



## Premier Safety Institute®

### Opioid analgesics: a double threat to patient safety

Misuse of controlled substances, and opioid analgesics in particular, has become a significant health threat in the United States. Non-medical use of these drugs has increased dramatically in recent years, eclipsing that of many other illicit substances with an escalation of related overdoses and death. In the hospital setting, errors in the prescribing, administration and inadequate monitoring of patients on opioid therapy are a serious patient safety issue and result in preventable adverse events. In both the ambulatory and inpatient settings opioid use is associated with considerable costs. In addition, drug diversion, or the transfer of prescriptions for non-medical uses, poses a significant danger to individuals and health care workers. Federal and state agencies, as well as professional organizations and physician groups, have called for urgent action to curb the epidemic of opioid misuse and reduce the avoidable errors associated with inpatient administration of these drugs.

#### Opioid Analgesics

- codeine
- dextropropoxyphene
- fentanyl
- hydrocodone
- hydromorphone
- meperidine
- methadone
- morphine
- oxycodone
- pentazocine

#### Opioid analgesics: a target for misuse

In the 1990s, increased recognition of the need to adequately address patient pain, along with business-related factors, led to an expansion in the use of opioids for non-cancer chronic pain. [Nelson 2012] As a result, the availability of opioid analgesics increased exponentially. This class of drugs, which includes codeine, fentanyl, hydromorphone, meperidine, morphine, oxycodone, pentazocine, dextropropoxyphene, methadone, and hydrocodone, has become a target for misuse because of the euphoria these drugs induce. [CMS 2012]

It was initially believed that long-acting analgesic opioids—those with a duration of effect of 8 to 24 hours—were less likely to be associated with misuse than short-acting agents, which have a more rapid increase in serum level. [Argoff 2009] However, some long-acting formulations can be physically altered to induce a more rapid onset of action, produce a greater psychogenic effect, and allow for non-oral routes of administration (e.g., snorting, injection). [Cone 2006]

#### Misuse of opioids now epidemic

In the past two decades, the number of annual retail pharmacy prescriptions for opioid analgesics increased from 76 to 210 million. [SDI's sector 1 (VONA)] Between 1997 and 2007 the distribution of these drugs increased more than 600 percent, from the equivalent of 96 mg of morphine per person in the US to about 700 mg per person. [CDC 2012] The retail sale of oxycodone alone increased almost 600 percent between 1997 and 2005. The Drug Abuse Reporting Network (DAWN) data indicate that since 1996, oxycodone-related deaths have increased 400 percent and in 2010 alone, adverse events related to misuse of narcotic

pain relievers (mostly oxycodone and hydrocodone) represented about half of all emergency department visits for misuse of drugs

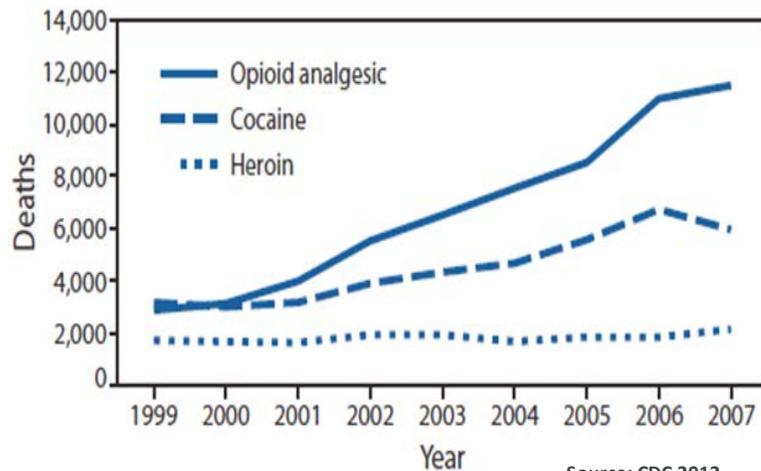
Expansion in the prescribing and availability of opioid analgesics fueled the nonmedical use of these drugs. In 2010, the number of new users of pain relievers for recreational use was second only to the number of new users of marijuana. [SAMHSA 2011] Every year since 2002, two million or more individuals have begun using pain relievers for nonmedical use. [SAMHSA 2011] Five hundred thousand of these users never used another illicit drug before using prescription pain relievers. [SAMHSA 2011]

With the sustained growth of nonmedical use of pain relievers over the past decade, the numbers of individuals with dependence on pain relievers has risen sharply: from 936,000 in 2002 to 1.4 million in 2010. [SAMHSA 2011] Six out of ten of those dependent on pain relievers are aged 26 or older. Evidence of the epidemic is also visible in the number of individuals who receive specialty substance abuse treatment. Between 2002 and 2010, the number doubled, from 199,000 to 406,000. [SAMHSA 2011]

### Escalating deaths from opioid misuse

The death rate from unintentional drug overdose has soared in the past decade, driven primarily by deaths associated with opioid analgesics. Since 2003, opioids have been responsible for more deaths by overdose than cocaine and heroin combined. [CDC 2012]

In the US, the two populations at greatest risk of lethal overdose due to prescription drugs are patient on long-term opioid use for a medical condition and those who use the drugs for nonmedical purposes. [CDC 2012] Of those who die of opioid overdose, almost two-thirds used drugs that were originally prescribed for someone else. [CDC 2012]



Source: CDC 2012

### Opioids associated with significant adverse events, even when used as prescribed

Opioid analgesics are associated with a number of side effects, the most serious of which is respiratory depression. [Joint Commission 2012] Sedation, nausea, vomiting, delirium, falls, and constipation are other common adverse effects associated with these drugs. [Joint Commission 2012] Even when used as prescribed and administered correctly, opioids are associated with significant adverse events, with certain patients at heightened risk for complications, whether in the inpatient or ambulatory setting. Risk factors include smoking, older age, pre-existing cardiac or pulmonary disease, simultaneous use of other sedating drugs, and the presence of sleep apnea or obesity. [Joint Commission 2012]

Opioids are one of the most frequent causes of drug-associated adverse reactions in the hospital setting, associated with 16 percent in one study of almost 4,000 patients. [Davies 2009] A recent analysis of 380

hospitals in Premier's Hospital Database found that adverse events related to opioid analgesics occurred in 12 percent of more than 300,000 surgeries performed between 2008 and 2010. [Oderda 2011]

Of the adverse events reported to the Joint Commission between 2004 and 2011 that involved opioids, almost half were due to wrong dose errors, almost one third due to inadequate monitoring of the patient, with the remainder due to factors such as excessive dosing, interactions with other drugs, or adverse drug reactions. [Joint Commission 2012]

### **The physicians' role in opioid misuse and drug-related errors**

In the past, physicians, concerned about the risk of abuse, may have undertreated pain. With the availability of new formulations of opioids and greater recognition of the need to address pain more adequately—and perhaps to meet accreditation standards on analgesia—the number of prescriptions written for analgesic opioids increased exponentially. In trying to better treat patients with pain, physicians have unwittingly become the primary source of the drugs feeding the epidemic among ambulatory patients. [Nelson 2012]

Treatment of ambulatory patients with non-cancer-related chronic pain can be complex and challenging, especially for providers who have received little training on safe opioid prescribing and the prevention of misuse. Physicians may be unfamiliar with screening tools for identifying the risk of misuse or with clinical practices, such as requiring patients to sign a opioid agreement, that can help prevent it.

Adequately and safely addressing pain in the inpatient setting can be challenging as well, although for different reasons. Provider-related causes of opioid-associated adverse events in the inpatient setting include lack of knowledge about the relative potency of different opioids, improper prescribing and administration, and inadequate monitoring of patients taking opioids. [Joint Commission 2012]

### **Opioids associated with higher costs**

Recent analyses of worker's compensation claims have clearly shown that analgesic opioid use—especially long-acting formulations—is costly. According to one insurer providing coverage in 18 states, medical and disability claims for a workplace injury averaged \$13,000 when no opioids were prescribed, \$39,000 when short-acting opioid analgesics were prescribed, and \$117,000 when longer-acting opioids were used. [Meier 2012] A published study by the same insurer of more than 12,000 claims filed in Michigan found that claims were 1.76 times more likely to result in a final cost greater than \$100,000 if short-term opioids were used and almost 4 times more likely to result in such a cost if long-term opioids were used, after controlling for factors such as number of ICD-9 codes per claim, legal involvement, and claim duration. [White 2012]

In the analysis of hospitals in the Premier's Hospital Database mentioned previously, the occurrence of opioid-related adverse events was associated with a longer hospital stay (an additional 3.3 days), greater risk of readmission, and increased cost of about \$4,700 compared with cases in which adverse events due to these drugs did not occur. [Oderda 2011]

### **Drug diversion a hazard to patients and health care workers**

Analgesic opioids and other prescription drugs are obtained legally through prescriptions or illegally through diversion. Drug diversion is the transfer of prescriptions from legal, medically necessary uses to illegal uses that are not medically necessary or authorized. Opioids are the most commonly diverted controlled prescription drugs. [US Dept of Justice 2010]

Although the full extent of diversion is not known, it is recognized as a growing problem. Drug diversion in the inpatient setting poses a hazard for both patients and health care workers. Drug diversion by medical personnel leads to a number of serious consequences, including inadequate analgesia in patients, falsification of records, and, as documented in a recent case report, the transmission of infectious diseases. Five cases of hepatitis C infection in an acute care hospital and affiliated multispecialty clinic were attributed to drug diversion by a health care worker in the facility. [Hellinger 2012]

Diversion of drugs from either the inpatient or outpatient setting fuels the epidemic of analgesic opioid misuse. According to a report by CMS, the impact of drug diversion extends beyond the cost of the prescription drugs that are no longer available for medical use to include the costs associated with physician visits, ED treatment, rehabilitation, and the human toll of dependence and abuse. [CMS 2012]

#### **Laws to prohibit “doctor shopping” among recommended strategies**

Recommended tactics to curb opioid misuse include stricter legislation and law enforcement, labeling changes, improved collection and sharing of information about prescribing activity, and other specific steps to prevent drug diversion. The CDC recently called for stricter enforcement of existing laws that prohibit “doctor shopping” and the adoption of new legislation to restrict “pill mills,” which distribute prescriptions for controlled substances without a physical exam. [CDC 2012]

More restrictive drug labeling use is another strategy for addressing opioid misuse. In July, a group of more than 30 physicians petitioned the FDA to change the prescription labeling for opioid analgesics. The petition requested the approved indications for non-cancer pain from “moderate to severe pain” to “severe pain.” [Meier 2012] Some experts have recommended labeling changes to reflect the current knowledge of the risks and benefits of analgesic opioids for non-cancer pain. [Nelson 2012]

Improving the collection and sharing of information about opioid prescriptions is another recommended strategy to curtail misuse. CDC has called for increased surveillance of prescription activity and insurance restrictions on opioid prescriptions from multiple providers to prevent misuse. [CDC 2012] The Centers for Medicare and Medicaid Services (CMS) has recommended that states implement prescription drug monitoring programs, allowing prescribers and pharmacists to access utilization records. [CMS 2012]

CMS also recommended the use of “lock-in” programs for Medicaid recipients who overutilize the drugs, based on state guidelines for appropriate utilization. [CMS 2012] Individuals who are identified as overutilizing opioids could be restricted for a period of time to obtaining prescriptions from a single provider or filling prescriptions at a single pharmacy.

Specific steps to prevent drug diversion are recommended. For more information, see Premier Safety Institute website on [drug diversion](#).

## Ten Strategies for Preventing Opioid-Related Adverse Events in Hospitals

As with opioid misuse, a number of specific strategies have been recommended to reduce adverse events associated with opioids in the inpatient setting. These include adequate screening of patients for the risk of respiratory depression, policies and procedures to monitor patients on opioid therapy, the use of information technology to flag possible errors and calculate conversions, and the use of patient-controlled analgesia. See the sidebar for ten strategies for preventing opioid-related adverse events in hospitals.

### **Additional education for prescribers needed**

Expanded prescriber education is needed to address both misuse and errors related to inpatient prescribing, as many physicians receive little training on the safe prescribing of opioids. Regulatory agencies have recommended specific education for providers. In July 2012, the FDA released a risk evaluation and

mitigation strategy (REMS) for extended-release and long-acting opioids, replacing several REMS for several individual drugs with a class-wide strategy. The REMS requires opioid manufacturers to distribute education for prescribers on patient selection, screening for misuse, and counseling in appropriate use of analgesic opioids. However, use of the educational materials is voluntary. Some experts have argued that manufacturer-provided educational materials are subject to bias due to financial motivations and may be insufficient to address the problem. [Nelson 2012]

In some states, opioid education is mandatory for practicing physicians. Medical boards in seven states now require physician education on safe prescribing of controlled substances, or opioids in particular, for licensure. [Federation of State Medical Boards 2012] In the future such training may be required for all prescribers of controlled drugs. The Obama Administration's national plan for addressing abuse of prescription drugs, which was released in 2011, calls for mandatory prescriber education. When

## Ten Strategies for Preventing Opioid-Related Adverse Events in Hospitals

1. Educate staff at all levels regarding safe opioid use, including the appropriate use of non-narcotic analgesia, the risks associated with opioids, and assessment for respiratory depression and other adverse drug reactions.
2. Ensure the availability of pharmacists or pain management experts to help providers with opioid conversion and dosing.
3. Create policies and procedures to ensure ongoing monitoring of patients on opioid therapy.
4. Require the use of standardized screening tools to assess the risk of respiratory depression.
5. Ensure that oxygen and reversal agents are available wherever opioids are administered.
6. Track and investigate opioid-related adverse events.
7. Create oversight committees and systems to identify and deter drug diversion by staff.
8. Establish clear policies and procedures for evaluating and addressing identified instances of drug diversion.
9. Provide written and oral education to patients on opioid therapy or to their caregivers, including risks and side effects, potential for sedation, the danger of use in combination with alcohol or other sedating drugs, and safe storage at home.
10. Use technology to support safe opioid use through decision support and alert systems in the electronic medical record and the use of patient-controlled analgesia (PCA) devices.

implemented, prescribers will need to complete the training to obtain or renew a controlled substance registration with the Drug Enforcement Administration. [CDC 2012]

### Conclusion

Opioid analgesics represent a double threat to patient safety. In the ambulatory setting, the misuse of these drugs has dramatically increased over the last decade, as has the incidence of opioid dependence and deaths due to overdose. Opioids are associated with a risk of serious side effects, even when used as prescribed and administered correctly. In the inpatient setting, prescribing errors or lack of adequate monitoring of patients on opioid therapy have been identified as important causes of adverse events.

Recommended strategies to curtail opioid misuse include stricter legislation and law enforcement, labeling changes, improved collection and sharing of information about prescribing activity, and specific steps to prevent drug diversion. Recommended strategies to prevent opioid-associated adverse events in the inpatient setting include adequate screening of patients for the risk of respiratory depression, policies and procedures to ensure adequate monitoring of patients on opioid therapy, the use of information technology to flag possible errors and calculate conversions, and the use of PCA devices. Effective prevention of opioid-related adverse events, including overdose and death, will require hospital leaders, health care providers, law enforcement officials, and other stakeholders to collaborate in implementing multidimensional mitigation strategies in both the inpatient and ambulatory settings.

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