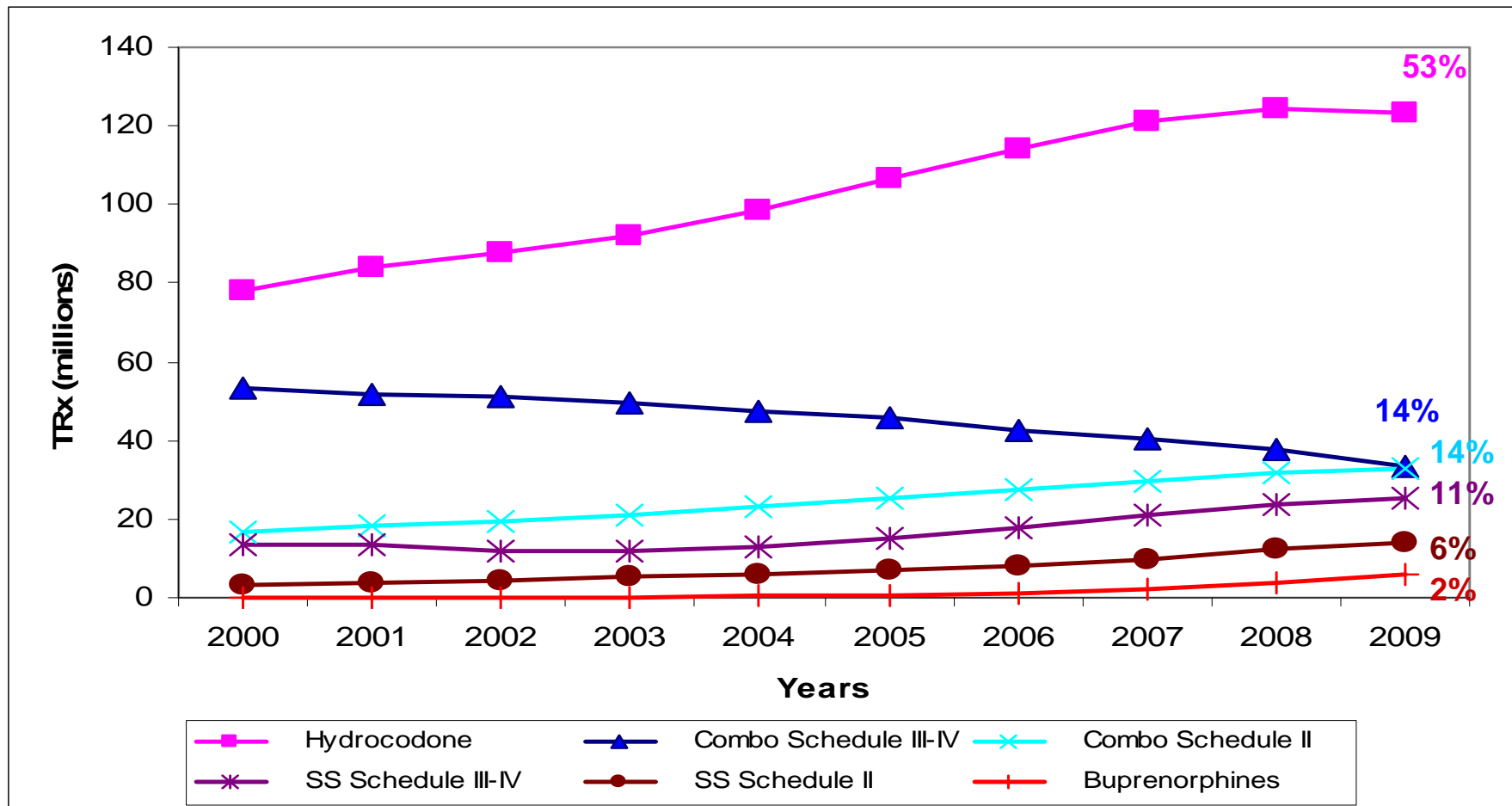
# Total number of prescriptions dispensed for ER/LA opioids from U.S. outpatient retail pharmacies, Years 2000 - 2009

SDI, Vector One®: National. Extracted June 2010.



# Total number of dispensed prescriptions for IR opioids from U.S. outpatient retail pharmacies, Years 2000 - 2009

SDI, Vector One®: National. Extracted June 2010.





## Mean Days of Therapy per Dispensed Opioid Prescription, Years 2000 – 2009

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	Days
ER/LA opioids	23 - 28
IR Single-Ingredient opioids	13 - 21
IR Combination, Hydrocodones, Buprenorphines	8 - 14

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SDI, Vector One®: National. Years 2000 - 2009. Extracted June 2010.

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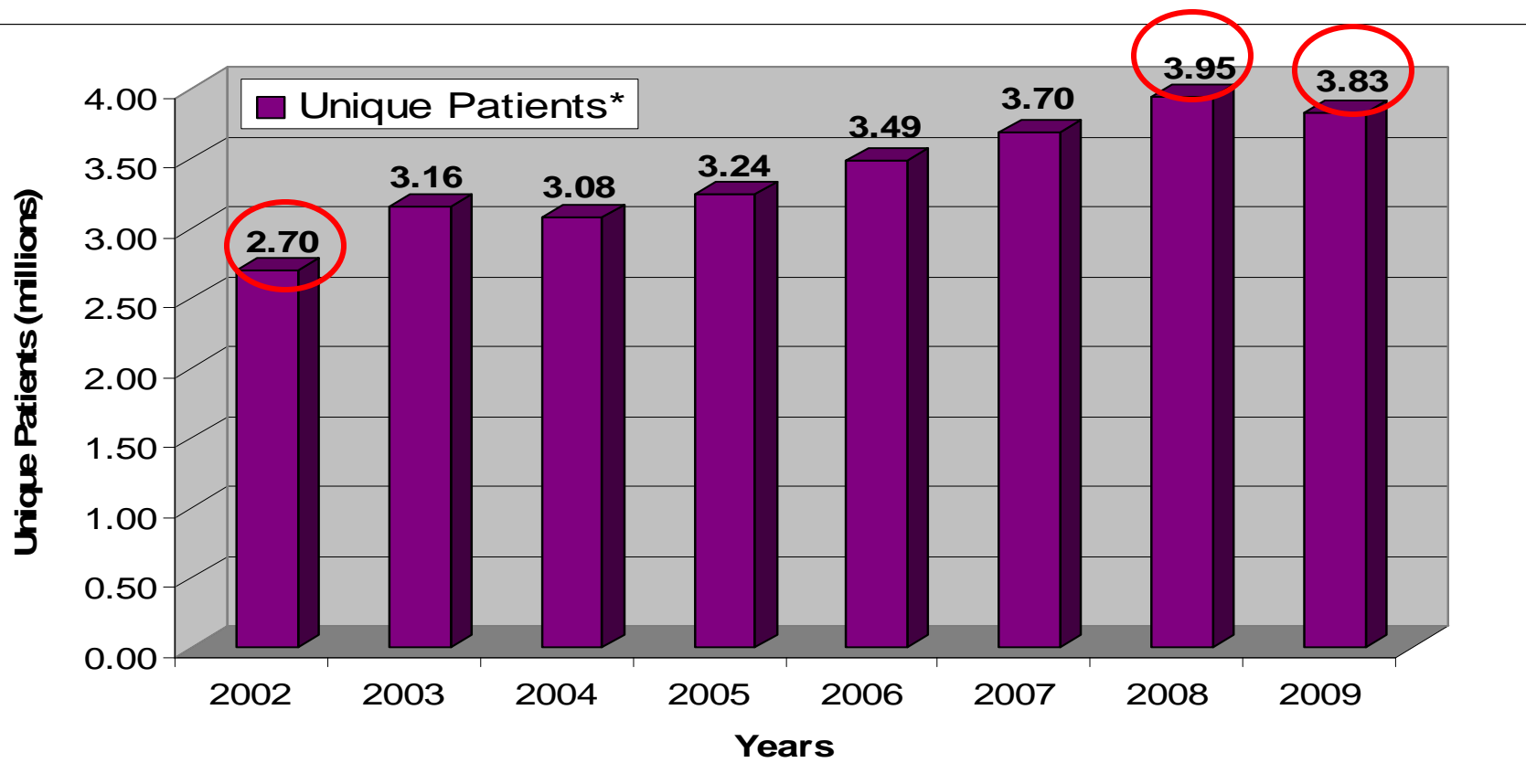
## Percent of new patient new prescriptions dispensed for IR and ER/LA opioid products, Year 2009

SDI: Vector One®: National. Extracted July 2010.

	2009 TRxs	2009 Share TRxs
<b>TOTAL MARKET</b>	257,706,624	100.0%
<b>IR Opioids</b>	234,794,592	91.1%
<b>New Patient Rxs</b>	93,883,495	40.0%
Continuing Patient Rxs	116,242,033	49.5%
Switch/Add-On Patient Rxs	24,669,063	10.5%
<b>ER Opioids</b>	22,912,032	8.9%
<b>New Patient Rxs</b>	6,582,010	28.7%
Continuing Patient Rxs	11,178,876	48.8%
Switch/Add-On Patient Rxs	5,151,146	22.5%

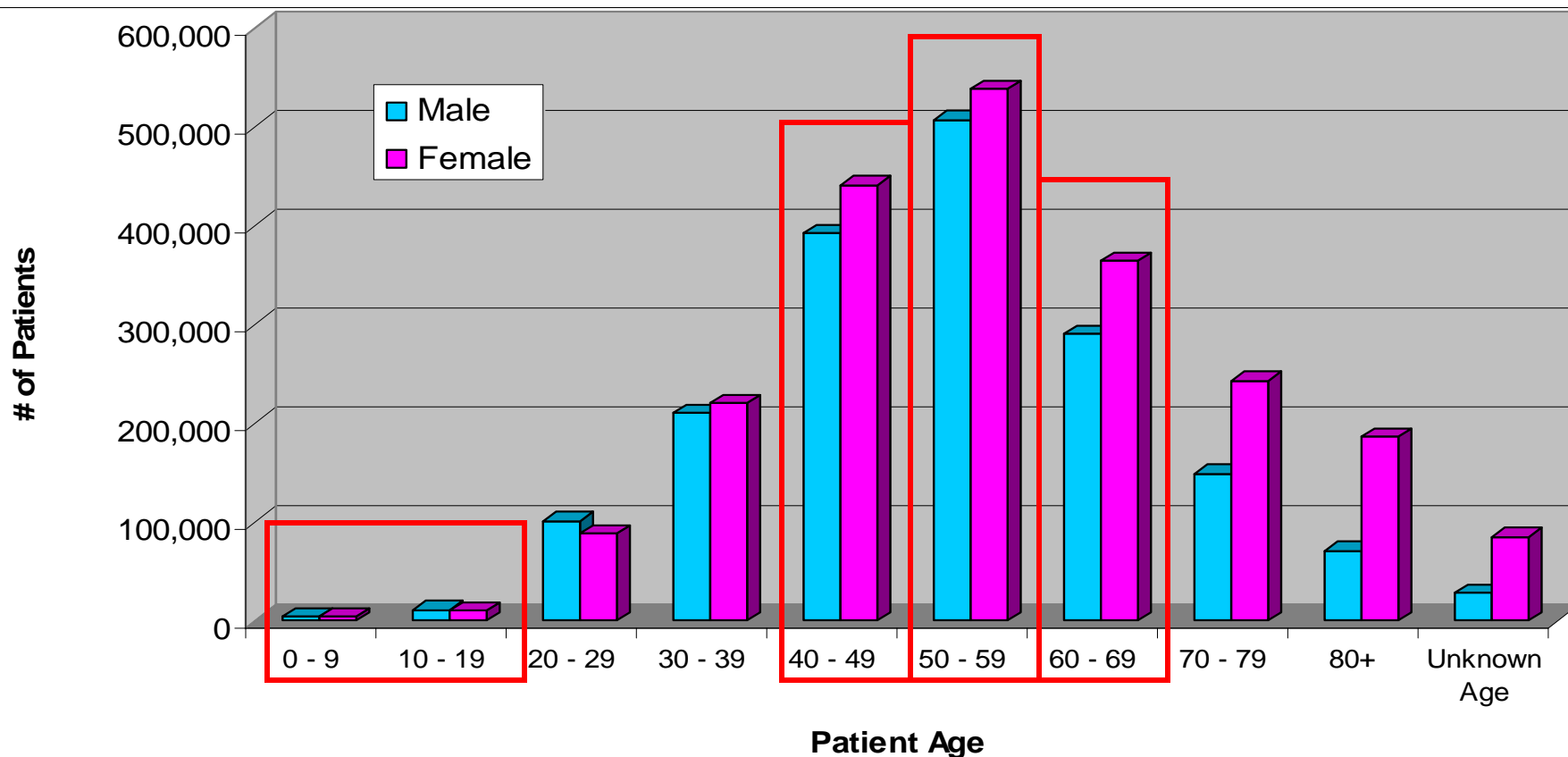
## Total number of unique patients receiving a dispensed prescription for a ER/LA opioid product from U.S. outpatient retail pharmacies, Years 2002 – 2009

SDI, Total Patient Tracker. Extracted June 2010.



# Total number of unique patients, stratified by age and sex, receiving a dispensed prescription for ER/LA opioid product from U.S. outpatient retail pharmacies, Year 2009

SDI, Total Patient Tracker, Extracted June 2010.



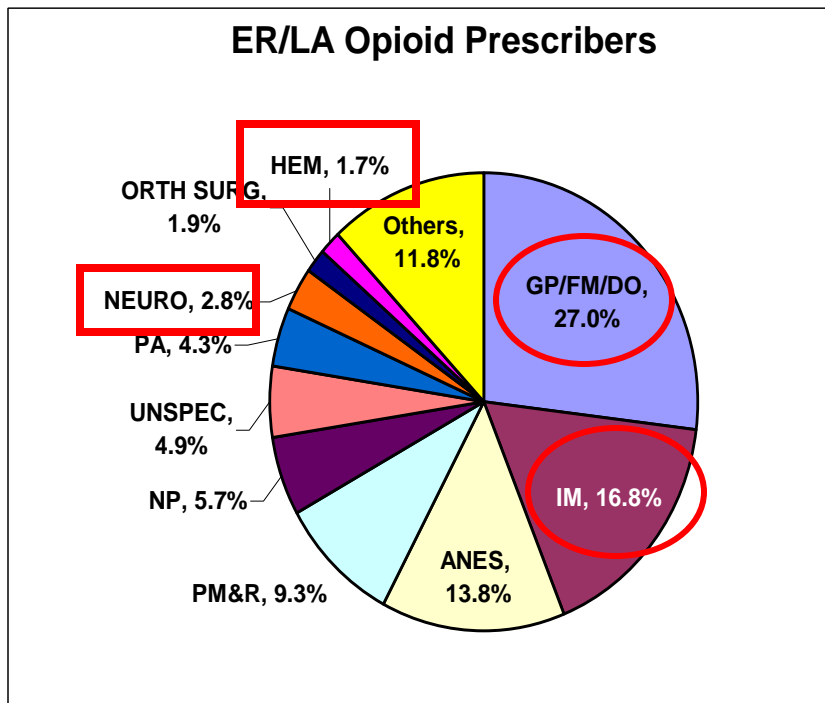
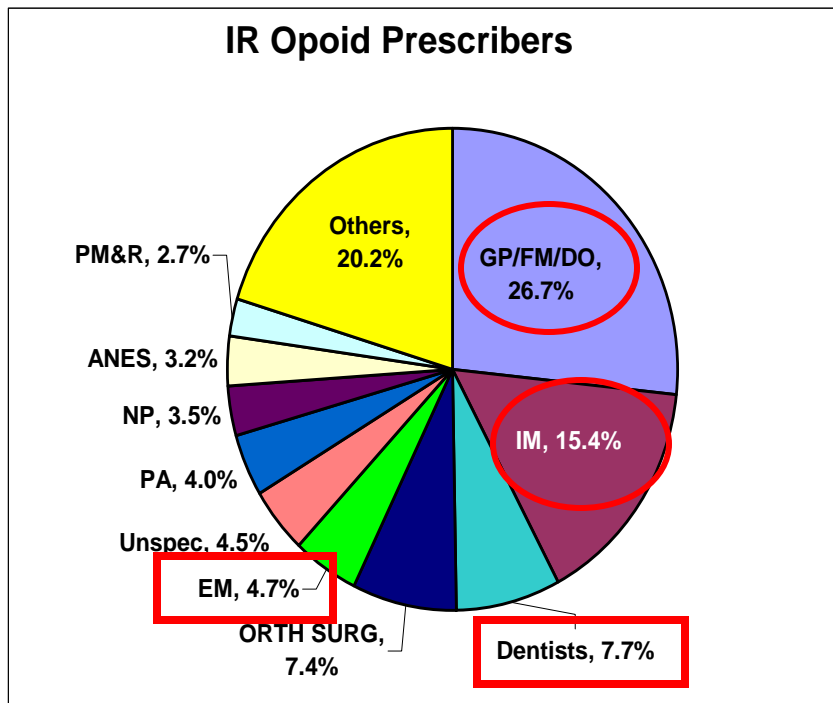


# Prescribing Specialties, Diagnoses Associated with Use...



## Total number of prescriptions dispensed in the U.S. by top 10 prescribing specialties for IR and ER/LA opioids, Year 2009

SDI: Vector One®: National. Extracted June 2010.



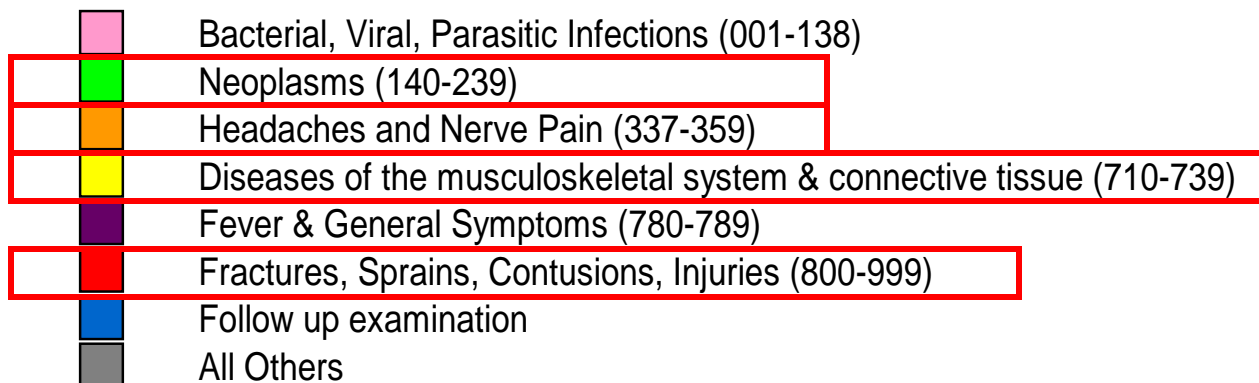
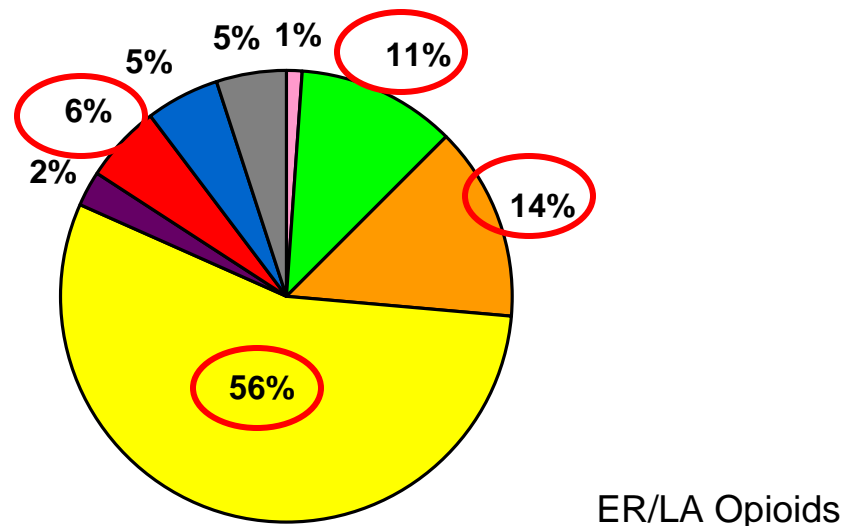
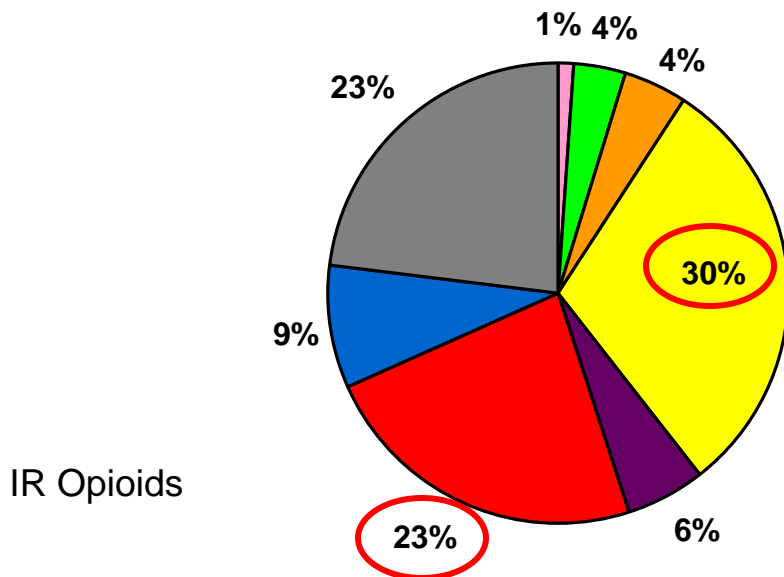
- GP/FM/DO, and IM were top 2 prescribers for IR and ER/LA opioids
- IR opioid prescribers:
- Dentists and EM specialists accounted for about 18 million and 11 million IR dispensed prescriptions

# Diagnoses associated with use SDI, Physician Drug and Diagnosis Audit™

- Office-based physician survey data
  - monthly survey composed of approximately 3,200 office-based physicians that monitors disease states and the physician intended prescribing habits on a national-level
  - designed to provide descriptive information on the patterns and treatment of diseases encountered in office-based physician practices in the U.S.
  - represents 30 specialties across the United States
    - Includes surveys of over 115 pain specialists physicians each month.

## Diagnoses associated with use (by grouped ICD-9 codes) for IR and ER/LA opioids as reported by office-based physicians in the U.S., Year 2009

SDI, Physician Drug and Diagnosis Audit, Extracted 6/10.



# Reason for switching to an ER/LA opioid product

SDI, Physician Drug and Diagnosis Audit, Year 2009, Extracted July 2010.

<b>Ineffective</b>	<b>57.7%</b>
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<b>Nausea</b>	<b>10.3%</b>
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<b>Short acting</b>	<b>7.1%</b>
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<b>Vomiting</b>	<b>5.1%</b>
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<b>Liver toxicity</b>	<b>4.8%</b>
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<b>Too strong</b>	<b>3.7%</b>
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<b>Longer duration of action</b>	<b>3.6%</b>
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<b>Inadequate</b>	<b>1.1%</b>
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<b>Unspecified</b>	<b>32.5%</b>
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Some of the most common reasons for switching to an ER opioid were the following

# Limitations

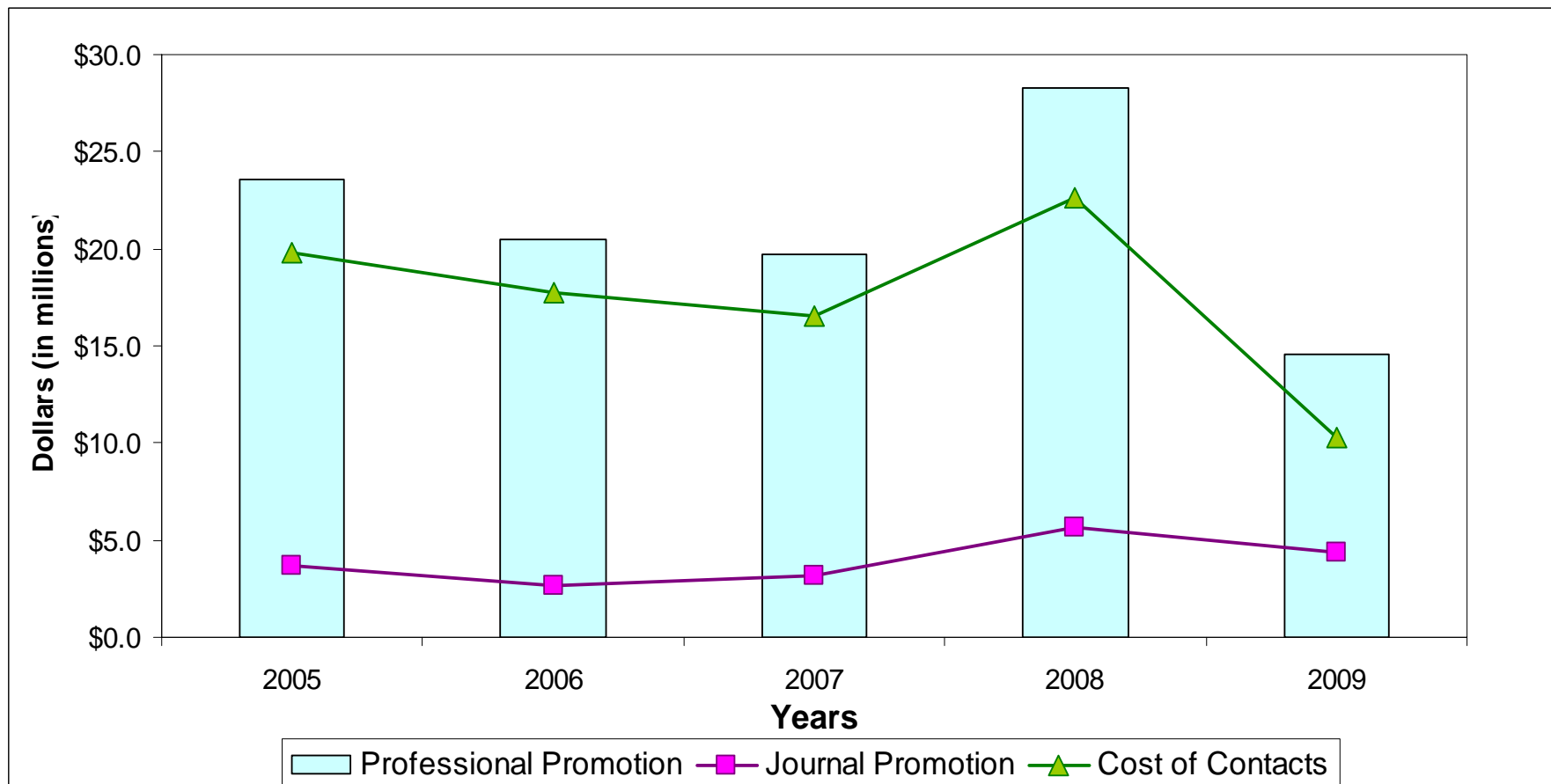
- Only outpatient opioid use assessed; inpatient, ED and other non-outpatient settings not included in analysis
- Unable to assess:
  - “chronic” versus “acute” pain using ICD-9 codes alone
  - opioid tolerance without longitudinal patient-level analysis that encompassing multiple settings of care

# Summary...

- Approximately 3.8 million patients, annually, receive prescriptions for an ER/LA opioid product in the outpatient setting
- About half of prescriptions for ER/LA opioid products are prescribed by primary care practitioners.
- Data suggests that about a quarter of patients on ER/LA opioids have not had an opioid prescription in the previous month
- ER/LA opioids were used more commonly for conditions that are often associated with chronic pain such as back pain and arthritis
- ER/LA opioids had longer mean days of therapy per dispensed opioid prescription than IR opioids

# Total cost of professional promotional activities for ER/LA opioids, Years 2005 - 2009

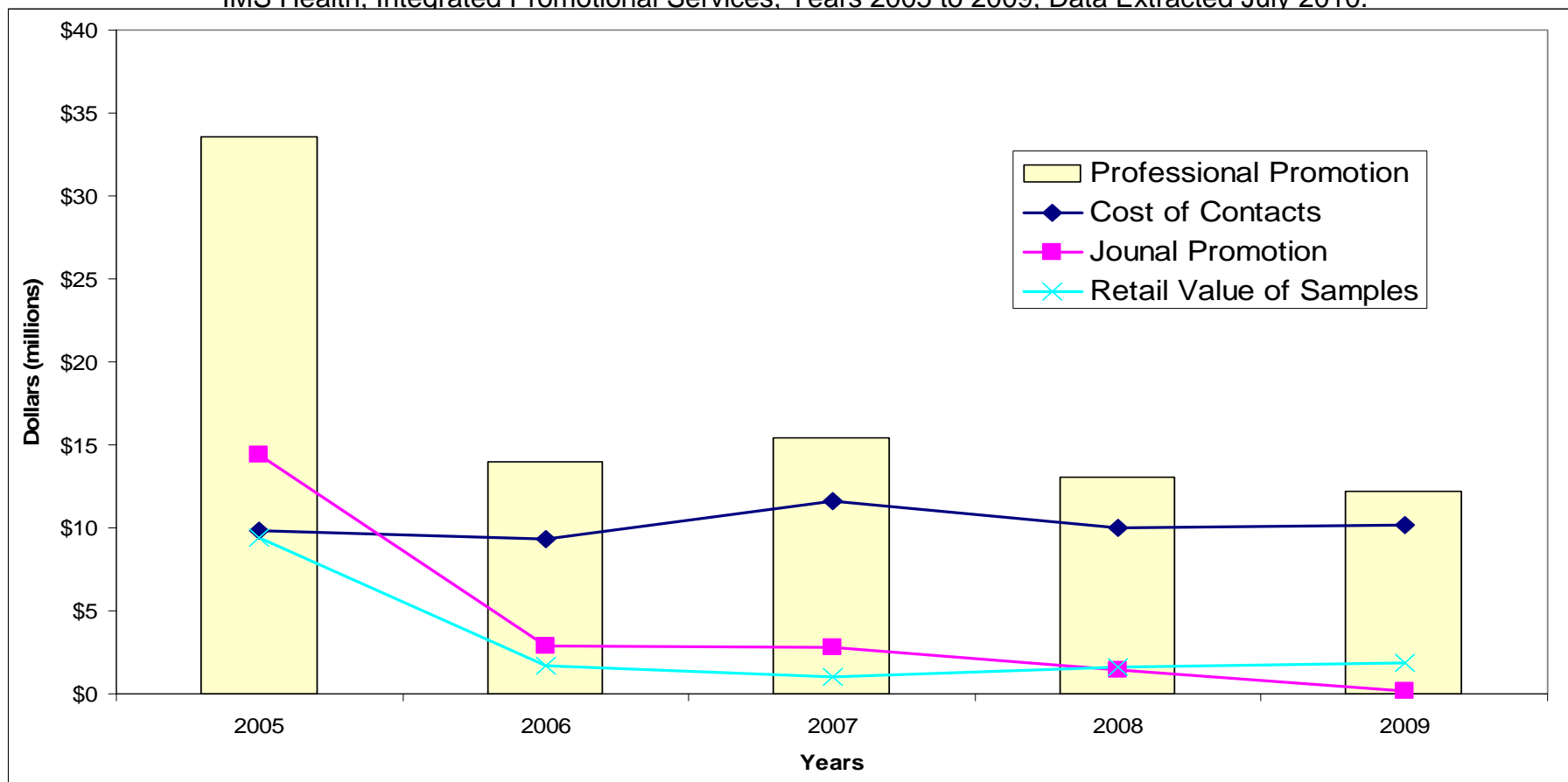
IMS Health, Integrated Promotional Services, Years 2005 to 2009, Data Extracted July 2010.



- Professional promotional activities decreased by 48% from year 2008 to 2009

# Total cost of professional promotional activities for IR opioids, Years 2005 - 2009

IMS Health, Integrated Promotional Services, Years 2005 to 2009, Data Extracted July 2010.



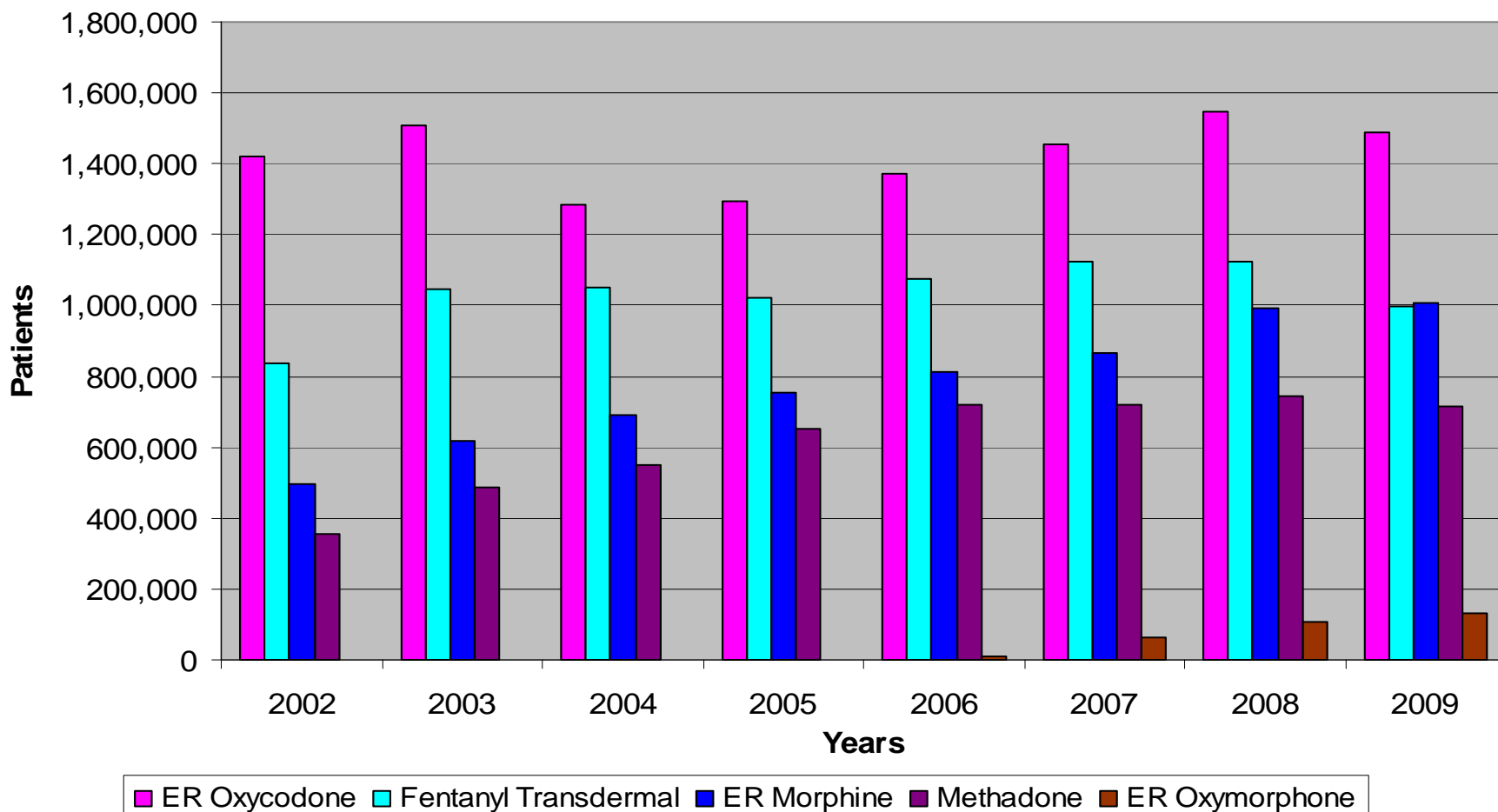
- Professional promotional activities decreased by 64% from year 2005 to 2009





## Total number of unique patients receiving a dispensed prescription for a ER/LA opioid product from U.S. outpatient retail pharmacies, Years 2002 – 2009

SDI, Total Patient Tracker. Extracted July 2010.



# **Opioid Abuse and Misuse: Data from the National Survey on Drug Use and Health and the Drug Abuse Warning Network**

Catherine Dormitzer, PhD, MPH  
Division of Epidemiology  
Office of Surveillance and Epidemiology

# Outline

- Background
  - National Survey on Drug and Health (NSDUH)
  - Drug Abuse Warning Network (DAWN)
- NSDUH -- Reported Findings
- DAWN – Estimates and Ratios
- Methods
- Summary
- Conclusions

# National Survey on Drug Use and Health (NSDUH)

- Representative nationally and in each State. 67,500 respondents each year
- Civilian, noninstitutional population, age 12+
- Face-to-face interview, 1 hour. Computer-assisted, mainly self-administered
- Survey changed in 1999 and in 2002, creating breaks in trends
- Response rates (2006):
  - 91% of Households selected
  - 74% of Persons selected within households (85% for youth, 73% for adults)

# Nonmedical Prescription Drug Use

- Nonmedical use of prescription drugs by therapeutic classes (TCs):
  - Pain Relievers,
  - Tranquilizers,
  - Stimulants,
  - Sedatives
- Specific pharmaceuticals asked for each TC:
  - Lifetime use only (except OxyContin® and methamphetamine)
  - Includes mix of brand-name and generic drugs
  - “Pill cards” show specific pharmaceuticals
- Recency and Frequency of use of TC
  - Lifetime, Past year, Past month
- Date of first use
  - Incidence/First time use within past year
- Dependence and abuse

# Nonmedical Prescription Drug Use: NSDUH Definition

“Not prescribed for you”

OR

“You took the drug only for the  
experience or feeling it caused”

(Excludes OTC)

# “PILL CARDS”

Drug groups above the red line are asked separately

Drug groups below the red line are asked in tandem with followup to identify which one(s)

Any other drugs in TC are specified by write-in.

## CARD A Pain Relievers

<p>1</p> <p><b>Darvocet-N®</b></p> <p><b>Darvon®</b></p> <p><b>Tylenol® with Codeine</b></p>	<p>2</p> <p><b>Percocet®</b></p> <p><b>Percodan®</b></p> <p><b>Tylox®</b></p>	<p>3</p> <p><b>Vicodin®</b></p> <p><b>Lortab®</b></p> <p><b>Lorcet®/Lorcet Plus®</b></p>
<p>4</p> <p><b>Codeine</b></p>	<p>9</p> <p><b>Hydrocodone</b></p>	<p>14</p> <p><b>Propoxyphene</b></p>
<p>5</p> <p><b>Demerol®</b></p>	<p>10</p> <p><b>Methadone</b></p>	<p>15</p> <p><b>SK-65®</b></p>
<p>6</p> <p><b>Dilaudid®</b></p>	<p>11</p> <p><b>Morphine</b></p>	<p>16</p> <p><b>Stadol®</b></p>
<p>7</p> <p><b>Fioricet®</b></p>	<p>12</p> <p><b>OxyContin®</b></p>	<p>17</p> <p><b>Talacen®</b></p>
<p>8</p> <p><b>Fiorinal®</b></p>	<p>13</p> <p><b>Phenaphen® with Codeine</b></p>	<p>18</p> <p><b>Talwin®</b></p>
		<p>19</p> <p><b>Talwin® NX</b></p>
		<p>20</p> <p><b>Tramadol</b></p>
		<p>21</p> <p><b>Ultram®</b></p>

# NSDUH: Nonmedical Use of Pain Relievers

- The proportion of the US population aged  $\geq 12$  years of age ever using prescription pain relievers non-medically has more than doubled in 10 years:

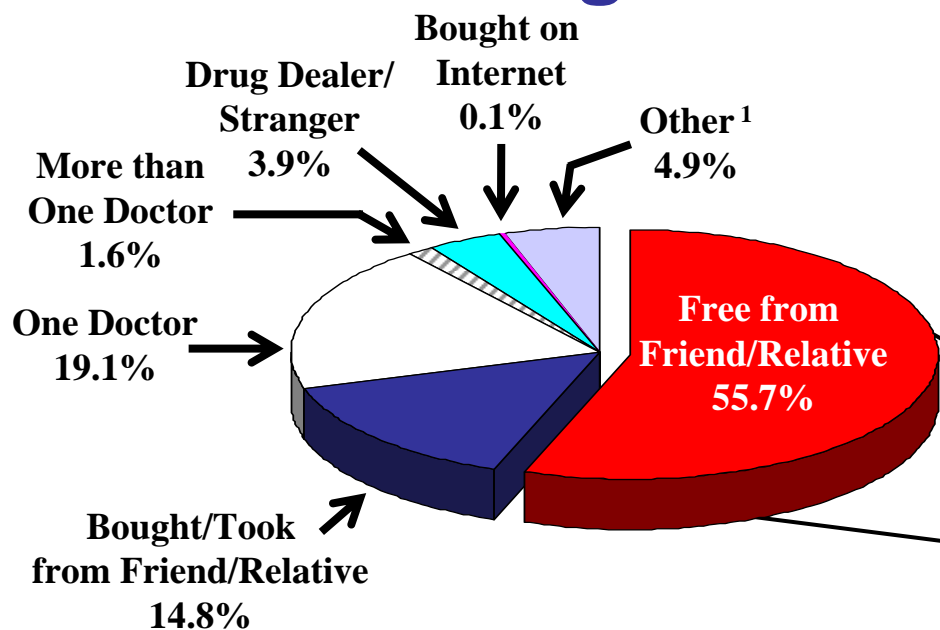
1998	2001	2008
5.8%	9.8%	13.6%

- Increase in incidence (initiates) of non-medical prescription pain relievers use over the years:

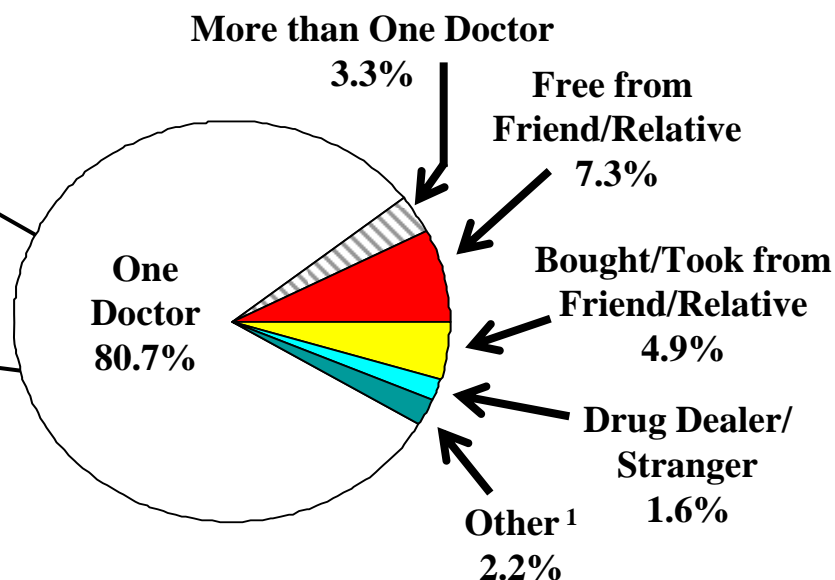
1990	2005
627,000	2.2 million



# NSDUH: Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users : 2006



## Source: Where Friend/Relative Obtained



## Source: Where Respondent Obtained

Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.

<sup>1</sup> Other category includes: "Wrote Fake Prescription," "Stole from Doctor's Office/Clinic/Hospital/Pharmacy," and "Some Other<sup>8</sup> Way." Source: SAMHSA, NSDUH

# Drug Abuse Warning Network (DAWN)

- Administered by the Substance Abuse and Mental Health Services Administration (SAMHSA)
- Stratified probability sample of hospitals
  - Short-term, general, non Federal hospitals with 24-hour emergency departments (EDs)
- National estimates account for:
  - Sample design
  - Hospital non-response
  - Partial non-response in responding hospital

## Selection of Opioid Drugs

- Opioid Analgesic products were selected that included both immediate and extended release formulations
  - Oxycodone (IR & ER)
  - Morphine (IR & ER)
  - Oxymorphone
  - Fentanyl (transdermal & transmucosal)
  - Hydrocodone
  - Methadone
- Relative Standard Errors (RSE) were greater than 50 so estimates were suppressed from all analyses:
  - Oxymorphone
  - Fentanyl transmucosal
  - Morphine IR

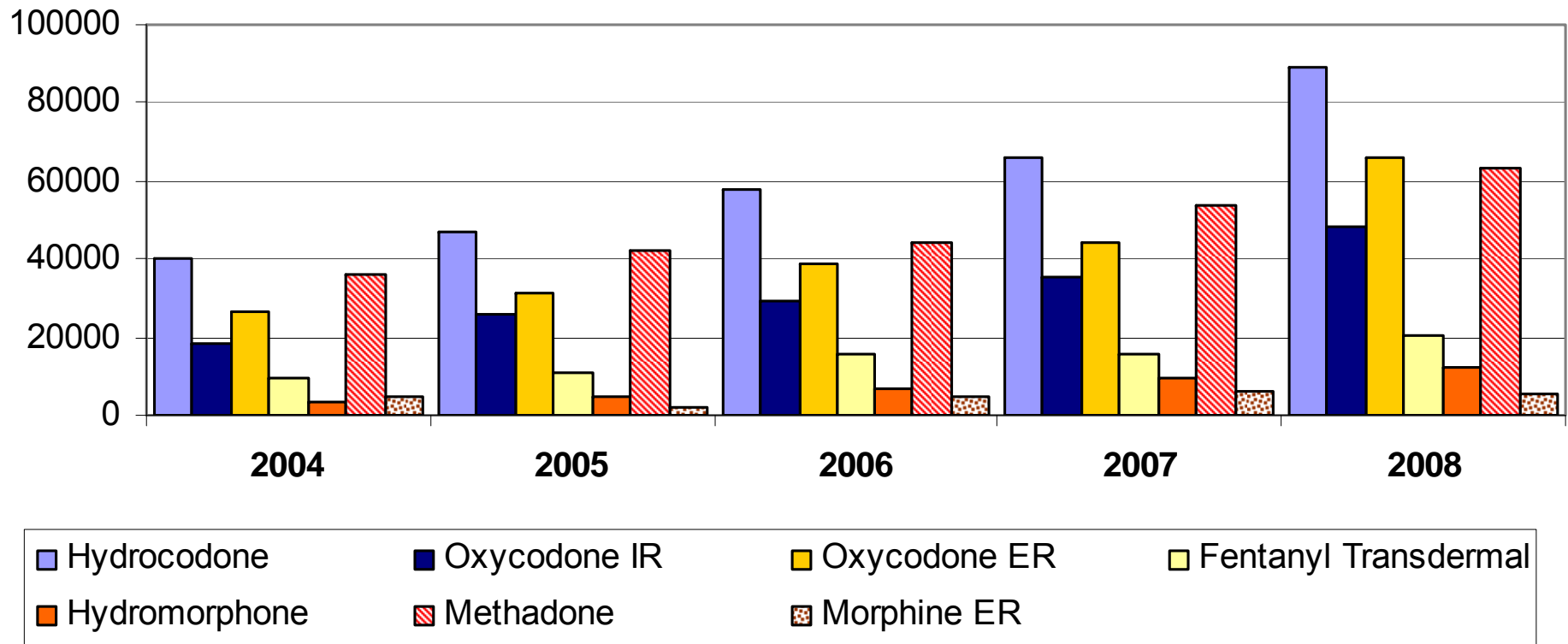
## NMUP & ALLMA Case Types

- SAMHSA constructed definitions
- **NMUP** – non-medical use of pharmaceuticals includes overmedication, seeking detox, “other”
- **ALLMA** – all misuse/abuse -- this classification includes all NMUP ED visits plus ED visits where there were illegal drugs or alcohol present

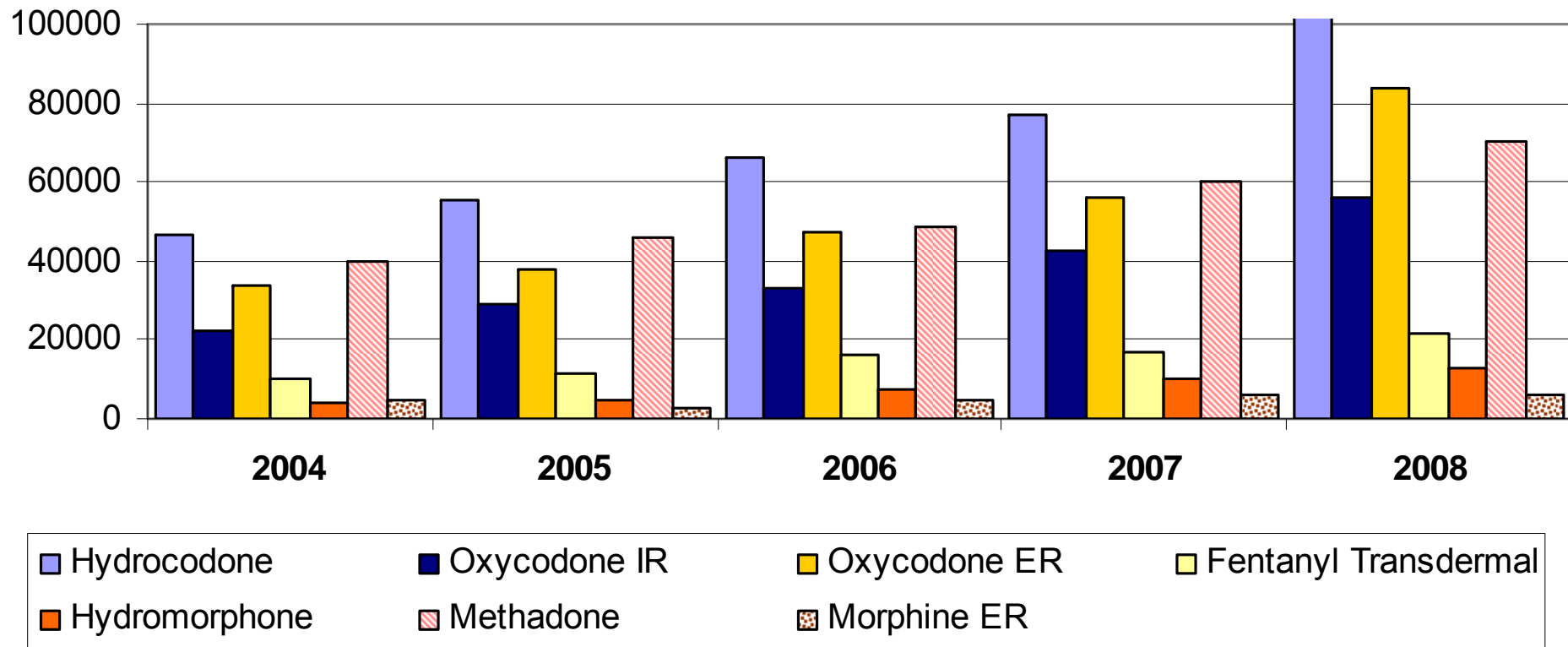
# Analysis – Abuse Ratios

- **Numerator data**
  - Number of NMUP & ALLMA related ED Visits (DAWN)
- **Denominator data**
  - Retail prescriptions used as proxy for drug availability
- **Abuse ratios**
  - number of NMUP ED visits /10,000 retail prescriptions
  - number of ALLMA ED visits /10,000 retail prescriptions

## DAWN: Number of NMUP Related ED Visits by Year and Release Type, 2004 - 2008



## DAWN: Number of AllMA Related ED Visits by Year and Release Type, 2004-2008



## NMUP Ratio: Number of NMUP ED Visits per 10,000 Retail Prescriptions 2004 – 2008

NMUP Ratios	2004	2005	2006	2007	2008
<b>IR</b>					
Oxycodone IR	7.3	9.1	9.5	10.2	12.4
Hydrocodone	4.0	4.4	5.0	5.4	7.1
<b>ER/LA</b>					
Oxycodone ER	42.0	48.9	55.5	59.1	84.5
Fentanyl Transdermal	23.5	25.8	33.1	30.4	37.4
Hydromorphone	34.3	38.6	48.4	58.3	64.6
Morphine ER	17.0	6.9	12.5	13.9	11.8



## AIIMA Ratio: Number of AIIMA ED Visits per 10,000 Retail Prescriptions 2004 – 2008

<b>AIIMA Ratios</b>	<b>2004</b>	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>2008</b>
<b>IR</b>					
Oxycodone IR	8.8	10.4	10.8	12.2	14.3
Hydrocodone	4.7	5.2	5.8	6.4	8.4
<b>ER/LA</b>					
Oxycodone ER	53.2	59.0	68.3	74.2	106.8
Fentanyl Transdermal	24.4	27.1	34.4	31.9	39.7
Hydromorphone	40.5	40.6	53.1	62.3	70.1
Morphine ER	17.1	7.6	13.5	14.0	12.7

# Ratio Not Assessed

- Methadone
  - Methadone is used for analgesia and for opioid dependence treatment
    - Numbers of ED visits are available for methadone, but the reason for the use is not identified
    - Denominator data are not available from opioid dependence treatment programs

# Limitations

- Calculating abuse ratios using different data sources for numerator and denominator estimates has limitations
  - Data are not linked
    - DAWN
    - SDI Vector One®: National (VONA)
  - Differences in Sampling Methodologies
    - DAWN
    - SDI Vector One®: National (VONA) -
  - Differences in Population
    - DAWN -
    - SDI Vector One®: National (VONA)
  - Large numbers produce more precise estimates,
    - i.e. small estimates have larger confidence intervals

# DAWN: Summary

- Prescription data serves as a proxy for drug availability and provides context for non-medical use.
- ED visits related to non-medical use of pain relievers increased from 2004 through 2008.
- The ratios (e.g. ED visits/Rx) are higher for ER/LA opioid products compared to immediate release opioid products.

# NSDUH: Summary

- In 2008, more than 13% of Americans aged 12 and older have used a prescription pain reliever non-medically at least once in their lifetime.
- More than 2 million Americans aged 12 and older, initiate non-medical use of a prescription pain reliever each year; this rate has remained unchanged for the past 5 years.
- Most non-medical users of prescription pain relievers obtained it from one doctor.

## Conclusion

- The non-medical use and abuse of opioid analgesics continues to be an important public health problem.



# Extended-Release and Long-Acting Opioid Labeling and Risk Management

Division of Anesthesia and Analgesia  
Products  
CDER/OND/Office of Drug Evaluation II

# Summary of Presentation

- Important Labeling Changes
- Risk Management



## 2000: Initial reports of OxyContin abuse and diversion

- Increasing media and state reports of abuse and diversion of OxyContin:
  - Crushing of tablets
  - Oral, inhalation, injection administration
  - Adverse events included addiction, withdrawal and fatalities
- Prominently affected areas:
  - Appalachian states: Kentucky, Virginia, W. Virginia, Pennsylvania
  - Maine; Ohio
- Involved recreational drug users, teenagers, pain patients

# Early Indication

- Indication for modified-release opioids:  
“For the management of moderate to severe pain where use of an opioid analgesic is appropriate for more than a few days.”

# Amended Indication

- For the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.
- Not intended for intermittent dosing or as an as needed analgesic.
- Not indicated for pain in the immediate post-operative period if the pain is mild or not expected to persist.

# Addition of a Boxed Warning

- Calls attention to the potential for abuse, misuse and diversion of the product.
- Highlights the proper treatment population.

# Addition of a Boxed Warning

## Potential for abuse

- Tradename contains (name of opioid), which is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

# Addition of a Boxed Warning

## Potential for abuse

- Tradename can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Tradename in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

# Addition of a Boxed Warning

## Proper patient selection

- Tradename is not indicated for the management of acute or postoperative pain.
- Tradename is not intended for use as an as needed analgesic.

# Addition of a Boxed Warning

## Proper patient selection

- Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse, abuse and addiction.



# Addition of a Boxed Warning

## Safe Use

- Tradename must be swallowed whole and must not be cut, broken, chewed, crushed, or dissolved. Taking cut, broken, chewed, crushed or dissolved Tradename tablets leads to rapid release and absorption of a potentially fatal dose of (opioid name)

# Risk Management Plan

OxyContin RMP - 2001

Key messages

- Proper patient selection messages
- Prevention of diversion and abuse messages
- Child safety messages

# Risk Management Plan

## Key features

- Education and outreach
- Labeling
- Surveillance
- Intervention

# Risk Management Plan

## Education

- Accredited Physician, Nursing, and Pharmacist Continuing Education Programs via unrestricted educational grants
- Symposia at National/Regional Organization/Society Meetings
- Seminars
- Targeted Antidiversion and Law Enforcement Programs
- Monographs— Symptoms and management of drug addiction
- Journal Supplement

# Risk Management Plan

## Surveillance

- Media Surveillance
- Exposure Data
- Basic Surveillance for Abuse and Addiction
  - Drug Abuse Warning Network (DAWN)
  - Toxic Exposure Surveillance System (TESS)
  - RADARS Surveillance System
    - estimates of rates of misuse, abuse, addiction, and diversion via treatment programs, contacts with law enforcement agencies, surveys of individuals knowledgeable about abuse and addiction trends in their region.

# Public Discussions

## January 30 & 31, 2002

- Advisory Committee meeting to discuss:
  - Opioid analgesic use and development.
  - Use of opioid analgesics in pediatric patients.
  - Abuse and misuse of opioid analgesics.
- Notable conclusions:
  - Abuse of opioid analgesics is a considerable public health problem.
  - However, opioid analgesics are an essential component of pain management.
  - Any RMP that restricts opioid treatment may prevent their appropriate utilization.

# Public Discussions

## September 9 & 10, 2003

- Advisory Committee meeting to discuss:
  - RMPs for opiate analgesic drug products
    - Particular attention to modified-release products
  - Abuse liability of and RMP for Palladone (extended-released hydromorphone)
- Key conclusions: RMP should include -
  - Appropriate prescriber education
  - Surveillance of misuse, abuse, diversion
  - Assessment of the source(s) of diverted drugs
  - Assessment of the RMP's impact on opioid prescribing practices

# Public Discussions

May 5 , 2008

- Advisory Committee meeting to discuss: OxyContin reformulation
  - Tamper-resistant properties
  - Adequacy of testing methods
  - Impact on abuse, misuse and diversion
  - Changes to the product label
  - RMP
- Notable conclusions:
  - Available data are not adequate to support tamper-resistance claims
  - Inclusion of the new physicochemical properties in the label may result in false security and adversely impact addiction and overdose
  - RMP: directed at the entire opioid class, targeted education, restricted indication



# OxyContin: Public Discussions

May 5 , 2008

- Advisory Committee meeting to discuss: OxyContin reformulation
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# Summary

- Identification of the problem
- Attempts to reduce abuse and misuse of extended-release opioids through labeling and RMPs



# **Education Campaigns on Misuse of Pain Relievers**

Ellen Frank

Director, Division of Public Affairs

July 22, 2010

# Objective

- Background on Mission of CDER's Division of Public Affairs
- Provide overview of Education Campaigns related to Misuse of Pain Relievers

## **Education Campaigns on Misuse of Pain Relievers**

- **Safe Use of Methadone (SAMHSA)**
- **Misuse of Prescription Pain Relievers (older adults)**
- **Misuse of Prescription Pain Relievers (teens)**
- **Prescription Drug Abuse (parents of teens)**
  - \* **Partnership for Drug Free America**
  - \* **Office of National Drug Control Policy**
- **Medicines In My Home**
- **Prescription Drug Abuse on College Campuses (NCPIE-SAMHSA)**

## **Example of Campaign Components**

- Brochures – English and Spanish
- Fact Sheet – English and Spanish
- Posters – English and Spanish
- Web Site
- Targeted Point-of-Sale material - English
- Patient Safety News Segments
- Print Public Service Ads
- Radio and TV ads
- Newspapers and magazines
- Dissemination through Partner Organizations

# Safe Use of Methadone

## Partnership with SAMHSA



### Methadone Is a Proven Road to Relief...If You Keep Your Eyes on the Road

Methadone provides relief to patients who do not respond to non-narcotic pain medications and to individuals who suffer from addiction and dependence on heroin and narcotic pain medicines.

Here are some simple ways to reduce the risks:

- Know and share your complete health history with health professionals, especially if you are a first-time user. Other medicines may interact with methadone and cause heart conditions.
- Take methadone exactly as prescribed. Follow your doctor's directions exactly.
- Never use more than the amount prescribed, at the times prescribed. If you miss a dose or if you feel it is not working, do not take extra.
- Use caution when taking methadone. Don't consume alcohol. Be careful driving or operating machinery.
- Take care not to abuse methadone. It can be addictive.
- Call 911 if you take too much methadone or overdose.
- Take steps to prevent children from accidentally taking methadone; never give methadone to anyone else.
- Store methadone at room temperature and away from light.
- Dispose of unused methadone by flushing it down the toilet.

**Take Side Effects Seriously**  
Some are emergencies.  
Patients should stop taking methadone—and contact a physician or emergency services right away—if they:

- Have difficulty breathing or shallow breathing
- Feel lightheaded or faint
- Get hives or a rash; have swelling of the face, lips, tongue, or throat
- Feel chest pain
- Have a fast or pounding heartbeat
- Have hallucinations or confusion

### Need More Information?

Patients who develop a problem with methadone or have questions should speak with a physician or contact 1-800-662-HELP.

Helpful information can also be found at the following Web sites:



U.S. Department of Health and Human Services (HHS)  
[www.hhs.gov](http://www.hhs.gov)

Substance Abuse and Mental Health Services Administration (SAMHSA)  
[www.samhsa.gov](http://www.samhsa.gov)

Center for Substance Abuse Treatment (CSAT)  
[www.csat.samhsa.gov](http://www.csat.samhsa.gov)

CSAT's Division of Pharmacologic Therapies  
[www.dpt.samhsa.gov/methadonesafety](http://www.dpt.samhsa.gov/methadonesafety)

Food and Drug Administration (FDA)  
[www.fda.gov](http://www.fda.gov)







## Prescription Pain Relievers and the Elderly

### Follow the prescription.



Prescription pain relievers are safe and effective when used correctly. If misused, you could become addicted or experience other problems.

Take your prescription as directed. To get answers about your pain reliever, call your doctor. For information about addictions, call **1-800-662-HELP**.  
**Do the right dose.**



### Do The Right Dose



Sometimes your pain seems overwhelming.

Prescription pain relievers are safe and effective when used correctly. If misused, you could become addicted or experience other problems.

Take your prescription as directed. To get answers about your pain reliever, call your doctor. For information about addictions, call 1-800-662-HELP.

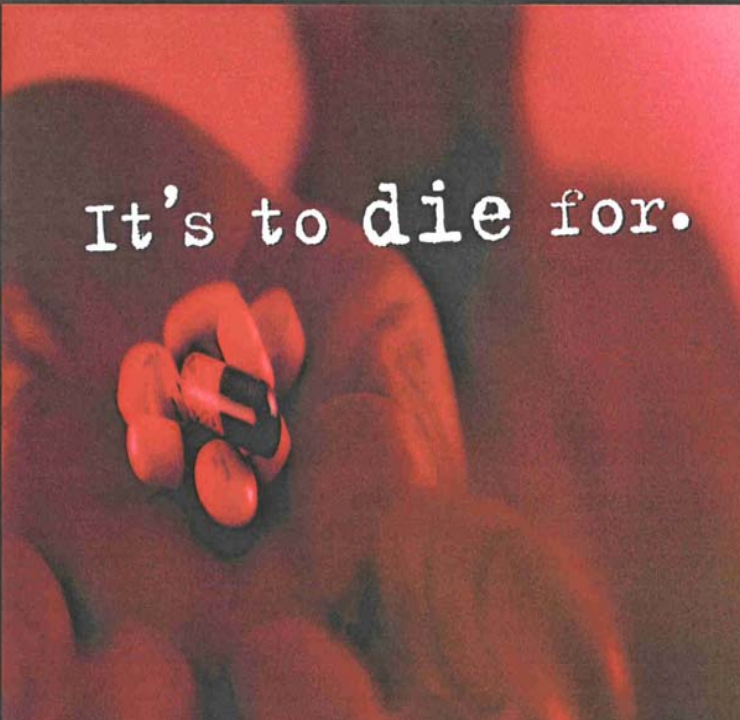
Do the right dose.








## Teens and Misuse of Prescription Pain Relievers



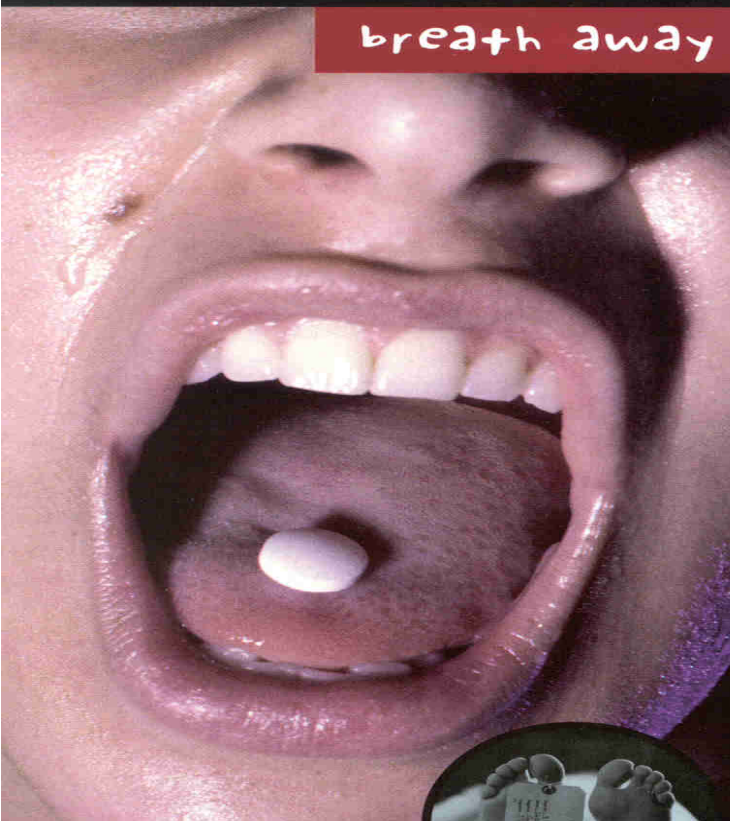
It's to die for.

It starts with "just this once," and it can end there.  
Misuse of prescription pain relievers can kill you.  
If someone offers you oxy, percs, vics or some other party drug,  
**think twice—because you only die once.**  
For information or help, call 1.800.662.HELP.

 U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Substance Abuse and Mental Health Services Administration  
Food and Drug Administration


Prescription pain relievers, when used correctly and under a doctor's supervision, are safe and effective.


The buzz takes your  
breath away



Permanently.

Misuse of prescription  
pain relievers can kill you.



 U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Substance Abuse and Mental Health Services Administration  
Food and Drug Administration



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

www.fda.gov

## Teens and Misuse of Pain Relievers

The Partnership for a Drug Free  
America

Ad in Newsweek



## MOST TEENS GO THROUGH PHASES. SOME GO THROUGH THE MEDICINE CABINET INSTEAD.

Teens are abusing prescription drugs at an alarming rate to cope with some of the problems in their lives. Moodiness, anxiety and peer pressure are often a common part of growing up but some teens are struggling with real adolescent depression and can't cope as well as others.

In fact, you may not know it, but 1 in 5 high school teens admits to abusing prescription drugs. That's a problem. And that's a problem we have to face.

The bigger problem is the misconception that these drugs are safe for everyone because they come from pharmacies, but taking drugs without a prescription can be as dangerous and addictive as using street drugs.

There are signs that can indicate your child needs help so look for them. Signs may include a dramatic change in your child's behavior that lasts longer than a few weeks. Watch for loss of interest in activities, difficulty concentrating or even anger and hostility.

These are signs that your teen might be depressed, which can lead some teens to abusing prescription drugs for help. If you'd like to find more information about how you can spot signs of teen depression, visit the Academy of Adolescent and Child Psychiatry at [www.aacap.org](http://www.aacap.org). If you think your teen may be exhibiting some of this behavior consult a doctor – ideally one specializing in adolescent mental health.

When used as directed, prescription drugs serve a helpful purpose but they should never (really, never) be used without a doctor's supervision. Be safe. Most of us have prescription drugs at home. If you need them, just be sure to keep careful track of them. If you don't, safely get rid of them.

For more information about the causes and dangers of prescription drug abuse and what you can do, visit [www.drugfree.org](http://www.drugfree.org).



U.S. FOOD & DRUG ADMINISTRATION

The Partnership for a Drug-Free America

Not all Dangerous  
Drugs are Illegal.

Learn about  
prescription drug  
abuse at  
[www.drugfree.org](http://www.drugfree.org)



U.S. Food and Drug Administration  
Protecting and Promoting Public Health

# Prescription Pain Reliever Abuse Among Teens and Young Adults

Letter to parents

Partnership with ONDCP

## IS THIS WHERE YOUR TEEN GOES TO GET HIGH?



A growing danger among teens today is the intentional abuse of prescription drugs and over-the-counter cough and cold medicines to get high.

One cause of the problem is how easily teens can find them. These drugs are most likely already in your own home. Over half of teens who abuse prescription pain relievers report they get them for free from the homes of family or friends, or they take them from family or friends without asking.<sup>1</sup>

Most frightening, however, is that teens often don't recognize the dangers of prescription and over-the-counter drug abuse; they don't see it to be as harmful as illicit drug use. After all, these drugs are approved for medical use. But when taken without medical supervision, intentionally abused, or mixed with other drugs or alcohol, prescription medicines can be dangerous. Teens who decide to abuse prescription drugs run the risk of addiction, strokes, seizures, comas, and even death.

Unfortunately, it's a growing trend. Teens are turning away from using street drugs to prescription medications to get high. New users of prescription drugs are actually catching up with new users of marijuana.<sup>2</sup>

The first step for parents is to recognize the potential risks and consequences of prescription drug abuse, and to help teens understand them as well. Learn the signs, symptoms, and tips on how to talk to your teens about prescription drug abuse. **Educate yourself to protect your teens; visit [www.TheAntiDrug.com](http://www.TheAntiDrug.com) or call 1-800-788-2800.**

Overall, teen use of street drugs is down. That's great; that means you've been doing your job. Now it's time to make sure that you stay updated on this latest threat to your teens' health and safety.

Signed,

American Academy of Pediatrics  
American College of Emergency Physicians  
American Medical Association  
American Pharmacists Association  
American Society of Addiction Medicine  
Association for Medical Education  
and Research in Substance Abuse (AMERSA)

National Association of Chain Drug Stores  
National Association of School Nurses  
National Council on Patient Information and Education  
Partnership for a Drug-Free America  
U.S. Department of Health and Human Services  
National Institute on Drug Abuse  
Substance Abuse and Mental Health Services Administration  
U.S. Food and Drug Administration



[www.TheAntiDrug.com](http://www.TheAntiDrug.com)

<sup>1</sup> SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2003  
<sup>2</sup> Ibid





U.S. Food and Drug Administration  
Protecting and Promoting Public Health

[www.fda.gov](http://www.fda.gov)



# Medicines In My Home



Department of Health and Human Services  
Food and Drug Administration



# **Opioids Safe Use Education Initiative**

## **More to Come!**

# Risk Evaluation and Mitigation Strategies (REMS) Requirements of the Food and Drug Administration Amendments Act of 2007 (FDAAA)

Presentation to the Joint Anesthetic and Life Support and  
Drug Safety and Risk Management Advisory Committees  
July 22, 2010

Jane A. Axelrad, J.D.  
Associate Director for Policy  
Center for Drug Evaluation and Research  
FDA

# Section 505-1 – Risk Evaluation and Mitigation Strategies (REMS)

FDA may require a REMS:

- Before approval: If FDA determines a REMS is necessary to ensure that the benefits of the drug outweigh the risks
- After approval: If FDA becomes aware of new safety information and determines a REMS is necessary to ensure the benefits of the drug outweigh the risks

# FDA Can Enforce REMS Requirements Against the Sponsor

- Sponsor may not introduce drug into interstate commerce if in violation of provisions
- Drug may be found to be misbranded
- FDA can impose civil penalties on sponsors for violations of the Act



# Factors that FDA must consider in determining the need for a REMS

- Size of the population likely to use the drug
- Seriousness of the disease
- Expected benefit of the drug
- Expected duration of treatment
- Seriousness of known or potential adverse events
- Whether the drug is a new molecular entity

# Elements of a REMS

- MedGuides (if meets regulations in 21 CFR Part 208) and Patient Package Insert (PPI) (if insert may help mitigate serious risk of the drug)
- Communication plan if FDA determines plan may support implementation of an element of the REMS
- Elements to assure safe use
- Implementation system, if REMS includes certain elements to assure safe use
- Timetable for assessment (only required element)

# Medication Guides

- Medication Guides were previously considered only part of labeling but may be included as part of a REMS if FDA determines the Medication Guide is necessary to inform patients about the risks or instructions for safe use of the drug.

# Communication Plans

- Communication plan may include letters to healthcare providers; disseminating information about the REMS to encourage implementation; disseminating information through professional societies about any serious risks of the drug and any protocol to assure safe use
- When an ANDA is approved for a drug with a REMS that includes a communication plan, FDA must implement the communication plan

# Elements to Assure Safe Use

- FDA may require elements to assure safe use when:
  - FDA determines that the drug is associated with a serious adverse drug experience and can be approved only if, or would be withdrawn unless, such elements are required as part of such strategy, and
  - For a drug that is approved initially without elements to assure safe use, FDA must determine that the other elements of a REMS would not be sufficient to mitigate the serious risk.

## FDAAA Requires that ETASU

- Be commensurate with specific serious risk(s) listed in the labeling of the drug
- Not be unduly burdensome on patient access to the drug, and
- To minimize the burden on the healthcare delivery system, must, to the extent practicable, conform with elements for other drugs with similar serious risks and be designed for compatibility with established distribution, procurement, and dispensing systems for drugs

# Elements to Assure Safe Use (ETASU)

- Healthcare providers who prescribe the drug have particular training or experience or special certifications
- Pharmacies, practitioners, or healthcare settings that dispense the drug are specially certified
- The drug may be dispensed only in certain healthcare settings
- The drug may be dispensed to patients with evidence of safe-use conditions
- Each patient must be subject to monitoring
- Patients must be enrolled in a registry

# ETASU: Certification of Healthcare Providers

- A REMS may require health care providers who prescribe the drug to have particular training or experience, or to be specially certified
- Certifications may require, for example, that prescribers:
  - Are familiar with educational materials, risks of the drug, and conditions for safe use
  - Counsel patients about the risks and appropriate use of the drug



# ETASU: Certification of Those Who Dispense

- A REMS may require pharmacies, practitioners, or health care settings that dispense the drug to be specially certified
- Certifications may require, for example, that dispensers:
  - Be familiar with educational materials, risks of the drug, and conditions for safe use
  - Verify that prescribers and patients are enrolled in the REMS program, enroll patients themselves, or counsel patients

# ETASU: Dispense in Certain Settings

- The REMS may require that the drug be dispensed to patients only in certain health care settings
  - for example, product can only be administered in hospitals or infusion centers

# ETASU: Documentation of Safe-Use Conditions

- The REMS may require that the drug be dispensed to patients with evidence or other documentation of safe-use conditions
- Evidence of safe use conditions may include
  - Laboratory tests
  - Documentation of consent or counseling by patient
  - Patients receive the drug only after specified authorization is obtained (e.g., documented negative pregnancy test)

# ETASU: Patient Monitoring

- The REMS may require each patient using the drug be subject to certain monitoring
  - Might require periodic blood tests or other monitoring at specified time periods
  - Might require follow up questionnaire at specified time periods and after discontinuation of drug

## ETASU: Registry

- The REMS may require each patient using the drug be enrolled in a registry
  - Provides information on patients prescribed the drug and allows follow-up on adverse events and trends

# ETASU: Summary

- Are not mutually exclusive; in fact, there is considerable overlap
- Educational materials are an important component of several of the elements; may eliminate need for specific communication plans if included as elements to assure safe use
- FDA working to standardize elements to assure safe use, but individual REMS are shaped by the characteristics of the drug and the risks the program is designed to address, and to some extent, sponsor preferences

# Implementation Systems

- REMS may include an implementation system related to ETASU requiring certification of pharmacies and hospitals, limiting use to certain healthcare settings, and requiring documentation of safe use conditions
- May require applicant to take reasonable steps to—
  - (A) monitor and evaluate implementation of such elements by health care providers, pharmacists, and other parties in the health care system who are responsible for implementing such elements; and
  - (B) work to improve implementation of such elements by such persons.

# Timetable for Assessments

- Only required element of a REMS approved under NDAs is a timetable for submission of assessments of the REMS
- FDAAA states that the timetable for assessment must be, at a minimum, by 18 months, three years, and in the seventh year after the REMS is approved
- FDA can require additional assessments
- FDA is requiring each REMS to have a goal against which it can be assessed



# REMS Assessment Plans

- When possible, at the time of approval of the REMS, FDA will describe in the REMS approval letter the types of data that should be collected and reported during the REMS assessment

# REMS and Generic Drugs

- Generic drugs only required to have REMS if the applicable listed drug has a REMS
- Elements limited to a Medication Guide or PPI, elements to assure safe use, and an implementation plan *if* the applicable listed drug has a REMS with these elements
- If there is a communication plan for the listed drug, FDA must carry out the plan when a generic is approved
- Generic drugs are not required to have a timetable for assessment

# Generics and Innovators Must Use Single Shared System for Elements to Assure Safe Use

- For a REMS with elements to assure safe use, generics and innovators must use a single shared system or the generic sponsor must obtain a waiver

# In Summary

- FDAAA provides FDA the authority to require sponsors to implement REMS when necessary to ensure that a product's benefits outweigh its risks
- A REMS may include a variety of risk management tools
- In deciding which tools to use, we must consider how best to manage the identified risks while maintaining patient access to pain medications and minimizing the burden on the healthcare system



# Development of the Opioid REMS

Division of Anesthesia and Analgesia

Office of Drug Evaluation II

CDER

## Opioid REMS – History

- **February 6, 2009** – Letters sent to sponsors of certain opioid products notifying them that their drugs will require a REMS.
  - Products include methadone and extended-release formulations of fentanyl, oxycodone, oxymorphone, morphine, and hydromorphone.
- **March 3, 2009** – Sponsor meeting held to discuss the REMS design to manage the risks while considering the burden on the health care system.
- **April 2009** – Opioid REMS Webinar created to better inform stakeholders about general issues related to REMS and specific issues related to REMS for certain opioid analgesics.

## Opioid REMS – History (Continued)

- **May 4-5, 2009** – Stakeholder meetings including prescriber, pharmacy, and patient advocacy organizations and insurance providers.
- **May 27-28, 2009** – Public meeting to allow affected sponsors and other interested persons to present comments and information on what a REMS should look like for these products, how to minimize the burden on the health care community and patients while achieving the objective of ensuring that the benefits of these drugs continue to outweigh the risks, and how FDA should evaluate the REMS to determine whether it is achieving these objectives.

## Opioid REMS – History (Continued)

- **August 2009 – January 2010** - Several months of work by 70+ people from FDA (CDER and OSHI) in 8 working groups examining data from the docket, gathering additional information, analyzing the issues, and developing recommendations.
  - The 8 working groups:
    - Scope
    - Access
    - Pharmacy Systems
    - Metrics
    - Patient Education
    - Pharmacist Education
    - Prescriber Education
    - Public Education



## Opioid REMS – History (Continued)

- **December 4, 2009** – Public Meeting with sponsors (the Industry Working Group) to hear about their collaborative effort to develop a proposed REMS.
- **January 7-8, 2010** - Off-site retreat of Steering Committee and Working Groups to develop proposal for FDA actions to address the opioid problem.
- **January 12 and 25, 2010** – Briefings for CDER Director and Commissioner on proposed path forward.

## FDA's approach to the problem involves both the REMS authority and the Safe Use Initiative, as well as collaborations with other Federal Agencies



### Prescribers

- Proper patient selection, proper prescribing (e.g., dose, schedule)
- Proper patient counseling, proper patient monitoring and follow-up

### Patients

- Proper patient education, proper use as prescribed
- Proper storage, proper disposal
- "No sharing", no illegal sales

### "Others"

- Avoid accidental exposure (e.g., household contacts), inappropriate therapeutic use (e.g., sharing for intended therapeutic use), recreational use, repeated non-therapeutic misuse (e.g., intentional abuse)
- Limit diversion and other illegal activities



# Elements of the Proposed REMS for Long-Acting and Extended-Release Opioid Drug Products

Bob A. Rappaport, M.D.  
Director, Division of Anesthetic and Analgesic Products  
CDER, FDA

Joint Meeting of the Anesthetic and Life Support Drugs and  
Drug Safety and Risk Management Advisory Committees

July 22, 2010

UMUC Conference Center at the Marriot, Adelphi, MD

# High Level Overview of Proposed REMS

- Proposed REMS elements
  - Medication Guide
  - Elements To Assure Safe Use (ETASU) for prescriber education
  - Mandatory sponsor-developed patient education materials made available to prescribers for voluntary use with patients
- Proposed REMS does NOT include
  - Enrollment of individual prescribers into a REMS program
  - Real-time electronic verification of prescriber training at the pharmacy level
  - Communication plan – any such plan would have to be implemented by FDA because there are generics for some of the long-acting/extended-release Schedule II opioid products

## Goals of Proposed REMS

- Reduce serious adverse outcomes resulting from inappropriate prescribing, misuse and abuse of long-acting and extended-release opioids while maintaining patient access to these medications. Adverse outcomes of concern include addiction, unintentional overdose, and death.

This will be accomplished by educating prescribers in appropriate patient selection, dosing, and patient monitoring, and by educating patients in the safe use, storage, and disposal of opioids.

## Scope of the Proposed REMS

- We recommend against broadening the scope of the REMS, as some have proposed, to include all Schedule II opioids
  - long-acting/extended-release Schedule II opioids present unique risks to patients related to their formulations and pharmacokinetics and represent a significant and growing problem of serious adverse events in patients and others when not used properly
  - While immediate-release Schedule II opioids also present serious risks to patients if not used properly, broadening the REMS to include all agents would be difficult to justify and would create a greater burden on the healthcare system
  - The broader problem of misuse and abuse of immediate-release Schedule II opioids (and lesser schedule opioids) is more appropriately addressed by the Safe Use Initiative and other federal agencies.

## Proposed ETASU – Prescriber Training

- FDA is proposing that sponsors be required to develop an educational program that would educate prescribers about appropriate patient selection, dosing, and patient monitoring. Prescribers would also be trained to counsel patients on the safe use, storage, and disposal of opioids.
  - We will encourage that the training be developed in partnership with an appropriate independent third party (e.g., Federation of State Medical Boards)
  - FDA will approve the content of the training

## Proposed ETASU – Prescriber Training

- Although prescribers would not be required to demonstrate evidence of training to prescribe these products, sponsors would be required to demonstrate that prescribers have been trained and that knowledge of appropriate use has improved via surveys of the prescribing community.
  - Sponsors will be encouraged to explore appropriate incentives (e.g., CME credit) to encourage prescribers to undertake training



## Prescriber Training (cont.)

- At this time we are not recommending individual enrollment of prescribers into a REMS program or real-time electronic verification of prescriber training at the pharmacy level. These would be very burdensome to the healthcare system.
  - There are currently over 1 million DEA registrants, of which approximately 700,000 are prescribers who may fall under the REMS program
  - A requirement for individual prescriber registration and real-time verification of training may create a “balloon effect” with some, perhaps many, prescribers “opting out” of the program with potential adverse consequences to access to pain medications
  - In the long term, linking education to the existing DEA registration system would be more efficient but would require legislation

## Prescriber Training (cont.)

- The question of allowing exemptions to the training requirement for certain prescribers has not been fully resolved. There is agreement that if there are exemptions they should be very limited and based on verifiable credentials (e.g., board certification)
- FDA believes that exemptions should NOT be based on the practice location (e.g., inpatient versus outpatient) since prescribers in all settings should understand how to use long-acting and extended-release Schedule II opioids properly

## Proposed patient education under REMS

- Medication Guides (we acknowledge their limitations)
  - Would be required for each long-acting and extended-release Schedule II opioid
  - Would include “class” language along with product specific information
- Patient education sheets for prescribers
  - Sponsors would be required to make these available to prescribers and encourage their use in counseling patients
  - Content would be FDA approved
  - Goal would be a one page tear-off sheet
- Pain treatment agreements or patient/provider agreements
  - Not required under the REMS
  - Partner under Safe Use Initiative to make existing models more broadly available for voluntary use

## Patient education (cont.)

- At this time we are not recommending individual enrollment of patients in a registration system. These would be very burdensome to the healthcare system and create a stigma for pain patients that could adversely affect patient access to necessary medications.
  - Nearly 4 million patients are prescribed long-acting or extended-release opioids annually.
  - Enrolling this many patients in a registration system would be an enormous undertaking with unpredictable effects on patient access.
- FDA will carefully monitor the effects of the program and may consider further steps if the REMS does not prove effective in curbing serious outcomes resulting from inappropriate prescribing, abuse and misuse.

## Safe Use Initiative

- We propose that we engage with partners under the Safe Use Initiative to initiate broader efforts to address the problem of misuse and abuse of prescription opioids
  - One proposal is for a government sponsored or endorsed web site that would contain information for patients and others on safe use of these products

## Summary

- Three-pronged strategy recommended for FDA
  - Require REMS for all long-acting and extended-release Schedule II opioids
    - Prescriber training
    - Patient education
  - Engage in Safe Use partnerships to achieve broader goals that do not fit well under FDA's REMS authorities
  - Work with other federal agencies to address the problem via alternative strategies



# **Metrics for Opioid REMS**

**Mary Willy, Ph.D.**  
**Deputy Director, DRISK**  
**OSE/CDER**

# Outline

- Goals for Opioid REMS
- Proposed Metrics
- Challenges
- Conclusions



# Goals for Opioid REMS

- Reduce serious adverse outcomes resulting from inappropriate prescribing, misuse and abuse of long-acting (LA) and extended-release (ER) opioids while maintaining patient access to pain medications.
  - Adverse outcomes of concern include addiction, unintentional overdose, and death.

# Summary of Metrics Working Group Recommendations

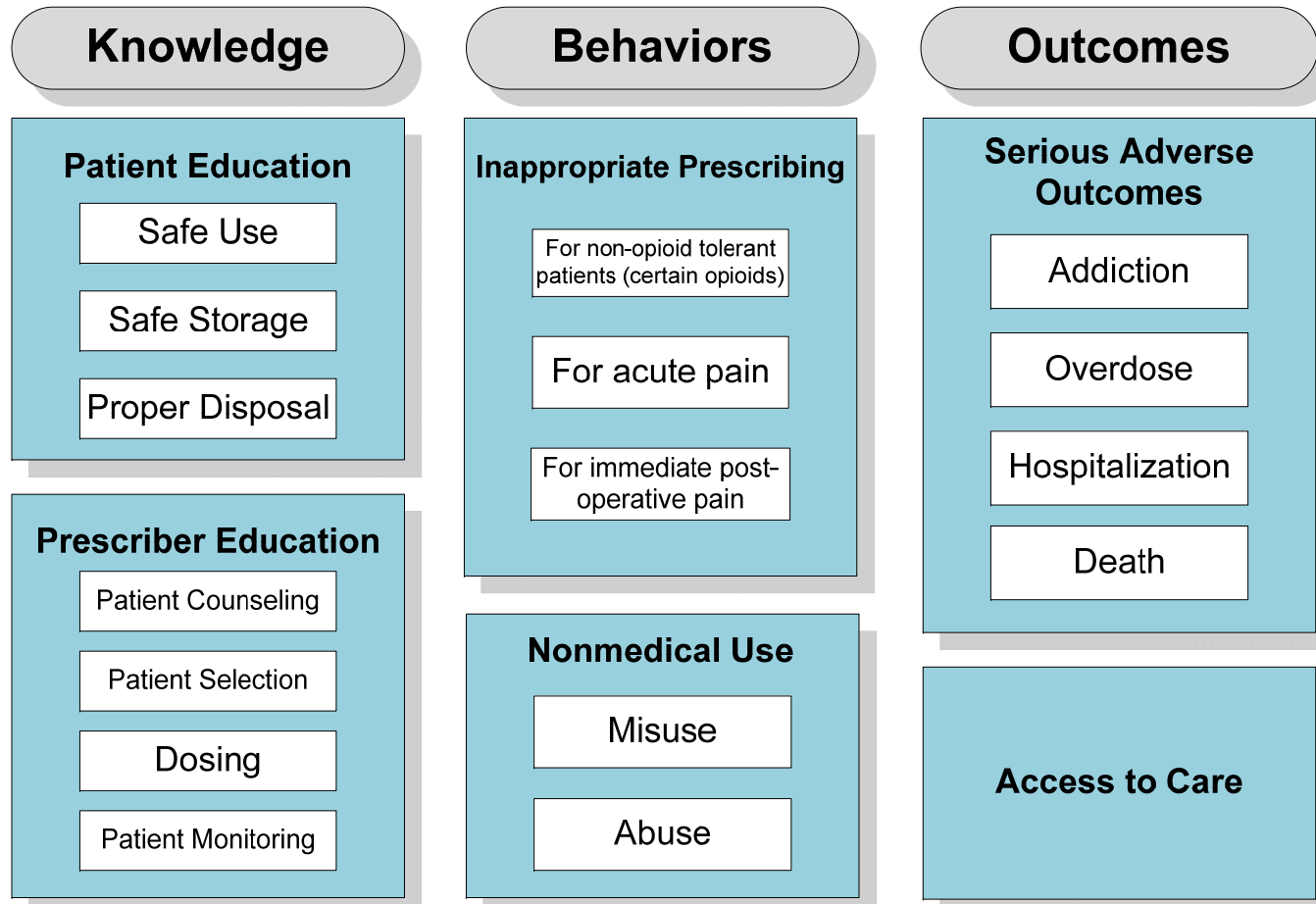
- Utilize multiple metrics and data sources to measure the impact of the REMS
- Create new data sources to measure certain components of the REMS (surveys and surveillance systems)
- Measure the impact of the REMS on outcomes related to both extended release products and all opioids

# Summary of Metrics Working Group Recommendations - 2

- Establish working definitions for outcomes of interest.
- Establish baseline metrics to determine the degree to which the REMS changes knowledge, behaviors, and health outcomes
- Account for other interventions and trends

## Metrics Data Needs

In order to measure the effect of the REMS on health outcomes, data should be collected in the following areas:





# Proposed Metrics

# Process Metrics

- System will need to be developed to collect training data
  - Depends on final REMS
- Source: to be determined

# Knowledge Metrics

- Percent prescriber and patient with understanding of risk
- Source: Surveys
- Strengths: will provide prescriber- and patient-level information
- Limitations: will require Sponsors to collaborate on funding and data collection
  - there are no Federal data sources that provide this information

# Inappropriate Prescribing

- Most challenging metric to monitor
  - Number (rate) prescriptions to non-opioid tolerant patients
  - Number (rate) prescriptions to immediate post-operative care/less invasive surgery; for acute pain (for example, discharge from Emergency Dept)
- Source: Prescription claims databases
- Strength: Provide timely information for specific drugs
- Limitation: Without review of medical records cannot be sure that analysis is valid



# Inappropriate Prescribing - 2

- Pilot study with Center for Medicare and Medicaid Services (CMS)
  - Look at Medicare and Medicaid patients in recent years
    - Prescriptions of certain opioids to non-tolerant patients
    - Look for markers of questionable patient behavior, such as increased number of prescribers and pharmacies, early refills per patient over 6 months.
      - Not clear if these markers can be used to monitor changes in prescriber behavior

# Non-medical use and abuse

- Number (Rate) identified with non-medical use and abuse in various settings
- Sources: National Survey on Drug Use and Health (NSDUH), Monitoring the Future, commercial surveillance systems
- Strength: Provide class specific (some drug-specific information) information; national data
- Limitations: Data are not as timely as would like; not all data are available to public; data not available for a subset of the proposed REMS drugs

# Unintentional overdoses

- Number (rate) of unintentional overdoses identified from opioids
- Sources: National Electronic Injury Surveillance System – Cooperative Adverse Drug Events Surveillance (NEISS-CADES), National Poison Data System (NPDS)
- Strengths: Provide class specific (some drug-specific information) information; national data
- Limitations: Data are not as timely as would like; not all data are available to public

# **National Electronic Injury Surveillance System – Cooperative Adverse Drug Events Surveillance (NEISS-CADES)**

- CDC and FDA collaboration with Consumer Product Safety Commission
  - Identifies emergency department (ED) visits due to unintended adverse events from medications
  - Nationally representative system
    - Updates once a year; 9 months after the end of the previous year

# National Poison Data System

- Data collected by American Association of Poison Control Centers
  - Collects information from 61 poison control centers
  - Exposures are classified into a number of groupings that reflect: unintentional use, therapeutic error, and abuse
- Data are not all publicly accessible; will need special funding

# Emergency Department Visits

- Number (rate) of ED visits identified from opioids
- Sources: Drug Abuse Warning Network (DAWN)
- Strengths: Provide class specific (some drug-specific information) information; national data
- Limitations: Data are available 9-12 months after the end of the previous year; not all data are available to public

# Addiction

- Number (rate) of admissions to Treatment programs
- Source: Treatment Episode Database (TEDS), commercial surveillance systems
- Strength: Provide class specific (some drug-specific information) information; nationally representative
- Limitations: Data are not as timely as would like; not all data are available to public

# Treatment Episode Data Set (TEDS)

- Data reported by over 10,000 facilities to the 50 States, District of Columbia, and Puerto Rico
  - Primarily from facilities receiving public funds
  - Estimated coverage – 80%
- Drugs of abuse reported in “generic” categories, not specific brand names or formulations
  - All States report on “opiates other than heroin” as a group; only 16 States report on specific opioid analgesics



# Deaths

- Number (rate) of identified deaths from opioids
- Source: National Vital Statistics
- Strength: Provide class specific information; nationally representative
- Limitation: Data are not as timely as would like

# Access

- Change in Access to opioids
- Source: Medical Expenditure Panel Survey (MEPS) funded by Agency for Healthcare Research and Quality (AHRQ)
- Strengths: Includes questions regarding access to care problems and the reasons for them; can account for drug taken, severity and cause of pain
- Limitations: Data comes with a two year delay; data reflect access to care for any drug taken by the patient

# Medical Expenditure Panel Survey (MEPS)

- Can ascertain share of moderate/severe chronic pain patients who could not get a prescription because
  - their healthcare provider refused to provide services and/or
  - the patient did not know where to get care
  - the patient had problems getting to the doctor's office

# Challenges

- Difficult obtaining timely data
  - Many systems have 2-3 year delay
- Most systems do not collect drug-specific data
  - eg. Oxycodone instead of OxyContin
- Most data will be population level and not patient level
- Small changes will be hard to find
- Many other efforts have been initiated, so difficult determining what changes related to opioid REMS

# Challenges, Continued

- Data lag: It may be several years until we have a complete set of data

Availability of first-year REMS data from some sample data sources:

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Process</b>	Administrative Data				
<b>Knowledge</b>		Prescriber & Patient Survey Data			
<b>Behaviors</b>		NSDUH Data			
<b>Outcomes</b>		DAWN Overdose Data			
		NEISS-CADES Unintentional Overdose Data			
				Death Data	

# Development of New Methodology with Federal and State Partners

- CMS:
  - Pilot study to look for inappropriate prescribing
- CDC:
  - Working to develop methods to identify unintentional overdoses in NEISS-CADES
- Other possible collaborations:
  - VA and Department of Defense
  - State Prescription Monitoring Programs

# Conclusions

- Many data sources are available
- None is specifically tailored to measure the outcomes of the opioid REMS
- Roles and responsibilities across multiple sponsors and the FDA need to be determined
  - Sponsors will be responsible for funding and implementing REMS

# Metrics Working Group Members

- Suzanne Barone, Office of Compliance
- Silvia Calderone, Controlled Substance Staff
- Cathy Dormitzer, Office of Surveillance and Epidemiology
- Adam Kroetsch, Office of Planning and Analysis
- Jeanne Perla, Office of Surveillance and Epidemiology
- Marta Wosinska, Office of Planning and Analysis
- Mary Willy, Office of Surveillance and Epidemiology
- Patrick Frey, Advisor, Office of Planning and Informatics





**Collaborating to reduce preventable harm  
from medications**

**Opportunities to Complement the REMS**

Karen D. Weiss, M.D., MPH  
Associate Director for Medical Affairs, FDA/CDER

## Safe Use

- FDA initiative to reduce risks (*preventable* harm) from Rx, OTC medications
- Promote drug safety outside of REMS, labeling, and other regulatory authorities (i.e., voluntary)
- FDA's regulatory authority alone is not sufficient
- Partner with healthcare: government, NGOs: to identify barriers, influence behaviors and practices
- Collaborations can more broadly address preventable harm, such as misuse and abuse of opioids

## Regulatory

- Risk Evaluation and Mitigation Strategy (REMS)
  - Measure impact
- Labeling changes
- Advisory committee
- Require new studies to assess observed safety signals
- Drug safety communications
- Develop guidance documents

## Safe Use

- Convene stakeholders:
  - Identify drug safety issue(s)
  - Discuss barriers
  - Propose interventions
- Form partnerships
  - Federal, non-federal partners
  - Implement interventions
  - Measure impact
- Join ongoing drug safety activities
- Support literacy, HIT activities

# Setting Priorities for Safe Use

- Associated with preventable harm
- Public health impact
- Amenable to collaborative approach to harm reduction
- Measureable
- Complement ongoing regulatory activities



# Opioids/Safe Use Initiative Activities

- Goals
  - Reinforce REMS programs
  - Expand into areas where REMS not appropriate
- Safe Use Initiative Opportunities
  - Education Campaign
  - Patient Provider Agreements
  - Potential for many more

# Education Campaign

- Main message; e.g.:
  - Opioids are powerful drugs
  - Must be used only as directed
- Ensure target audiences understand potential for misuse and abuse
  - Consumers: Patients, caregivers, other intermediaries
  - Healthcare providers: Physicians, pharmacists, others
- Communicate safe prescribing, dispensing, storage, and disposal
- Educate about all opioids, not only ER/LA class

# Education Campaign

- Partnership development
  - Public and private partners
- Media outreach; diverse channels
  - Kick-off event
  - Satellite media tour
  - Speakers bureau
  - Online and social media
- Materials dissemination
  - Print and broadcast Public Service Announcements (PSAs)
  - Collateral materials (brochures, etc)



# Patient Provider Agreements (PPA)

- Describe patient responsibilities, e.g.
  - Take as prescribed
  - Attend required follow up visits
  - Inform doctor of side effects
  - Use one doctor, one pharmacy
  - Will not sell, lend, give to another person
- Provide information, e.g.:
  - Proper use of opioid medication
  - Proper storage of medication
  - Risks associated with taking opioid medication
- Few contain provider responsibilities





# Patient Provider Agreements

## Positives

- Provide tool for discussion
- Increase patient awareness
  - Appropriate use
  - Benefit/Risk
  - Storage/Sharing
- Reference tool for at home
- Develop health plan/re-evaluate therapy
- Clarify provider & patient roles and responsibilities

## Negatives

- May not be geared to appropriate literacy level
- May adversely impact patient provider trust
- Emphasis on patient compliance
- Lack provider responsibilities
- Inadequately highlights benefit & risk
- Can be long
- Limited data on effectiveness

# PPA – Safe Use Initiative

## Areas for research

- Who uses an opioid PPA and why?
- How well do they work? What do you measure?
  - Health outcomes for patient
- What information? Type and format?
  - Essential elements, layout
  - Consistency of information
  - Balance between responsibility of provider and patient
- How do you ensure/encourage use?

## Summary

- Highlighted two Opioid/Safe Use Initiatives
  - Education Campaign
  - Patient Provider Agreement Activities
  - Many issues to consider, including how to measure impact
- Anticipate developing other Safe Use programs to enhance Opioid safety
- Seeking input and partnerships

# Contact Us

- The Safe Use Initiative
  - [www.fda.gov/safeuseinitiative](http://www.fda.gov/safeuseinitiative)
- Safe Use Initiative docket
  - <http://www.regulations.gov>
  - Docket number: [FDA-2009-N-0526](https://www.fda.gov/oc/ohrt/fda-2009-n-0526)
- CDER Safe Use e-mail
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