The treatment of chronic pain, therapeutic opioid use and abuse, and the nonmedical use of prescription drugs have been topics of intense focus and debate. After the liberalization of laws governing opioid prescribing for the treatment of chronic non-cancer pain by state medical boards in the late 1990s, and with the introduction of new pain management standards implemented by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in 2000, opioids, in general, and the most potent forms of opioids including Schedule II drugs, in particular, have dramatically increased.

Despite the escalating use and abuse of therapeutic opioids, nearly 15 to 20 years later the scientific evidence for the effectiveness of opioids for chronic non-cancer pain remains unclear. Concerns continue regarding efficacy; problematic physiologic effects such as hyperalgesia, hypogonadism and sexual dysfunction; and adverse side effects – especially the potential for misuse and abuse – and the increase in opioid-related deaths.

Americans, constituting only 4.6% of the world's population, have been consuming 80% of the global opioid supply, and 99% of the global hydrocodone supply, as well as two-thirds of the world's illegal drugs. Retail sales of commonly used opioid medications (including methadone, oxycodone, fentanyl base, hydromorphone, hydrocodone, morphine, meperidine, and codeine) have increased from a total of 50.7 million grams in 1997 to 126.5 million grams in 2007. This is an overall increase of 149% with increases ranging from 222% for morphine, 280% for hydromorphone, 319% for hydromorphone, 525% for fentanyl base, 866% for oxycodone, to 1,293% for methadone. Average sales of opioids per person have increased from 74 milligrams in 1997 to 369 milligrams in 2007, a 402% increase.

Surveys of nonprescription drug abuse, emergency department visits for prescription controlled drugs, unintentional deaths due to prescription controlled substances, therapeutic use of opioids, and opioid abuse have been steadily rising. This manuscript provides an updated 10-year perspective on therapeutic use, abuse, and nonmedical use of opioids and their consequences.

Key words: Controlled prescription drug abuse, opioid abuse, opioid misuse, nonmedical use of psychotherapeutic drugs, nonmedical use of opioids, National Survey on Drug Use and Health, National Center on Addiction and Substance Abuse at Columbia University.
dramatically increased (15-17). This dramatic increase has been due to a shift in the regulations largely driven by published, albeit weak, evidence suggesting that opioids could be used safely in selected persons with chronic non-cancer pain (18,19), by the advocacy of physicians and others who felt constrained by the near absolute prohibition of such before that time (6) and by consensus of professional societies of pain specialists who believe that chronic pain had been previously undertreated (13). Despite the escalating use and abuse of therapeutic opioids (4), nearly 15 to 20 years later the scientific evidence for the effectiveness of opioids for chronic non-cancer pain remains unclear. Concerns continue regarding efficacy (3-5,19,20); problematic physiologic effects such as hyperalgesia (21), hypogonadism and sexual dysfunction (22); and adverse side effects – especially the potential for misuse and abuse (23,24) – and the increase in opioid-related deaths (25-40). Meanwhile, numerous efforts by organizations for appropriate use and exercise of constraints have been misrepresented, with these opinions used to a minimum extent (3,4,10,41-47).

The treatment of chronic pain, therapeutic opioid use and abuse, and the nonmedical use of prescription drugs have been topics of intense focus and debate (3-5,47-99). Due in some measure to the campaign of alleged undertreatment of pain (100-122), Americans, constituting only 4.6% of the world’s population, have been consuming 80% of the global opioid supply, and 99% of the global hydrocodone supply, as well as two-thirds of the world’s illegal drugs (4,10-12,122,123). Retail sales of commonly used opioid medications (including methadone, oxycodone, fentanyl base, hydromorphone, hydrocodone, morphine, meperidine, and codeine) have increased from a total of 50.7 million grams in 1997 to 126.5 million grams in 2007. This is an overall increase of 149% with increases ranging from 222% for morphine, 280% for hydrocodone, 319% for hydromorphone, 525% for fentanyl base, 866% for oxycodone, to 1293% for methadone (14). In 2005 and 2006, over 120 million prescriptions for hydrocodone were issued and hydrocodone continues to be the number one prescribed drug in the United States (10,14,123-125). Average sales of opioids per person have increased from 74 milligrams in 1997 to 369 milligrams in 2007, a 402% increase. It is no surprise then that surveys of nonprescription drug abuse (4,126-131), emergency department visits for prescription controlled drugs (132-138), unintentional deaths due to prescription controlled substances (28-40,139-145), therapeutic use of opioids, and opioid abuse (15-17,48-103,140,146-174) have been steadily rising.

Chronic pain has been defined by the American Society of Interventional Pain Physicians (ASIPP) (175,176) as, “pain that persists 6 months after an injury and beyond the usual course of an acute disease or a reasonable time for a comparable injury to heal, that is associated with chronic pathologic processes that cause continuous or intermittent pain for months or years that may continue in the presence or absence of demonstrable pathology; may not be amenable to routine pain control methods; and healing may never occur.”

Chronic persistent pain can cause significant impairment of physical and psychological health, and performance of social responsibilities, including work and family life (175-182). While modern medicine has shown significant improvements in the understanding of pain (including diagnosis and treatment) (175,176,183-227), chronic pain continues to be an epidemic resulting in vocational, social and family discord, which may make the difference between life and death, and is accompanied by claims of inadequate treatment (100-121,175,176,228-231).

Prevalence and associated disability continue to increase. Harkness et al (179), in a 2000 publication, showed that there was a large difference in the prevalence of musculoskeletal pain over a 40-year period of investigation. The results showed that overall, the prevalence of low back pain increased from 8.1 to 17.8% in males, and it increased from 9.1 to 18.2% in females. Similarly, Freburger et al (180) reported the rising prevalence of chronic low back pain following an evaluation of North Carolina (USA) households conducted in 1992 and repeated in 2006. The results showed an increasing prevalence of chronic impairing low back pain over the 14-year interval from 3.9% in 1992 to 10.2% in 2006, with an overall increase of 162% in low back pain and an annual increase of 11.6% associated with care-seeking and disability.

1.0 Nonmedical Use of Psychotherapeutic Drugs

Results of the 2008 National Survey on Drug Use and Health (NSDUH) (126), an annual survey sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), showed that an estimated 20.1 million, or 8.0% of Americans, aged 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 nonmedically. Marijuana was the most commonly used illicit drugs with 15.2 million current (past month) users, or 6.1% of the US population. Cocaine was used by 1.9 million, whereas hallucinogens were used in the past month by 1.1 million persons (Fig. 1 and Table 1). Next to marijuana, 6.2 million (2.5%) persons aged 12 or older had used prescription-type psychotherapeutic drugs nonmedically in the past month (current use). Of these, 4.7 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 LSD.

1.1 Current Nonmedical Use

The increases for current (past month) nonmedical use of psychotherapeutics from 1998 to 2008 was 151% compared to 33% for marijuana and hashish and 61% for cocaine as shown in Table 1 (4,126). In fact, psychotherapeutics were the only ones that showed significant increases from 2002 to 2008, whereas, marijuana and cocaine were similar over a period of 5 years. Table 1 also illustrates a 10-year increase of 175% in the nonmedical use of tranquilizers in contrast to 109% from 1997 to 2006 with increases of stimulants and sedatives of 43% and 11%.

Overall, there has been some decrease in the current use of all illicit drugs from 2002 to 2008, as shown in Fig. 2.

1.2 Past Year Initiates

In 2008, there were 2.5 million persons aged 12 or older who used psychotherapeutics nonmedically for the first time within the past year. Numbers of new users for specific psychotherapeutics in 2008 were 2.2 million for pain relievers, 1.1 million for tranquilizers, 599,000 for stimulants, and 181,000 for sedatives (Table 2 and Fig. 3). The specific drug categories with the largest number of recent initiates among persons aged 12 or older were nonmedical use of pain relievers (2.176 million) and marijuana (2.208 million), followed by nonmedical use of tranquilizers (1.127 million), cocaine

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1 Illicit drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription type psychotherapeutics used nonmedically.
Table 1. Types of illicit drug use in the past month among persons aged 12 or older: Numbers in thousands, from 1998 to 2008.

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<td>Nonmedical Use of</td>
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<tr>
<td>Psychotherapeuticsa</td>
<td>2,477</td>
<td>3,952</td>
<td>3,849</td>
<td>4,811</td>
<td>6,287</td>
<td>6,451</td>
<td>6,110</td>
<td>6,491</td>
<td>7,095</td>
<td>6,895</td>
<td>6,224</td>
<td>151%</td>
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<tr>
<td>Pain Relievers</td>
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<tr>
<td>OxyContin*</td>
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<td>325</td>
<td>334</td>
<td>276</td>
<td>369</td>
<td>435</td>
<td></td>
<td>NA</td>
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<tr>
<td>Tranquilizers</td>
<td>655</td>
<td>1,097</td>
<td>1,000</td>
<td>1,358</td>
<td>1,804</td>
<td>1,830</td>
<td>1,616</td>
<td>1,817</td>
<td>1,766</td>
<td>1,835</td>
<td>1,800</td>
<td>175%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>633</td>
<td>950</td>
<td>788</td>
<td>1,018</td>
<td>1,303</td>
<td>1,310</td>
<td>1,312</td>
<td>1,188</td>
<td>1,385</td>
<td>1,053</td>
<td>904</td>
<td>43%</td>
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<tr>
<td>Sedativesb</td>
<td>210</td>
<td>229</td>
<td>175</td>
<td>306</td>
<td>436b</td>
<td>294</td>
<td>265</td>
<td>272</td>
<td>385b</td>
<td>346</td>
<td>234</td>
<td>11%</td>
</tr>
<tr>
<td>Marijuana and Hashish</td>
<td>11,016</td>
<td>10,458</td>
<td>10,714</td>
<td>12,122</td>
<td>14,584</td>
<td>14,638</td>
<td>14,576</td>
<td>14,626</td>
<td>14,813</td>
<td>14,448</td>
<td>15,203</td>
<td>38%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>1,750</td>
<td>1,552</td>
<td>1,213</td>
<td>1,667</td>
<td>2,020</td>
<td>2,281</td>
<td>2,021</td>
<td>2,397</td>
<td>2,421</td>
<td>2,075</td>
<td>1,855</td>
<td>6%</td>
</tr>
<tr>
<td>TOTAL ILLICIT DRUGSb</td>
<td>13,615</td>
<td>13,829</td>
<td>14,027</td>
<td>15,910</td>
<td>19,522</td>
<td>19,470</td>
<td>19,071</td>
<td>19,720</td>
<td>20,357</td>
<td>19,857</td>
<td>20,077</td>
<td>47%</td>
</tr>
</tbody>
</table>

- 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 - 2008. Source: http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf (126) Access date 3/16/2010.

Fig. 2. Past month illicit drug use among persons aged 12 or older, by age: 2008. Source: http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf Access date 3/16/2010.

www.painphysicianjournal.com
(0.722 million), ecstasy (0.9 million), stimulants (0.599 million), and inhalants (0.729 million) (Fig. 3). More strikingly, in 2008, the number of new nonmedical users of OxyContin (oxycodone) aged 12 or older was 478,000 with an average age at first use of 22.6 years among those aged 12 to 49 (126).

1.3 Past Year Use

Analysis of long-term statistics based on yearly use of illicit drugs are concerning, despite some decreases. The past year use of illicit drugs in 2008 was 35.525 million, or 14.2% of the population (Table 3). Nonmedical use of psychotherapeutics for the past year in the 2008

Table 2. Past year initiates for illicit drugs from 1998 to 2008 (numbers in thousands) for 10 years.

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<td>Pain Relievers</td>
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<td></td>
<td>1,548</td>
<td>1,810</td>
<td>2,268</td>
<td>2,400</td>
<td>2,320</td>
<td>2,456</td>
<td>2,422</td>
<td>2,193</td>
<td>2,150</td>
<td>2,147</td>
<td>2,176</td>
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<td></td>
<td>41%</td>
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<td>Tranquilizers</td>
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<td></td>
<td>860</td>
<td>916</td>
<td>1,298</td>
<td>1,212</td>
<td>1,184</td>
<td>1,071</td>
<td>1,180</td>
<td>1,286</td>
<td>1,112</td>
<td>1,232</td>
<td>1,127</td>
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<td>31%</td>
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<tr>
<td>Stimulants</td>
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<td></td>
<td>648</td>
<td>706</td>
<td>808</td>
<td>853</td>
<td>783</td>
<td>715</td>
<td>793a</td>
<td>647</td>
<td>849b</td>
<td>642</td>
<td>599</td>
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<td>Sedatives</td>
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<td>147</td>
<td>164</td>
<td>191</td>
<td>225</td>
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<td>267</td>
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<td>181</td>
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<td>23%</td>
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<td>Marijuana</td>
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<td>2,498</td>
<td>2,640</td>
<td>2,746</td>
<td>2,793</td>
<td>2,196</td>
<td>1,973</td>
<td>2,142</td>
<td>2,114</td>
<td>2,063</td>
<td>2,090</td>
<td>2,208</td>
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<tr>
<td>Cocaine</td>
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<td>868</td>
<td>917</td>
<td>1,002</td>
<td>1,140</td>
<td>1,032b</td>
<td>986b</td>
<td>998b</td>
<td>872b</td>
<td>977b</td>
<td>906b</td>
<td>722</td>
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<td>Heroin</td>
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<td>1154</td>
<td>117</td>
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-- Not available. Note: 2002 to 2008 data is based on 2008 National Survey on Drug Use and Health 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: http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf (126) Access date 3/16/2010
### Table 3. Types of illicit drug use in the past year among persons aged 12 or older: numbers in thousands from 1998 to 2008 (10 years).

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<tbody>
<tr>
<td>Nonmedical Use of Psychotherapeuticsa, b</td>
<td>5,759 (2.6%)</td>
<td>9,220 (4.2%)</td>
<td>8,761 (3.9%)</td>
<td>11,102 (4.9%)</td>
<td>14,795 (6.3%)</td>
<td>15,163 (6.4%)</td>
<td>14,849 (6.2%)</td>
<td>15,346 (6.3%)</td>
<td>16,482 (6.7%)</td>
<td>16,280 (6.6%)</td>
<td>15,166 (6.1%)</td>
<td>163%</td>
</tr>
<tr>
<td>Pain Relievers</td>
<td>6,582 (3.0%)</td>
<td>6,466 (2.9%)</td>
<td>8,353 (3.7%)</td>
<td>10,992 (4.7%)</td>
<td>11,671 (4.9%)</td>
<td>11,256 (4.7%)</td>
<td>11,815 (4.9%)</td>
<td>12,649 (5.1%)</td>
<td>12,466 (5.0%)</td>
<td>11,885 (4.8%)</td>
<td>NA</td>
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<td>OxyContinc</td>
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<td>NA</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>1,940 (0.9%)</td>
<td>2,728 (1.2%)</td>
<td>2,731 (1.2%)</td>
<td>3,673 (1.6%)</td>
<td>4,849 (2.1%)</td>
<td>5,051 (2.1%)</td>
<td>5,068 (2.1%)</td>
<td>5,249 (2.2%)</td>
<td>5,058 (2.1%)</td>
<td>5,282 (2.1%)</td>
<td>5,103 (2.0%)</td>
<td>163%</td>
</tr>
<tr>
<td>Stimulantsd</td>
<td>1,489 (0.7%)</td>
<td>2,291 (1.0%)</td>
<td>2,112 (0.9%)</td>
<td>2,486 (1.1%)</td>
<td>3,380 (1.4%)</td>
<td>3,031 (1.3%)</td>
<td>3,254 (1.4%)</td>
<td>3,088 (1.3%)</td>
<td>3,791 (1.5%)</td>
<td>2,998 (1.2%)</td>
<td>2,639 (1.1%)</td>
<td>77%</td>
</tr>
<tr>
<td>Sedatives</td>
<td>522 (0.2%)</td>
<td>631 (0.3%)</td>
<td>611 (0.3%)</td>
<td>806 (0.4%)</td>
<td>981 (0.4%)</td>
<td>831 (0.3%)</td>
<td>737 (0.3%)</td>
<td>750 (0.3%)</td>
<td>926 (0.4%)</td>
<td>864 (0.4%)</td>
<td>621 (0.2%)</td>
<td>19%</td>
</tr>
<tr>
<td>Marijuana and Hashish</td>
<td>18,710 (8.6%)</td>
<td>19,102 (8.6%)</td>
<td>18,589 (8.3%)</td>
<td>21,086 (9.3%)</td>
<td>25,755 (11.0%)</td>
<td>25,231 (10.6%)</td>
<td>25,451 (10.6%)</td>
<td>25,375 (10.4%)</td>
<td>25,378 (10.3%)</td>
<td>25,085 (10.1%)</td>
<td>25,786 (10.3%)</td>
<td>38%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>3,811 (1.7%)</td>
<td>3,742 (1.7%)</td>
<td>3,328 (1.5%)</td>
<td>4,186 (1.9%)</td>
<td>5,902 (2.5%)</td>
<td>5,908 (2.5%)</td>
<td>5,658 (2.3%)</td>
<td>5,523 (2.3%)</td>
<td>6,069 (2.5%)</td>
<td>5,738 (2.3%)</td>
<td>5,255 (2.1%)</td>
<td>38%</td>
</tr>
<tr>
<td>TOTAL ILLICIT DRUGS f</td>
<td>23,115 (10.6%)</td>
<td>25,402 (11.5%)</td>
<td>24,535 (11.0%)</td>
<td>28,409 (12.6%)</td>
<td>35,132 (14.9%)</td>
<td>34,993 (14.7%)</td>
<td>34,807 (14.5%)</td>
<td>35,041 (14.5%)</td>
<td>35,775 (14.5%)</td>
<td>35,692 (14.4%)</td>
<td>35,525 (14.2%)</td>
<td>54%</td>
</tr>
</tbody>
</table>

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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: [http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf](http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf) (126) Access date 3/16/2010

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Survey was 15.166 million or 6.1% population aged 12 or older, compared to 16.280 million or 6.5% in 2007 and 16.482 million in 2006, or 6.7% of the population. Of importance is the fact that nonmedical use of psychotherapeutics was just behind marijuana and hashish with 10.3% of the population aged 12 or older in 2008 which increased from 10.1% in 2007. Overall, nonmedical use of psychotherapeutics increased 163% from 1998 to 2008 in contrast to 167% from 1997 to 2006, compared to marijuana 31% versus 38%, 46% in cocaine to 38%, and overall illicit drug use of 48% versus 54% during the past year.

### 1.4 Lifetime Use

Lifetime use of illicit drugs (lifetime use indicates use of a specific drug at least once in the respondent's lifetime), including psychotherapeutics, among persons aged 12 or older has been increasing over the years (Table 4). In 2008, the lifetime use of illicit drugs among persons aged 12 or older was slightly more than 2007 with 117,325 or 47% of the population, an increase from 46.1% of the population in 2007. In contrast, nonmedical use of psychotherapeutics increased to 20.8% in 2008, or almost 52 million using prescription psychotherapeutic drugs for nonmedical purposes. Among the
Table 4. Types of illicit drugs of lifetime use among persons aged 12 or older: numbers in thousands, 1998 – 2008.

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonmedical Use of Psychotherapeutics&lt;sup&gt;2&lt;/sup&gt;</td>
<td>20,193</td>
<td>34,076</td>
<td>32,443</td>
<td>36,028</td>
<td>47,958&lt;sup&gt;1&lt;/sup&gt;</td>
<td>49,001&lt;sup&gt;1&lt;/sup&gt;</td>
<td>49,157&lt;sup&gt;1&lt;/sup&gt;</td>
<td>50,965</td>
<td>50,415</td>
<td>51,970</td>
<td>51,707</td>
<td>157%</td>
</tr>
<tr>
<td>Pain Relievers</td>
<td>--</td>
<td>19,888</td>
<td>19,210</td>
<td>22,133</td>
<td>29,611&lt;sup&gt;1&lt;/sup&gt;</td>
<td>31,207&lt;sup&gt;1&lt;/sup&gt;</td>
<td>31,768&lt;sup&gt;1&lt;/sup&gt;</td>
<td>32,692&lt;sup&gt;1&lt;/sup&gt;</td>
<td>33,472</td>
<td>33,060&lt;sup&gt;2&lt;/sup&gt;</td>
<td>34,861</td>
<td>NA</td>
</tr>
<tr>
<td>OxyContin&lt;sup&gt;1&lt;/sup&gt;</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1,924&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2,832&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3,072&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3,481&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4,098&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4,354</td>
<td>4,842</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>7,726</td>
<td>13,860</td>
<td>13,007</td>
<td>13,945</td>
<td>19,267&lt;sup&gt;1&lt;/sup&gt;</td>
<td>20,220</td>
<td>19,852&lt;sup&gt;1&lt;/sup&gt;</td>
<td>21,041</td>
<td>21,303</td>
<td>20,208</td>
<td>21,476</td>
<td>178%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>9,614</td>
<td>15,922</td>
<td>14,661</td>
<td>16,007</td>
<td>23,490&lt;sup&gt;1&lt;/sup&gt;</td>
<td>23,004&lt;sup&gt;1&lt;/sup&gt;</td>
<td>22,297</td>
<td>20,983</td>
<td>22,468</td>
<td>21,654</td>
<td>21,206</td>
<td>121%</td>
</tr>
<tr>
<td>Sedatives</td>
<td>4,640</td>
<td>7,747</td>
<td>7,142</td>
<td>7,477</td>
<td>9,969&lt;sup&gt;1&lt;/sup&gt;</td>
<td>9,510</td>
<td>9,891</td>
<td>8,982</td>
<td>8,822</td>
<td>8,396</td>
<td>8,882</td>
<td>91%</td>
</tr>
<tr>
<td>Marijuana and Hashish</td>
<td>72,070</td>
<td>76,428</td>
<td>76,321</td>
<td>83,272</td>
<td>94,946&lt;sup&gt;1&lt;/sup&gt;</td>
<td>96,611&lt;sup&gt;1&lt;/sup&gt;</td>
<td>96,772&lt;sup&gt;1&lt;/sup&gt;</td>
<td>97,545&lt;sup&gt;1&lt;/sup&gt;</td>
<td>97,823&lt;sup&gt;1&lt;/sup&gt;</td>
<td>100,518</td>
<td>102,404</td>
<td>14.8%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>23,089</td>
<td>25,406</td>
<td>24,896</td>
<td>27,788</td>
<td>33,910&lt;sup&gt;1&lt;/sup&gt;</td>
<td>34,891&lt;sup&gt;1&lt;/sup&gt;</td>
<td>34,153&lt;sup&gt;1&lt;/sup&gt;</td>
<td>33,673&lt;sup&gt;1&lt;/sup&gt;</td>
<td>35,298</td>
<td>35,882</td>
<td>36,773</td>
<td>59%</td>
</tr>
<tr>
<td>TOTAL ILLICT DRUGS&lt;sup&gt;3&lt;/sup&gt;</td>
<td>78,123</td>
<td>87,734</td>
<td>87,931</td>
<td>94,140</td>
<td>108,255&lt;sup&gt;1&lt;/sup&gt;</td>
<td>110,205&lt;sup&gt;1&lt;/sup&gt;</td>
<td>112,085&lt;sup&gt;1&lt;/sup&gt;</td>
<td>111,774&lt;sup&gt;1&lt;/sup&gt;</td>
<td>114,275&lt;sup&gt;1&lt;/sup&gt;</td>
<td>117,325</td>
<td>117,970</td>
<td>50%</td>
</tr>
</tbody>
</table>

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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, and 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.


Subgroups, only OxyContin increased significantly from 3,481 in 2005 to 4,842 in 2008, or 1.4% of the population in 2005 to 1.9% in 2008. Lifetime use of illicit drugs in persons aged 12 or older was topped by marijuana (41.0% of the population) followed by nonmedical use of psychotherapeutics (20.8% of the population). Further, nonmedical use of psychotherapeutics was 157% higher than the lifetime use of cocaine (59%) or marijuana (42%), from 1998 to 2008.

### 1.5 Abuse Based on Age

In 2008, young adults aged 18 to 25 demonstrated rates of current use of illicit drugs to be higher (19.6%) than for youths aged 12 to 17 (9.3%) and adults aged 26 or older (5.9%), with 16.5% using marijuana, 5.9% using psychotherapeutics nonmedically, 1.5% using cocaine, and 1.7% using hallucinogens (Fig. 4). Past month nonmedical use of prescription-type drugs among young adults increased from 5.5% in 2002 to 5.9% in 2008. 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. Further, during the same period of time, the nonmedical use of tranquilizers also increased from 1.6% to 2%. Lifetime, past year, and current nonmedical use
of psychotherapeutic drugs among young adults aged 18 to 25 also increased between 2002 and 2006, 27.7% vs. 30.3% for lifetime use, 14.2% vs. 15.5% for past year use, and 1.9% vs. 2.1% for current use, with increases in the rates of pain relievers and tranquilizer use (126).

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 2008 increased from 3.3% at ages 12 or 13, to 8.6% at ages 14 or 15, to 15.2% at ages 16 or 17. The highest rate of 21.5% was noted among persons aged 18 to 20 (Fig. 5) (126). In 2008, adults aged 26 or older were less likely to be current drug users than youths aged 12 to 17 or young adults aged 18 to 25 (5.9 vs. 9.3 and 19.6 percent, respectively). However, there were more drug users aged 26 or older (11.3 million) than users in the 12-to-17-year age group (2.3 million) and 18-to-25-year age group (6.5 million) combined.

1.6 Abuse Based on Gender

In 2008, the survey results were similar to prior years with males being more likely than females to be current illicit drug users (9.9% vs. 6.3%). Males were more likely than females to be past month users of marijuana (7.9% vs. 4.4%). However, males and females had similar rates of past month nonmedical use of psychotherapeutic drugs (2.6% and 2.4%, respectively), pain relievers (2.0% and 1.8%), tranquilizers (0.7% and 0.8%), stimulants (0.4% for both), and sedatives (0.1% for both) (126).

1.7 Abuse During Pregnancy

Among pregnant women aged 15 to 44 years, a significantly lower proportion of women used illicit drugs (5.1%) compared to their nonpregnant counterparts of 9.8% in the past month based on data averaged for 2007 and 2008 (126).

1.8 Abuse Based on Employment

Employment also seems to have a significant influence in 2008. Among adults aged 18 or older, the rate of illicit drug use was higher for unemployed persons (19.6%) than for those who were employed full time (8%) or part time (10.2%) (126).

1.9 Regional Variations

There were also differences based on geographic area among persons aged 12 or older in 2008. The rate of current illicit drug use in 2008 was 9.8% in the West,
8.2% in the Northeast, 7.6% in the Midwest, and 7.1% in the South (126). Further, the rate of current illicit drug use in metropolitan areas was higher than the rate in non-metropolitan areas with 8.5% in large metropolitan counties, 8.1% in small metropolitan counties, and 6.3% in non-metropolitan counties as a group (126).

1.10 Drug Abuse Among Criminals
In 2008, adults aged 18 or older who were on parole or a supervised release from jail during the past year had higher rates of dependence on or abuse of a substance (27.8%) than their counterparts who were not on parole or supervised release during the past year (8%). In 2008, probation status was associated with substance dependence or abuse. The rate of substance dependence or abuse was 34% 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 8.4% (126).

1.11 Driving Under the Influence
Driving under the influence of illicit drugs is criminal and dangerous to the public. In 2008, 10 million persons, or 4.0% of the population aged 12 or older, reported driving under the influence of illicit drugs during the past year. This rate was highest among young adults aged 18 to 25 with 12.3% (126).

1.12 Frequency of Abuse
Among past year marijuana users aged 12 or older in 2008, the following patterns were revealed (126):
- 15.0% used marijuana on 300 or more days within the past 12 months, translating to 3.9 million using marijuana on a daily or almost daily basis over a 12-month period.
- 35.7%, or 5.4 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 2008 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 (126). 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 2008 was shown in 9.8 million adults, representing 4.4% of all adults, with the highest rates being in adults aged 18 to 25 (7.4%) and lowest for adults aged 50 or older (2.3%) as shown in Fig. 6 (126). The prevalence of SPD among women aged 18 or older was higher (5.6%) than among men (3.0%) in that age group (126).

Past year illicit drug use was higher among adults aged 18 or older with past year SMI (30.3%) than among adults without SMI (12.9%). SMI in the past year was associated with past year substance dependence of abuse in 2008 in 25.2% or 2.5 million dependent on or abusing illicit drugs or alcohol, compared to adults without SMI, this population was 8.3% or 17.9 million.

### 2.2 Major Depressive Episodes and Drug Abuse

The prevalence of a MDE in 2008 was 6.4% of persons aged 18 or older, or 14.3 million adults, with at least one MDE in the past year. Over one in 25 adults or 4.2% (9.5 million) people had past year MDE with severe impairment. Even then, the past year prevalence of MDE in 2008 was lower for those aged 50 or older (4.5%) compared with rates among persons aged 18 to 25 (8.7%) and those aged 26 to 49 (7.4%). However, the past year prevalence of MDE was higher among adult females than among adult males, 8.1% versus 4.6%. In addition, among women, past year MDE rates were higher with 12.1% for 18 to 25 year olds, 8.8% for 26 to 49 year olds compared with those of 50 or older with only 6%. Further, the prevalence of MDE also varied by race and ethnicity with highest rate among persons reporting 2 or more races (12.7%), while rates for single race groups were 7% among whites, 5.2% among Hispanics, 4.9% among American Indians or Alaska Natives, 4.9% among blacks, and 3.6% among Asians.

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**Fig. 6.** Serious medical illness, psychological distress, and nontherapeutic drug use, among persons aged 18 or older, by age: 2008.

Source: [http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf](http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf) (126)
In addition, in 2008 the past prevalence of MDE with severe impairment for adults aged 18 or older was higher among unemployed persons (6.6%) than among persons employed full time (3.2%).

In 2008, an adult aged 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 (27.2% vs 13.0%) (126). 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. Thus, having MDE in the past year was associated with higher past year substance dependence or abuse among adults aged 18 or older, with approximately 20.3% being dependent on or having abused alcohol or illicit drugs, while among adults without MDE only 7.8% were dependent on or had abused alcohol or illicit drugs (126). These numbers have slightly decreased from 2006. Figure 7 illustrates substance abuse in adults by MDE.

The prevalence of a MDE in youths aged 12 to 17 in 2008 showed that 2.0 million (8.3%) reported at least one MDE during the past year. Among youths aged 12 to 17, the past year prevalence of MDE ranged from 3.9% among 12-year-olds to 11.6% among those aged 16, and 10.6% among those aged 17 (126).

Among youths with MDE aged 12 to 17, 37.4% had used illicit drugs in 2008, in contrast to 34.6% in 2006. This was higher than the 17.2% 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 (126).

### 2.3 Serious Psychological Distress and Drug Abuse

In 2008, the prevalence of past 30-day SPD among adults aged 18 or older was an estimated 10.2 million representing 4.5% of all US adults. The rates of SPD were highest for adults aged 18 to 25 and lowest for adults aged 50 or older (7.5% versus 2.9%). In addition, the rates were higher among unemployed adults that among adults employed full-time (10.2% versus 3.3%), part-time (4.4%), or other persons not in the labor force (6.1%).

Illicit drug use was higher among patients with SPD than adults without SPD (19.6% versus 7.3%). In 2008, past 30-day use of illicit drugs other than marijuana was higher among adults with SPD than among adults without SPD (12.3% versus 2.9%).
2.4 Mental Health Services

The 2008 survey showed that 30 million adults received mental health services during the past 12 months which was similar to 2007 (13.4% versus 13.2%) (Fig. 8).

In 2008, the type of mental health services most often received by adults aged 18 or older was prescription medication (11.3%), followed by outpatient services (6.8%). Even though the rates of these services were similar to those in 2007, the percentage of adults between 2002 and 2008, who received outpatient services declined from 7.4% to 6.8%, while the percentage increased from 10.5% to 11.3% in those receiving prescription medication. In contrast, approximately 2 million adults or 0.9% of the population aged 18 years or older received inpatient care for mental health problems during the past year, which was similar findings in 2007.

Age, gender, and ethnicity variables affected the rate of mental health services received. The 2008 report showed that adults aged 18 to 25 had a lower rate of mental health service use (10.8%) than adults aged 26 to 49 (14%) and aged 50 or older (13.6%). Further, men were less likely than women to receive both outpatient mental health services (5% versus 8.5%) and prescription medication (7.5% versus 14.8%) for mental health problems in the past year. Regarding race, the rates of mental health service use for adults reporting 2 or more races was 18.8%, 16% for whites, 13.2% for American Indians or Alaska Natives, 8.7% for blacks (up from 6.8% in 2007), 6.8% for Hispanics, and 4.5% for Asians.

Despite widespread use of mental health services in 2008, there were 10.6 million adults (4.7%) who reported an unmet need for mental health care in the past year, including 5.1 million adults who did not receive any type of mental health service in the past year and 17.9% or 5.4 million reporting an unmet need for mental health care. The barriers to mental health care included the inability to afford care (42.7%), the belief at the time that the problem could be handled without care (28.5%), not knowing where to go for care 19.8%, and not having the time to go for care (13.9%). As shown in Fig. 9, 8.5% of the patients were concerned with confidentiality. Health insurance either did not cover care or did not cover care appropriately in 15.2% of patients, and 7.2% believed that the treatment would not help.

Fig. 8. Past year mental health service use among adults aged 18 or older, by type of care: 2002-2008.
Source: http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf (126)

*Difference between this estimate and the 2008 estimate is statistically significant at the .05 level.
Among youths aged 12 to 17, 3.1 million or 12.7% received treatment or counseling, either inpatient or outpatient, for problems with behavior or emotions in a specialty mental health setting. In addition, 11.8% of youths received services in an educational setting, and 2.9% received mental health services in a general medical setting in the past 12 months. However, female youths were more likely than male youths to report using outpatient specialty mental health services (13.6% versus 9.3%), educational services (13% versus 10.5%), or general medical-based services (3.2% versus 2.6%), even though there was no significant gender difference in the use of inpatient specialty mental health services.

**3.0 Source of Prescription Drugs**

Of importance to the medical profession is the source of prescription-type pain relievers used nonmedically. Among persons aged 12 or older who used pain relievers nonmedically in the past 12 months, 55.9% reported that they received the drug for free from a friend or relative (126). Another 8.9% bought the drug from a friend or relative, and 5.4% took them from a friend or relative without asking. An additional 18% reported that they got the drug from just one doctor. In contrast, only 4.3% got the pain relievers from a drug dealer or other stranger, and only 0.4% reported buying the drug on the internet (Fig. 10).

In 81.7% of the cases where nonmedical users of prescription pain relievers obtained their drugs for free from a friend or relative, the individuals indicated that their friend or relative had obtained the drugs from just one doctor (126). Only 1.6% reported that a friend or relative had bought the drug from a drug dealer or other stranger. Even more striking is the fact that in 2007-2008, 42.8% 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 30.1% buying it from a friend or relative. Only one in 5 users of methamphetamine (21.17%) bought it from a drug dealer or other stranger (126).

*Fig. 9. Reasons for not receiving mental health services in the past year among adults aged 18 or older with an unmet need for mental health care who did not receive mental health services: 2008.*

*Source: [http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf](http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.pdf) (126)*
4.0 Therapeutic Opioids

Opioids have been used for thousands of years to treat pain and continue to be one of the most commonly prescribed medications for pain (3,19,46,140). Opioids are a class of drugs that relieve pain by binding to and blocking certain receptors located in the brain and spinal cord. However, while opioid use for acute pain, post surgical pain, and palliative care is accepted in the United States, and many other countries, there is debate about whether opioids are appropriate for the treatment of chronic non-cancer pain (3,5,19,46,140,232-243). In fact, the United States, which differs from other western countries, made it illegal for physicians to prescribe opioids for addiction. Consequently, physicians in the United States could face loss of license, loss of practice, and possible imprisonment, and in fact still do (19). The efficacy of opioids for chronic non-cancer pain has been demonstrated in only short-term trials, which includes opioids for neuropathic pain, but, evidence on the efficacy and effectiveness of these agents for a long duration of treatment which is typical for chronic non-cancer pain is limited (3,5,19,46,140,232,233). In addition, numerous concerns have been raised about adverse effects including the development of psychologic addiction or abuse, or both, that may arise with long-term use (232). Even then, it has been stated that the chilling effect United States regulations had on opioid treatment of pain have been countered by pain (opiate) advocacy, which successfully restored opioid treatment of acute and cancer pain. Further, based on the ability of opioids to effectively and safely treat acute and cancer pain, several arguments have been made to support extending opioid treatment to patients with chronic pain, attempting to remove the previously exercised caution based on fears of addiction. It is argued that physicians should be encouraged to prescribe opioids because they are indispensable for the treatment of pain and suffering (19,236), because uncontrolled pain may have deleterious physical effects (19,237-239), and because persistent pain destroys people’s autonomy, dignity, and decision-making capacity (19). Thus, with advocacy groups and physician advocating unlimited opioids, mainly due to politics and emotional issues involved with efforts to improve awareness and treatment of chronic pain, the availability and utilization of opioids has increased dramatically in the past few decades (4).

The frequent and escalating use of opioids in managing chronic non-cancer pain has become a major health care issue in the United States placing a
significant strain on the economy with the majority of patients receiving opioids for chronic pain. This necessitates an increased production of opioids, leading to escalating cost of opioid use, even with normal intake (3-5,19,46,140,232-235). Above all, the additional costs of misuse, abuse, and addiction are incalculable (3,5,14,47-99,126-174,240-247). Finally, comorbidities including psychological and physical conditions and numerous other risk factors are common in chronic pain and add significant complexities to the physician managing these patients (175,176,248-260).

Several published guidelines and consensus statements recommend the judicious use of opioids in appropriately selected patients with chronic non-cancer pain who have not responded to other treatments and analgesic medications (3,5,13,19,46,140,232-235,260-262). However, serious issues remain along with uncertainty about the optimal use of opioids for chronic non-cancer pain. The adverse effects, lack of functional status improvement, excessive use, abuse, and diversion are common issues with opioid administration (3,5,19,46,140,232-235).

4.1 Escalating Therapeutic Opioid Use

In a large US survey, the proportion of office visits for chronic musculoskeletal pain in which opioids were prescribed doubled from 8% in 1980 to 16% in 2000 (15). Over the same 2 decades, the proportion of office visits in which prescriptions for potent opioids were given increased from 2% to 9% with usage of more potent opioids such as morphine, hydromorphone, oxycodone, and fentanyl increasing. In a study of commercial and medicare insurance plans from 2000 to 2005, Sullivan et al (17) evaluated trends in opioid therapy for chronic non-cancer pain into different types of populations – national and commercially insured population, and state-based and publicly-insured (Arkansas Medicaid) population – over a 6-year period. The results showed that the proportion of the enrollees receiving the diagnosis of chronic non-cancer pain increased 33% in the health care population and 9% in the medicare population, along with a proportion of enrollees with chronic pain who received opioids in 58% of HealthCore and 29% of medicaid. Cumulative yearly opioid dose (in mg morphine equivalents) received by chronic pain patients treated with opioids increased 38% in HealthCore and 37% in medicare due to increase in number of days supplied rather than dose/day supplied. Use of short-acting Schedule II opioid increased most rapidly, in both groups 54% versus 38% and in cumulative over year dosage of 95% in HealthCore and 191% in medicaid. However, these trends have occurred without any significant change in the underlying population prevalence of chronic pain or new evidence of the efficacy of long-term opioid therapy. Consequently, the authors concluded that this phenomenon likely represents a broad-based shift in opioid treatment philosophy. In another study, Boudreau et al (16) evaluated trends in long-term opioid therapy for chronic non-cancer pain in adult enrollees for 2 health plans serving over 1% of the US population from 1997 to 2005. Over the study period, incident long-term use increased from 8.5 to 12.1 per 100,000 in group health (6%) percent change in rates annualized (PCA), and 6.3 to 8.6 per 100,000 at Kaiser Permanente of Northern California (5.5% PCA). Prevalent long-term use doubled from 23.9 to 46.5 per 1,000 at group health (8.5% PCA), and 21.5 to 39.2 per 1,000 at Kaiser Permanente (8.1% PCA). Non-Schedule II opioids were the most commonly used opioid among patients engaged in long-term opioid therapy, particularly at Kaiser Permanente. Long-term use of Schedule II opioids also increased substantially at both health plans. They also showed that among prevalent long-term users in 2005, 28.6% at group health and 30.2% at Kaiser Permanente were also regular users of sedative hypnotics. They concluded that long-term opioid therapy for non-cancer pain is increasingly prevalent, but the benefits and risks associated with such therapy are inadequately understood. Further, concurrent use of opioids and sedative-hypnotics was unexpectedly common and concerning.

Vogt et al (156) evaluated analgesic usage for low back pain and its impact on health care costs and service use. In 2001, 55.5% of members with claims for low back services received analgesics costing a total of $1.4 million, of which 68% were opioids. They also found that opioid use was associated with the high volume usage of low back pain services and correlated with the higher use of opioids in patients with psychogenic pain and low back pain related to orthopedic devices (fusion, etc.).

Luo et al (98) also evaluated patterns and trends in opioid use among individuals with back pain in the United States. They showed overall opioid use among 11.6% of individuals with back pain from a sample of 23.6 million in 1996 increasing to 12.6% in 1999 with a sample of 24.7 million individuals. The prescriptions showed an increase in oxycodone and hydrocodone with a decrease in propoxyphene.
Dhalla et al (39) showed opioid analgesic prescriptions in Ontario increasing from January 1991 to May 2007 by 29%, from 458 to 591 prescriptions per 1,000 individuals annually. However, the number of oxycodone prescriptions rose more than 850% during the same period, from 23 per 1,000 individuals in 1991 to 197 per 1,000 in 2007. In addition, the prescribing of hydromorphone, fentanyl, and morphine also increased considerably over the same period — even though the total number of prescriptions for these drugs was far lower than that for oxycodone-containing products. By 2006, oxycodone accounted for 32% of the almost 7.2 million prescriptions for opioids dispensed that year. Of the 2.3 million oxycodone prescriptions dispensed in 2006, 28% were for long-acting formulation. In addition, from 2001 to 2007, the average amount of long-acting oxycodone dispensed per prescription increased by 24%, from 1,830 mg to 2,280 mg. Similarly, opioid-related deaths doubled from 13.7 per million in 1991 to 27.2 per million in 2004. The addition of long-acting oxycodone to the drug formulary was associated with a 5-fold increase in oxycodone-related mortality and a 41% increase in overall opioid-related mortality. Further, use of health care services in the month before death was common with 66.4 of them visiting a physician in the month before death and 56.1% had filled a prescription for an opioid in the month before death. The authors (40) suggested that a significant portion of the increase was associated with the addition of long-acting oxycodone to the provincial drug formulary.

4.2 Evidence Synthesis

Multiple systematic reviews have been conducted evaluating the efficacy, effectiveness, side effects, abuse and diversions of opioids (5,18,48,166,170,171,232-235,263-279). However, concrete evidence of the effectiveness and safety of opioids in chronic pain has not been demonstrated. The foundation of the argument for use of opioids is the unique analgesic efficacy of opioids, and based on surveys, case series, occasional open-label follow-up studies, as well as some randomized controlled trials and epidemiological studies, opioid use has escalated in the United States. It is also argued, based on the clinical experience of opioid maintenance treatment for addicts that patients on stable regimens can be fully functional in society, and in the workplace despite their choice use of substances known to effect cognitive function. Nevertheless, the argument to apply the same knowledge and experience to chronic pain patients seems to be reasonable (271-274). In addition, the early experience with tolerance to the analgesic effects of opioids was treated by dose escalations as a therapeutic maneuver, while the ongoing experience suggests a less rosy state of affairs (19). Recent systematic reviews by Chou et al (5,233-235) and Noble et al (232) yielded useful guidance. Noble et al (232) concluded that many patients discontinue long-term opioid therapy due to adverse events or insufficient pain relief; however, weak evidence suggests that patients were able to continue opioids long-term and experience clinically significant pain relief. The findings with regards to quality life or functional improvement were inconclusive. They also reported many minor adverse events like nausea and headache, but serious adverse events including iatrogenic opioid addiction were rare. In plain language summary, they concluded that proper management of a type of strong pain killer (opioids) in well-selected patients with no history of substance, addiction, or abuse, can lead to long-term pain relief for some patients with a very small risk of developing addiction, abuse, or other serious effects. They however cautioned that the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are more likely to benefit from treatment. Chou et al (5,233-235), concluded that chronic opioid therapy can be an effective therapy for carefully selected and monitored patients with chronic non-cancer pain. They also reported that opioids are also associated with potentially serious harms, including opioid-related adverse effects and outcomes related to the abuse potential of opioids. Thus, both guidelines or manuscripts recommended opioids in the face of weak evidence and escalating use, abuse, and serious adverse effects, though in a small proportion of patients (4,48-56,61-66).

4.3 Escalating Quantity of Opioids

In pain management settings, it has been reported that as many as 90% of the patients receive opioids for chronic pain management in spite of the numerous issues involved (49-70,146,147). Further, it also has been shown that the majority of these patients were on opioids prior to presenting to an interventional pain management setting (49).

The therapeutic use of opioids has exploded in the United States, witnessed by increased sales of hydrocodone by 280% from 1997 to 2007, whereas methadone usage increased 1,293% and oxycodone increased 866% (Table 5). Overall, opioids increased from 50.7 million grams of medication in 1997 to 126.5 million
grams of medication in 2007, an increase of 149%. The estimated number of prescriptions filled for controlled substances increased from 222 million in 1994 to 354 million in 2003 (123-125).

The milligram per person use of therapeutic opioids in the US increased from 73.59 milligrams in 1997 to 369.19 milligrams per person in 2007, an increase of 402% (Table 6 and Fig. 11). During the same period the therapeutic use of methadone increased by 1,124 mg/person, and oxycodone by 899% mg/person. This is also confirmed by the fact that between 1992 and 2003, the population of the United States increased by 13%, whereas, the number of prescriptions written for non-controlled drugs increased by 154%.

### 4.4 Adverse Consequences

Opioids are associated with some well-known common side effects including nausea, sedation, euphoria,

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<tbody>
<tr>
<td>Methadone</td>
<td>518,737</td>
<td>692,675</td>
<td>964,982</td>
<td>1,428,840*</td>
<td>1,892,691</td>
<td>2,649,559</td>
<td>3,683,881</td>
<td>4,730,157</td>
<td>5,362,815</td>
<td>6,623,687</td>
<td>7,728,219</td>
<td>1293%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>4,449,562</td>
<td>6,579,719</td>
<td>9,717,600</td>
<td>15,305,913</td>
<td>19,927,286</td>
<td>22,376,892</td>
<td>26,655,152</td>
<td>29,177,530</td>
<td>30,628,973</td>
<td>37,034,220</td>
<td>42,977,043</td>
<td>866%</td>
</tr>
<tr>
<td>Fentanyl Base</td>
<td>74,886</td>
<td>90,618</td>
<td>107,141</td>
<td>146,61*</td>
<td>186,083</td>
<td>242,027</td>
<td>317,200</td>
<td>370,739</td>
<td>387,928</td>
<td>428,668</td>
<td>463,340</td>
<td>525%</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>241,078</td>
<td>260,009</td>
<td>292,506</td>
<td>346,57*</td>
<td>400,642</td>
<td>473,362</td>
<td>579,372</td>
<td>655,395</td>
<td>781,287</td>
<td>901,663</td>
<td>1,011,028</td>
<td>319%</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>8,669,311</td>
<td>10,389,503</td>
<td>12,101,621</td>
<td>14,118,637</td>
<td>15,594,692</td>
<td>18,822,619</td>
<td>22,342,174</td>
<td>24,081,900</td>
<td>25,803,543</td>
<td>29,856,368</td>
<td>32,969,527</td>
<td>280%</td>
</tr>
<tr>
<td>Morphine</td>
<td>5,922,872</td>
<td>6,408,322</td>
<td>6,884,935</td>
<td>7,807,511</td>
<td>8,810,700</td>
<td>10,264,264</td>
<td>12,303,956</td>
<td>14,319,243</td>
<td>15,054,846</td>
<td>17,507,148</td>
<td>19,051,426</td>
<td>222%</td>
</tr>
<tr>
<td>Codeine</td>
<td>25,071,410</td>
<td>26,018,054</td>
<td>23,917,088</td>
<td>23,474,86*</td>
<td>23,032,641</td>
<td>22,633,733</td>
<td>21,865,409</td>
<td>20,264,555</td>
<td>18,960,038</td>
<td>18,762,919</td>
<td>18,840,329</td>
<td>-25%</td>
</tr>
<tr>
<td>Meperidine</td>
<td>5,765,954</td>
<td>5,834,294</td>
<td>5,538,592</td>
<td>5,494,99*</td>
<td>5,450,204</td>
<td>5,412,389</td>
<td>5,239,932</td>
<td>4,856,642</td>
<td>4,272,520</td>
<td>4,160,033</td>
<td>3,936,179</td>
<td>-32%</td>
</tr>
<tr>
<td>Total</td>
<td>50,713,010</td>
<td>56,273,194</td>
<td>59,445,465</td>
<td>35,962,089</td>
<td>75,294,939</td>
<td>82,874,845</td>
<td>92,987,076</td>
<td>98,456,163</td>
<td>101,253,958</td>
<td>115,272,706</td>
<td>126,477,091</td>
<td>149%</td>
</tr>
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Table 5. Retail sales of opioid medications (grams of medication) from 1997 to 2007.

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.

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<tbody>
<tr>
<td>Methadone</td>
<td>1.94</td>
<td>2.60</td>
<td>3.47</td>
<td>5.14*</td>
<td>6.81</td>
<td>9.54</td>
<td>13.26</td>
<td>17.03</td>
<td>19.31</td>
<td>23.84</td>
<td>25.50</td>
<td>1214%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>16.68</td>
<td>24.66</td>
<td>34.99</td>
<td>55.11</td>
<td>71.75</td>
<td>80.56</td>
<td>95.97</td>
<td>105.05</td>
<td>110.27</td>
<td>133.33</td>
<td>154.73</td>
<td>899%</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.28</td>
<td>0.34</td>
<td>0.39</td>
<td>0.53*</td>
<td>0.67</td>
<td>0.87</td>
<td>1.14</td>
<td>1.33</td>
<td>1.40</td>
<td>1.54</td>
<td>1.67</td>
<td>496%</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>32.49</td>
<td>38.93</td>
<td>43.57</td>
<td>50.83</td>
<td>56.15</td>
<td>67.77</td>
<td>80.44</td>
<td>86.70</td>
<td>92.90</td>
<td>107.49</td>
<td>118.70</td>
<td>265%</td>
</tr>
<tr>
<td>Morphine</td>
<td>22.20</td>
<td>24.01</td>
<td>24.50</td>
<td>28.11</td>
<td>31.72</td>
<td>36.95</td>
<td>44.30</td>
<td>51.55</td>
<td>54.20</td>
<td>63.03</td>
<td>68.59</td>
<td>209%</td>
</tr>
<tr>
<td>Total</td>
<td>73.59</td>
<td>90.54</td>
<td>106.92</td>
<td>139.72</td>
<td>167.1</td>
<td>195.69</td>
<td>235.11</td>
<td>261.66</td>
<td>278</td>
<td>329.23</td>
<td>369.19</td>
<td>402%</td>
</tr>
</tbody>
</table>

Table 6. The increase in therapeutic opioids use in the U.S. (mg/person) from 1997 to 2007.

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

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dysphoria, constipation, and itching. However, with chronic use, a different breed of side effects develops, which includes hormonal and immune system effects, abuse and addiction, tolerance, and hyperalgesia. More importantly, opioid use has been associated with increased disability, medical costs, subsequent surgery, and continued or late opioid use (15,154-157).

Vogt et al (156) reported an association between opioid prescribing and an increase in overall health care costs for low back pain, implying higher levels of utilization. Similarly Mahmud et al (157) found an association between opioid use for more than a week for acute low back pain and disability duration in a worker’s compensation cohort. Webster et al (154) showed that patients receiving more than a 450 mg equivalent of morphine over a period of several months were, on average, disabled 69 days longer than those who received no early opioids, had 3 times increased risk for surgery, and had 6 times greater risk of receiving late opioids. Fillingim et al (153) indicated that opioid use was associated with greater self-reported disability and poorer function.

Franklin et al (275) studied early opioid prescription and subsequent disability among 18,443 workers with lost work time work-claims with nearly 14% of the sample were receiving work disability compensation at one-year, more than one-third of the worker’s received an opioid prescription within 6 weeks, and 50.7% of these received at the first medical visit. Rhee et al (276) showed in a sample of 13,760 patient with low back pain due to mechanical causes, 45% of the patients used narcotic drugs. Narcotic-use in patients with low back pain had significantly higher rates of co-morbid conditions than patients with low back pain not using narcotic drugs including hypertension, arthritis, depression, anxiety, and cancer. Emergency room visits were also higher for patients with narcotics along with health care costs which were approximately 3 times per patients using narcotic drugs compared to those not using them.

An epidemiological study from Denmark (174), where opioids are prescribed liberally for chronic pain, demonstrated worse pain, higher healthcare utilization, and lower activity levels in opioid-treated patients compared with a matched cohort of chronic pain patients not using opioids, suggesting that when opioids are prescribed liberally, even if some patients benefit, the overall population does not.

Overall, it appears that epidemiological studies are less positive with regard to function and QOL and report the failure of opioids to improve QOL in chronic pain patients (277). By contrast, Eriksen et al (167) demonstrated worse pain, higher healthcare utilization, and lower activity levels in opioid-treated patients compared with a matched cohort of chronic pain patients not using opioids. Other studies have also shown that instead of improving functional status, opioid use has been associated with increased disability, medical costs,
subsequent surgery, and continued or late opioid use (15,154-157).

Apart from pain relief, functional status improvement and healthcare utilization, another important function when patients are on chronic opioid therapy is driving capability (278,279). Fishbain et al (279) in a structured, evidence-based review of impairment in driving-related skills in opioid-dependent or opioid-tolerant patients, concluded that the majority of the reviewed studies appeared to indicate that opioids do not impair driving-related skills in opioid-dependent or tolerant patients. However, the research was inconclusive in one of the 5 areas relating to the potential impairment in cognitive function of opioid-maintained patients. The research was conclusive that there was no impairment of psychomotor abilities of opioid-maintained patients; no impairment of psychomotor abilities immediately after being given doses of opioids; no greater incidence in motor vehicle violations or motor vehicle accidents versus comparable controls of opioid-maintained patients; and no impairment as measured in driving simulators and on-road driving by opioid-maintained patients. These opinions did not correlate with a narrative review by Strassels (278), indicating that cognitive function can be influenced by the use of opioid analgesics, although the effects vary among drugs.

4.4.1 Complications

Complications due to opioid administration concern all medical practitioners (12,25,27,36,37,42,144,2 14,280-283). Commonly known side effects of opioids include constipation, pruritus, respiratory depression, nausea, vomiting, delayed gastric emptying, sexual dysfunction (42), muscle rigidity and myoclonus (284,285), sleep disturbance (286), pyrexia, diminished psychomotor performance (278,279), cognitive impairment (287), hyperalgesia (19,42,46,288), dizziness and sedation, all reflecting the effects of opioids on multiple organ systems (44).

Adverse events, in general, appear to fall into 2 broad categories: non-life-threatening and life-threatening. Hydrocodone may cause sensorineural hearing loss due to possible genetic polymorphisms (289). More serious adverse events, such as respiratory depression and death, have been seen with the use of fentanyl buccal tablets for breakthrough pain. Drug deaths from opioids are a serious and increasing issue (25,36,37,144,280,282,283).

Opioids have also been described to have multiple drug interactions. A drug interaction occurs when the amount or the action of a drug is altered by the administration of another drug or multiple drugs. Multiple hepatic drug interactions may influence opioid drug levels (42,44).

5.0 Prescription Opioid Abuse

Prescription opioids are abused among the populations with or without pain, and in patients receiving or not receiving opioids. The abuse is associated with substantial risks to the patients and the nation as a whole with increasing emergency department visits, deaths, and federal drug spending.

Along with the increase of prescriptions for controlled drugs from 1992 to 2003 of 154% (151), there was also a 90% increase in the number of people who admitted abusing controlled prescription drugs. Mahowald et al (158) and White et al (290) evaluated opioid abuse in the insured population of the United States. Opioid abuse was determined to be present in 6.7 to 8 per 10,000 persons insured. However, opioid abusers also presented with multiple comorbidities and expenses 8 times higher than for nonabusers ($15,884 vs. $1,830).

The cost of opioid abuse is enormous. The White House Budget Office estimated drug abuse costs to the US Government to be approximately $300 billion a year (10,123). The White House Office of National Drug Control Policy (ONDCP), a component of the Executive Office of the President, established by the Anti-Drug Abuse Act of 1998, has been spending $12-13 billion each year.

5.1 Opioid Abuse in Chronic Pain

The central question when prescribing opioids for chronic noncancer pain is how best to balance the risk of opioid abuse with the pain relief provided by these medications (4,10,19,25,36,37,45,46,51-55,60,61,63-66,14 4,164,234,235,280,282,283,291-295). While proponents claim extremely low levels of opioid abuse (296), opioids are by far the most abused drugs, especially in chronic pain management settings (4,12,19,25,36,37,46,144,2 34,235,280). Numerous investigations have illustrated drug abuse in 18–41% of patients receiving opioids for chronic pain (10,48,49,51-55,60,61,63-66,294,295,297).

Martell et al (48), in a systematic review of opioid treatment for chronic back pain, estimated the prevalence of lifetime substance use disorders to range from 36 to 56%, with a 43% current substance use disorder rate. Furthermore, aberrant medication-taking behaviors ranged from 5 to 24%.
Multiple investigators have also studied the issue of illicit drug use in chronic pain patients receiving controlled substances (51,61,63-66,294,295). The results showed that illicit drug use in patients without controlled substance abuse was found in 14–16% of patients and illicit drug use in patients with controlled substance abuse was present in 34% of the patients (51,53,54). Illicit drug use was significant in chronic pain patients in general, but illicit drug use was similar in patients using either long-acting or short-acting opioids (64). In a study on effective monitoring of opiates in chronic pain patients evaluating 111,872 specimens collected over a 1-year time period from pain treatment facilities throughout the USA (294), and in another study evaluating 938,586 specimens, a significant proportion were shown to have abnormal drug testing with nonprescribed medications, illicit drugs and inappropriate intake of drugs (295). In other evaluations, it was shown that adherence monitoring will in fact decrease controlled substance abuse and illicit drug use (61,66).

Along with an increase of prescriptions for controlled drugs from 1992 to 2002 of 154%, there was also a 90% increase in the number of people who admitted abusing controlled prescription drugs. Studies also evaluated opioid abuse in the insured population of the USA (290). Opioid abuse was determined to be present in 6.7–8 per 10,000 persons insured; however, opioid abusers presented with multiple comorbidities and expenses 8-times higher than for nonabusers (US $15,884 vs. $1830).

5.2 Drug Diversion

Prescription drug ‘diversion,’ defined as the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit market place, has been a topic of widespread commentary, and is of interest to regulators and providers (298). The abuse of many different prescription drugs has been escalating since the early to mid-1990s (298,299). Diversion can occur in many ways, including the illegal sale of prescriptions by physicians, patients and pharmacists, doctor shopping, forgery, robbery and theft. However, it has been shown that the majority of the drugs come from a single physician’s prescription and that family members share it (4). Inciardi et al (298) described diversion as a disorganized for-profit industry. They described it as ‘disorganized’ because there are so many different players involved in the phenomenon, including physicians, pharmacists and other healthcare professionals; drug abusers, patients, students, street dealers and white collar criminals; tourists, saloon keepers and all types of service personnel, to name but a few. Federal agencies maintain that the diverted drugs enter the illegal market primarily through ‘doctor shoppers,’ inappropriate prescribing practices by physicians and improper dispensing by pharmacists (298). Inciardi et al (298) in a study of the mechanisms of prescription drug diversion among drug-involved club- and street-based populations, concluded that while doctor shoppers and the internet receive much of the attention regarding diversion, the data showed there are numerous active street markets involving patients, Medicaid recipients and pharmacists as well. They also suggested that the contributions of residential burglaries, pharmacy robberies and thefts and ‘sneak thefts’ to the diversion problem may have been understated.

In an updated manuscript, Inciardi et al (299) described the results of an ultra-rapid assessment of prescription opioid abuse and diversion in an urban community. They reported that the primary sources of prescription drugs on the street were the elderly, patients with pain and doctor shoppers, as well as pill brokers and dealers who work with all of the former. They also described that the popularity of prescription drugs in the street market was rooted in the abusers’ perceptions of these drugs as less stigmatizing, less dangerous and less subject to legal consequences than illicit drugs. Furthermore, they showed that the abuse of prescription opioids also appears to serve as a gateway to heroin use.

6.0 Drug Poisoning And Deaths

Unintentional drug poisonings in the United States are common. Unintentional, or accidental, with no harm intended, includes drug overdoses resulting from drug misuse, drug abuse, and taking too much of a drug for medical reasons (300).

6.1 Emergency Department Visits

The Drug Abuse Warning Network (DAWN) publishes results of emergency department visits with drug misuse and abuse. In 2008, DAWN (132) published results with over one million emergency department visits involving an illicit drug.

♦ Hydrocodone/combinations in 89,047 emergency department visits,
♦ Oxycodone/combinations in 105,208 emergency department visits, and;
Methadone in 63,629 emergency department visits.

Emergency department visits for narcotics were 305,885 in 2008 compared to 42,857 in 1995, a 614% increase over a period of 13 years (Fig. 12). Among the psychotherapeutic agents, the anxiolytics (anti-anxiety agents, sedatives, and hypnotics) were the most frequent, occurring in 30% of the visits associated with nonmedical use of pharmaceuticals (132). DAWN estimated that 271,700 emergency department visits were associated with nonmedical use of pharmaceuticals involving benzodiazepines in 2008, compared to 71,609 in 1995, a 279% increase over a period of 13 years (71,132-134).

In 2008, DAWN estimates show that prescription or over-the-counter drugs used nonmedically were involved in 1.0 million emergency department visits, and illicit drugs were involved in 1.0 millions visits (Fig. 13).

6.2 Deaths Due to Opioids

Drug overdose death rates have risen steadily in the United States since 1970 as illustrated in Fig. 14. In 2007, 27,658 unintentional drug overdose deaths occurred in the United States. Drug overdose deaths were second only to motor vehicle crash deaths among leading causes of unintentional injury death in 2007 in the United States. Consequently, rates have increased roughly 5-fold since 1990. Age-adjusted rates of drug overdose deaths for whites have exceeded those among African-Americans since 2003. It has been stated that increasing drug overdose death rates is largely because of prescription opioid painkillers. In 2007, the number of deaths involving opioid analgesics was 9.3 times the number involving cocaine and 5.38 times the number involving heroin. Figure 15 illustrates unintentional drug overdose deaths by major type of drug in the United States from 1999 to 2007. It has been reported that these deaths are secondary to an unusual increase of prescription opioids during the last 20 years which has been over 10-fold because of a movement toward more aggressive management of pain.

Significant regional variations also have been reported in relations to overall drug overdose death rates. It has been shown that states in the Appalachian region and the Southwest have the highest death rates (Fig. 16). The highest drug overdose death rates was found in West Virginia, which was nearly 7 times that of state with the lowest drug overdose death rate, South Dakota. In 2007,
states such as California and New York had some of the lowest overall death rates among all states because of low opioid overdose rates. In contrast, in the early 1990’s these states had some of the highest overall rates, largely because of high heroin and cocaine overdose rates.

It also has been demonstrated that men and middle aged people are more likely to die from drug overdose. In 2007, 18,029 drug overdose deaths occurred among males and 9,626 among females (Fig. 17). Essentially, male rates have doubled and female rates

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**Fig. 13.** Estimated numbers of emergency department visits involving legal drugs used nonmedically and illegal drugs, United States, 2008.

Source: Drug Abuse Warning Network.

**Fig. 14.** Rate of unintentional drug overdose deaths in the United States, 1970-2007.

Source: National Vital Statistics System
have tripled since 1999. In general, it has been stated that men have historically had higher rates of substance abuse than women.

Further, for both sexes, the highest rates were in the 45 to 54 years old age group with rates declining dramatically after the age of 54. Finally, after age 64, the male and female rates become comparable, probably as a result of the reduction of the rates of substance abuse with age.

6.3 Methadone Deaths

As previously indicated, the 2007 DAWN results (132) found methadone to be the number 3 opioid related to emergency room visits, causing 63,629 visits. Of greater concern is the shocking increase in methadone-related deaths.

Until the late 1990s, methadone was predominantly used for the management of heroin addiction. In 2006, with 4 million methadone prescriptions written for pain relief, and steady increases since then, it has become one of the most widely prescribed opioid painkillers (301). Table 7 illustrates this fact by comparing the alarmingly steady increase in methadone distribution activity (33). This table shows that the 2002-2007 distribution of methadone by business categories associated with pain management such as pharmacies, hospitals and practitioners, almost tripled, rising from about 2.3 million grams to about 6.5 million grams (33).

In November 2008, the Methadone Mortality Work Group of the Office of Diversion Control, Drug Enforcement Administration showed that from 2000 to 2005 methadone ranked at the top in percent of increase in the cause of poisoning deaths in the United States and has shown a dramatic percentage of increase over all other causes of poisoning deaths over this time period. This coincides with the Centers for Disease Control (CDC) report of the number of poisoning deaths involving methadone increasing from 790 in 1999 to 5,420 in 2006.

According to Nicholas Reuter, a public health analyst (301), the increasing use of methadone also coincides with concern over the abuse potential of OxyContin and the search for a relatively inexpensive long-acting opioid pain-killer alternative. Reuter’s data indicates that only one-third of all methadone prescriptions in 2008 were for treatment of drug addiction. There is a danger in this differential usage of methadone as it is able to suppress withdrawal symptoms for 24 hours, but is only effective as a painkiller for 4-8 hours. It can stay in the system for as long as 59 hours and pain patients may inadvertently overdose by taking the methadone too often or at excessive dosages allowing for the build-up of toxic levels and possible life-threatening changes in respiratory and cardiac function (301).

Another complicating issue is that methadone has unique pharmacological properties that many physician and consumers are unaware of especially as it enters...
Fig. 16. Drug overdose death rates by states, 2007.
Source: National Vital Statistics System

Fig. 17. Unintentional drug overdose death rates by sex and age group, United States, 2007.
Source: National Vital Statistics System
into the world of street abuse (301). Both professional continuing education and public service announcements are focused on this in order to ameliorate this problem, which also includes ignorance about the lethal potential of mixing methadone with benzodiazepines. At least one-half of all reported opioid-related deaths involved other drugs such as heroin or cocaine in 15% of cases and benzodiazepines such as Xanax or Valium in 17% of cases (301). CDC’s National Center for Health Statistics reports mortality rates, but they are derived from death certificates and there are no current estimates of whether these deaths were the result of legally prescribed drugs or not (301). We can be certain, however, that based on all of the other evidence and indicators that a significant proportion of these deaths were due to illicit drug usage, abuse, misuse, or illegal diversion.

The picture that emerges from the available data clearly indicates that methadone is not simply a benign management tool for the treatment of drug addiction nor is it any less benign in its role as a painkiller. The current age demographics show an increasing danger for younger age groups with an 11-fold increase in the 15-24 year age group (301), especially when used in conjunction with benzodiazepines and/or alcohol. Its potential for diversion is, to some degree, compromised by the huge utilization in narcotic treatment programs, a group already prone to habits of diversion, abuse, and experimentation. What is also clear is that 73-79% of the deaths are unintentional (301) and with increased professional education, public education and pro-active programs such as the National All Schedules Prescription Electronic Reporting (NASPER) legislation are to some extent preventable.

### 6.4 Deaths in Interventional Pain Management Practices

The literature on prevalence of deaths in pain management or specifically interventional pain management settings is not available.

From March 2003 to February 2007, Manchikanti et al (27) evaluated 2,179 patients were receiving opioids in 2003, 2,445 in 2004, 2,804 in 2005, and 2,965 in 2006. There were a total of 91 deaths, of which 60 were categorized as natural deaths, 25 were characterized as accidental deaths, and 6 were characterized as suicidal. Of the 18 drug poisoning deaths, 5 deaths were positively related to prescription drugs, 7 deaths were probably related to prescription drugs, and 6 deaths had no relation to the prescription drugs provided.

They concluded that, in an interventional pain management practice (a tertiary referral center), the total prevalence of opioid related deaths varied from 0.46 to 1.78 per 1,000 from 2003 to 2006 with a total of 12 deaths over a period of 4 years. The deaths definitely related to opioid prescriptions were 5 with a rate of 0 to 1.43 per 1,000 over a period of 4 years.

### Conclusions

What emerges from the available data utilized in this review is the conclusion that over the past 10 years there has been an escalation of the therapeutic use of opioids and other psychotherapeutics and of their abuse and nonmedical use as well. 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

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**Table 7. Methadone Distribution by Type of Business, 2002 to 2007**

<table>
<thead>
<tr>
<th>Year</th>
<th>OTPS</th>
<th>Hospitals</th>
<th>Pharmacies</th>
<th>Other practitioners</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>5,262,052</td>
<td>309,315</td>
<td>2,329,083</td>
<td>10,381</td>
</tr>
<tr>
<td>2003</td>
<td>5,743,272</td>
<td>393,685</td>
<td>3,274,331</td>
<td>15,113</td>
</tr>
<tr>
<td>2004</td>
<td>6,584,721</td>
<td>466,352</td>
<td>4,246,007</td>
<td>35,492</td>
</tr>
<tr>
<td>2005</td>
<td>6,892,025</td>
<td>521,216</td>
<td>4,863,736</td>
<td>43,260</td>
</tr>
<tr>
<td>2006</td>
<td>7,345,623</td>
<td>584,144</td>
<td>5,986,488</td>
<td>51,046</td>
</tr>
<tr>
<td>2007</td>
<td>6,451,288</td>
<td>590,649</td>
<td>6,442,516</td>
<td>49,503</td>
</tr>
</tbody>
</table>

Source: GAO analysis of DEA methadone distribution data. GA-09-341

Notes: Methadone distribution numbers are in grams. Prior to 2002 DEAs methadone distribution data did not track sales to OTPs, therefore, data prior to 2002 is not included.

- DEA reports that in hospitals methadone may be dispensed or administered for pain management. Hospitals may also dispense or administer methadone for addiction treatment when patients are admitted to the hospital for another condition but require treatment for opiate addiction during their stay.

- In addition to issuing prescriptions for controlled substances that patients can have filled in retail pharmacies, appropriately licensed practitioners may also dispense controlled substances directly to patients. DEA officials said that while practitioners may dispense methadone directly in their offices for pain management purposes, it is not a common practice. Officials did not have information on the specific types of practitioners who are dispensing methadone directly.
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 now is diversion through family and friends and their source is more likely to be from 1 physician and not from doctor shopping.

We must also consider the highly interactive pattern of effect and impact that exists in the general areas of substance abuse, mental health, and overall healthcare. Due to the close interrelationship between mental disorders and substance abuse, “dual diagnosis” is becoming more prevalent. This begs the age-old question of which comes first, the chicken-or-the-egg? We will probably never know.

We are clearly left with the challenge to be aware of the difficulties presented by our increased reliance on the use of therapeutic opioids to treat chronic and acute pain and to remember the physician’s dictum: Do no harm. Because of the alarming patterns described in this article we are required as physicians to become more diligent in our efforts to ensure proper prescrip-
tion and utilization of therapeutic opioids and to investig-ate in more depth the real therapeutic advantages of opioid use, especially for chronic pain. We need to be sensitive to our responsibilities in mitigating these problems and to ask ourselves whether we need to be more conservative in our therapeutic use of opioids. We are challenged to invent newer strategies for the pre-
vention of diversion among which perhaps the greatest would be the proactive education of our patients, their families, our congressional representatives and the general public of the limitations of therapeutic use, and the dangers of abuse and nonmedical use of opioids. There is an urgency created by this alarming trend that requires our immediate attention and it behooves us to take action now.

**Acknowledgements**

The authors wish to thank Sekar Edem for assistance in the search of the literature, Tom Prigge for manuscript review, and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in prepa-
ration of this manuscript.

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