

# prescription Painkillers

HISTORY, PHARMACOLOGY, AND TREATMENT

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with Mark E. Rose, M.A.



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THE LIBRARY OF ADDICTIVE DRUGS

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**Hazelden®**

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Center City, Minnesota 55012  
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Printed in the United States of America

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*Library of Congress Cataloging-in-Publication Data*

Seppala, Marvin D.

Prescription painkillers : history, pharmacology, and treatment / Marvin D. Seppala, with Mark E. Rose.—1st ed.

p. cm.—(The library of addictive drugs)

Includes bibliographical references and index.

ISBN 978-1-59285-901-6 (softcover)

1. Analgesics. I. Rose, Mark E., 1962- II. Title. III. Series.

RM319.S47 2010

615'.783—dc22

2010035596

*Editor's note*

The names, details, and circumstances may have been changed to protect the privacy of those mentioned in this publication.

This publication is not intended as a substitute for the advice of health care professionals.

14 13 12 11 10 1 2 3 4 5 6

Cover design by Theresa Jaeger Gedig  
Interior design and typesetting by Madeline Berglund

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## INTRODUCTION

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Eighty percent of the world's supply of opioid medications is used in the United States, in a country with only 4.6 percent of the world's population. This reveals the opportunity for both tremendous therapeutic advances using these medications, often simply called prescription painkillers, to address pain and suffering, as well as the potential for abuse. This quandary—that these medications are the best and basically the only available medications for moderate to severe pain and are highly reinforcing and potentially addicting—has driven clinical decision-making and government policy throughout U.S. history. The dramatic increase in prescription opioid abuse over the past fifteen years has received significant attention from diverse branches of the federal government. The Drug Enforcement Administration (DEA) has directed more resources to address issues of prescription opioid diversion; the National Institute on Drug Abuse (NIDA) has funded research to examine the appropriate treatment of prescription opioid addicts at the same time pain has become a vital sign to be used in hospitals accredited by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) around the country; and the National Institutes of Health (NIH) has funded research into the use of these medications in the treatment of a growing medical problem—chronic pain. Despite these efforts, opioid abuse has become commonplace, and opinions vary widely on the appropriate government response, medical care, and treatment of people who are addicted to opioids.

This book provides an overview of the major aspects of the tremendous dilemma associated with the prescription opioids in the United States. Here is a chapter-by-chapter outline of the topics covered:

- Prescription opioid abuse is the fastest-growing addiction in the United States. These medications are readily available, and many people naively believe they are safe for recreational use, because they are prescribed. All of the problems and tragedies associated with opioid abuse are increasing proportionally to the increased



use of the prescribed opioids. Chapter 1 documents the chilling extent of the problem.

- The historical background of opioid use and public policy in the United States is examined in chapters 2 and 3 to provide a context for understanding our current status and make sense of the federal system as it pertains to current law, oversight, and control of these medications. The medical sciences have not provided the entire framework for our policies—fear and stigma have played a major role in federal decision making regarding these medications, and continue to do so.
- In chapter 4, the availability and use of these medications will be described in a manner that links the extent of the problem to those contributing to the supply network. Some risk factors associated with the use of these medications are identical to all other drugs of abuse; others are specific to the prescribed opioids, such as treatment for pain. People obtain these medications in diverse ways. Some people see multiple physicians to obtain enough medication to maintain active addiction; others purchase medications from drug dealers who get their supplies by diversion at every step of the distribution path from the manufacturer to the physician's office. The network includes pill brokers purchasing opioids from older adults on fixed incomes, who sell some or all of their prescribed opioids, whether they need them or not, to supplement their income. Our access to these medications has changed dramatically with changing views of the treatment of pain.
- There are numerous opioids available in the United States and many routes of administration for which they are intended, resulting in many drugs available for abuse and multiple ways to use them to get high. The use of the drugs and those that are available in the United States are described in chapters 5, 6, and 7. They are most often used orally, as intended, but they can be snorted, smoked, and injected, among other means. Sometimes they must be modified for alternative use; the Internet provides quick and reliable descriptions of these methods. In chapter 8,

the case of OxyContin is used to reveal how a medication thought to have a lower potential for addiction was easily altered to provide an immediate, potent high. OxyContin is also used to examine not just illicit diversion of a new opioid, but also marketing of opioid medications and controversy associated with the treatment of pain.

- Treatment for opioid addiction completes the text, in chapters 9 and 10. Opioid addiction, being the oldest drug addiction, has been treated for centuries, yet we do not have tremendous success rates (especially for heroin) and continue to have controversies. The prescribed opioids may require different treatment methods than heroin, but at this time, one can summarize by saying we have adapted treatments for heroin addiction to treat this rapidly growing problem. Perhaps that is reasonable—we're talking about opioids, not different classes of drugs—but the research is not clear about this. Prescribed opioids are commonly taken orally, but can be used intravenously, like heroin. They are smoked like heroin, and have identical effects in the brain. Some say heroin is more potent, but prescribed opioids like fentanyl and sufentanil are tremendously more powerful. The common treatment methods—maintenance and abstinence—and their attributes and shortcomings will be described. The availability of Twelve Step groups for opioid addiction is also discussed in-depth.

This book provides readers with a solid foundation regarding the multifaceted problems associated with prescription opioids in the United States. Although the United States uses the majority of the world's prescription opioids, we are not the only country experiencing increasing problems with opioid addiction and all the regulatory questions associated with them. Knowledge of the problem provides the opportunity for healthy debate.

In my professional work, I oversee the care and treatment of people struggling with addiction, and I use that perspective to provide a broad examination of the current situation. I hope this book gives you an opportunity to learn more about this troubling, growing problem and even spurs you to become active in finding solutions.



## CHAPTER 1

### The Current Problem

**T**he misuse of opioids has become a tremendous problem in the United States. Prescribed opioids are currently the fastest-growing addiction. All of the measures used to examine drug abuse reveal the incredible destruction caused by these medications. Americans have a voracious appetite for illegal drugs, and for opioid drugs in particular. As the introduction revealed, Americans make up only 4.6% of the world's population but consume 80% of the global supply of opioids; we also use 99% of the global supply of hydrocodone, and 66% of all illegal drugs (Manchikanti 2007; Califano 2007; Kuehn 2007). Retail sales of prescription opioids increased 127% between 1997 and 2006, from a total of 50.7 million grams of commonly utilized opioids (including methadone, oxycodone, fentanyl base, hydromorphone, hydrocodone, morphine, meperidine, and codeine) to 115.3 million grams. During the same time period, increases in specific prescription opioids include 196% for morphine, 244% for hydrocodone, 274% for hydromorphone, 479% for fentanyl base, 732% for oxycodone, and 1,177% for methadone (table 1.1). These figures not only underscore the massive increase in the prescribing of opioids, but also the failure of the current "war on drugs" to reduce the nation's substance abuse and addiction problem right in our own backyard (Manchikanti and Singh 2008).

Table 1.1

Retail Sales of Prescription Opioids  
(Grams of Medication), 1997–2006

	1997	2006	Change
Methadone	518,737	6,621,687	1,177%
Oxycodone	4,449,562	37,034,220	732%
Fentanyl Base	74,086	428,668	479%
Morphine	5,922,872	17,507,148	196%
Hydrocodone	8,669,311	29,856,368	244%
Hydromorphone	241,078	901,663	274%
Meperidine	5,765,954	4,160,033	–28%
Codeine	25,071,410	18,762,919	–25%
<b>Total</b>	<b>50,713,101</b>	<b>115,272,706</b>	<b>127%</b>

(Manchikanti and Singh 2008)

As these figures indicate, the use of prescription opioids has increased dramatically over the last decade, and nonmedical use of prescription opioids has caused increasing concern among law enforcement officials and regulatory, pain relief advocacy, and drug abuse organizations (Zacny et al. 2005). The increase in opioid abuse is particularly troubling because respiratory depression and death can result from the doses at which these drugs are frequently used, especially when mixed with other central nervous system (CNS) depressants such as alcohol and benzodiazepines (Compton and Volkow 2006). The two populations for whom prescription opioid

abuse is especially troubling are adolescents, because of the uncertain implication of future addiction, and the elderly, because of increased vulnerability to toxicity. The brain is still developing until our mid-twenties, so early exposure to opioids may cause neurobiological changes and behavioral consequences that are different from what adults experience from chronic opioid use (Compton and Volkow 2006).

### **Figures from U.S. Government Agencies**

Several U.S. government agencies have documented the pattern of increased prescription opioid use. Here are a few of the highlights from their findings:

*An estimated 63 million people in the United States have used a prescription opioid for nonmedical purposes at least once during their lifetime* (Woolf and Hashmi 2004). The recent peak of prescription opioid use occurred in 2004, and the numbers have leveled off since. At the peak, an estimated 4.4 million individuals age twelve or older had used prescription opioids nonmedically in the past month, according to the 2004 National Survey on Drug Use and Health (NSDUH), resulting in an estimated 158,281 emergency department visits. The opioids that were identified most frequently were oxycodone products (24.1% of opioids), hydrocodone products (23.1%), and methadone (21.3%). Among persons admitted to the emergency department for opioids, 64.6% involved the use of multiple drugs (or alcohol) (Substance Abuse and Mental Health Services Administration [SAMHSA] 2005).

*Opioids now surpass marijuana as the drug class most often used by people for their first “high.”* In 2007, the specific drug categories with the largest number of initiates age twelve or older were prescription opioids

(2,147,000) followed by marijuana or hashish (2,090,000) (National Drug Intelligence Center [NDIC] 2009). The most recent data from NSDUH, 2008, shows that marijuana and opioids are approximately equal as the most common illicit substance for new users, but if heroin (an opioid) is added to the prescribed opioids, they easily exceed marijuana as the most common drug class to be used by people over twelve to get their first high. In 2007, 2.1% of persons age 12 or older (an estimated 5.2 million people) reported using prescription pain relievers nonmedically in the past month, a rate not significantly different from that in 2002.

The number of people who used prescription painkillers nonmedically for the first time in the past year (past-year initiates) was estimated at 2.3 million individuals (SAMHSA 2007c). The rate of past-year initiation decreased with age, with 3.8% of those age 12 to 17, 3.4% of those age 18 to 25, 0.9% of those age 26 to 34, 0.4% of those age 35 to 49, and 0.2% of those age 50 or older initiating use in the past year (SAMHSA 2007c).

*The number of people seeking treatment for prescription opioid abuse has risen.* The number of admissions to treatment centers for people with prescription opioids as their primary drug of choice increased 71% between 2003 and 2007, from 52,840 admissions in 2003 to 90,516 admissions in 2007. During this same period, the number of admissions to treatment centers for people with heroin as their drug of choice decreased from 273,996 in 2003 to 246,871 in 2007 (NDIC 2009).

*Some prescription opioid abusers (particularly teens and young adults) switch to heroin.* Prescription opioids are usually more expensive than heroin, and people abusing prescription opioids many switch to heroin

because it is more affordable in many areas of the United States. OxyContin abusers with a high tolerance may use 400 milligrams of the drug daily (five 80-milligram tablets), for an average cost of \$400. A comparable amount of heroin, roughly 2 grams, could be purchased at a cost of one-third to one-half that of the OxyContin (NDIC 2009).

*Males age 18 and older were more likely than females to have used a prescription painkiller nonmedically in the past year (5.2% versus 4.4%).* However, youths age 12 to 17, and females in all age groups were more likely than males to have used prescription opioids nonmedically in the past year (7.9% versus 6.8%). Among adults 35 and older, there were similar rates of nonmedical use of prescription pain relievers between males and females (SAMHSA 2007a). This is a dramatic shift in drug use patterns and consistent with the patterns in some states in which 12- to 17-year-old girls are drinking more frequently than their male counterparts. Historically, illicit substances are much more likely to be used by males. This change suggests a significant longer-term problem for the young women in the United States.

## Definitions

Many different terms have been used by professionals, patients, and the media to describe patterns of use of prescription opioids, or painkillers. Each of these means different things to different people. Therefore, a useful place to begin our discussion of prescription painkillers is to clarify these terms.

**Nonmedical use** refers to using a prescription pain reliever “even once, that was not prescribed for you, or that you took only for the experience or feeling that it caused” (SAMHSA 2006c). Thus, *nonmedical use* refers to



use of prescription drugs not prescribed to the user by a physician, or used only for the experience or feeling they caused (Zacny and Lichtor 2008).

**Misuse** refers to a patient's incorrect use of a medication, including use for other than the intended purpose, exceeding the prescribed amount, or taking the drug more frequently or for longer than prescribed (Ling, Wesson, and Smith 2005). *Misuse* and *nonmedical use* are comparable terms.

**Abuse** is a term that varies widely depending on the context. The Drug Enforcement Administration (DEA) defines *abuse* as the use of prescription drugs in a manner or amount inconsistent with the medical or social pattern of a culture. *Abuse* is also defined as the use of prescription medications beyond "the scope of sound medical practice" (Ling, Wesson, and Smith 2005). Abuse and misuse often overlap when referring to prescription medication. The American Psychiatric Association (APA 2000) defines *abuse* as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress as manifested by one or more behaviorally based criteria." Patterns of behavior in patients who engage in the abuse of prescription opiates include escalating use, manipulation of doctors, losing prescriptions, and doctor shopping (Longo et al. 2000).

**Addiction, or substance dependence**, is the term usually used to describe the condition of someone who is hooked on a drug. *Addiction* is defined by the American Society of Addiction Medicine as a primary chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing the development and manifestations. People with a drug addiction exhibit behaviors that include being unable to control their drug use, compulsive drug use, continued drug use despite harm, and urges and cravings for the drug (Ling, Wesson, and Smith 2005).

**Physical dependence** refers to neurobiological adaptation to the opioid drug from chronic exposure manifested by tolerance and withdrawal. A very important point is that physical dependence is not the same as addiction. Many patients who take a prescribed opioid for pain for an extended period will need more medication over time to relieve pain, an example of tolerance, and have opioid withdrawal symptoms if they stop abruptly, which is evidence that the body has acclimated to the constant presence of the drug. However, although many of these patients may experience

some degree of drug withdrawal (also referred to as the *discontinuation syndrome*), most will not experience the overwhelming urge to recapture the drug effect and the intense drive to continue or increase the use of the drug, as is seen with addiction (Ling, Wesson, and Smith 2005).

The most widely used term to describe addiction to a prescription painkiller is **opioid dependence**. *Opioid dependence* is defined as an abnormal pattern of opiate use that leads to consequences or distress in the patient, as manifested in three or more of the following (APA 2000; Miller and Greenfield 2004):

- tolerance (the need to increase the dose to achieve the desired effect)
- withdrawal symptoms when use stops or abruptly declines
- loss of control
- persistent desire or unsuccessful attempts to cut down or control the opiate use
- preoccupation with obtaining opiate medications (such as multiple doctors, trips to the emergency department)
- important social, occupational, or recreational activities that are abandoned or reduced because of the opiate use
- continued opioid use despite awareness of adverse physical or psychological problems caused or worsened by opioids

In other words, the term *dependence* is used to describe two separate phenomena: (1) The *pharmacological* definition of drug dependence is characterized by development of tolerance and a withdrawal syndrome from prolonged use, and (2) the *psychiatric* definition of drug dependence, which is equivalent to the term drug addiction, is characterized by compulsive use, inability to reduce use, preoccupation and drug-seeking behaviors, and a heightened vulnerability to relapse after abstinence (Schwartz 1998).

**Pseudo-addiction** describes drug-seeking behaviors in pain patients that result from inadequate pain relief, and manifest as preoccupation with and pursuit of opioid medication for pain relief, not for the drug's pleasurable effects. Pseudo-addiction develops in three phases: initially,

the patient receives an inadequate level of pain relief (*analgesia*), which leads to the escalation of demands for painkillers and changes in behavior. This may be exaggerated to convince others of the pain severity and the need for more medication, which results in a crisis of mistrust between the patient and the health care team. Pseudo-addiction is preventable when the patient report of pain is accepted as valid (Ling, Wesson, and Smith 2005). The DEA recently acknowledged pseudo-addiction, in a pamphlet addressed to doctors, pharmacists, and regulators about the appropriate use of narcotics, by stating that some patients exhibiting addict-like behavior may simply be desperate for pain relief. It notes that “drug-seeking behaviors” such as visits to several doctors, requests for specific narcotics, demands for more medication, and unilateral dose escalation “cannot immediately be ascribed to addiction” and may instead be due to unrelieved pain (Sullum 2004). No single aberrant behavior can determine whether one is drug seeking secondary to pain or due to addiction. Table 1.2 provides a summary of these terms and their definitions.

Opioids are the first choice of painkiller for the relief of acute pain. They are very effective in managing moderate to severe pain, which other medications are not strong enough to handle. Opioids are also the most likely choice for treatment of *chronic pain*, defined as “pain that persists beyond the usual course of an acute disease or a reasonable time for any injury to heal that is associated with chronic pathologic processes that cause continuous pain or pain at intervals for months or years,” “persistent pain that is not amenable to routine pain control methods,” and “pain where healing may never occur” (Manchikanti 2006). By most definitions, chronic pain lasts at least six months. Unfortunately, medical research has not adequately proven the best treatments for chronic pain. Studies have shown significant problems with the long-term use of opioids for treatment of chronic pain (Eriksen et al. 2006).

There can be considerable overlap between the overt behavior of the person using prescription opioids and the underlying cause of that behavior. A person abusing prescription opioids daily for extended periods and a person in chronic pain taking the same opioid daily for an extended period may both become physically dependent on the opioid and experience withdrawal if they abruptly stop taking the drug. This is a physiologic

Table 1.2

**Definition of Terms Related to Prescription Opioid Use, Misuse, and Dependence**

Term	Definition
Addiction/substance dependence	Substance abuse involving loss of control and compulsive use of a drug despite harm
Chemical coping	Reliance on a drug for psychological stability
Diversion	Redirection of a prescription drug from its lawful purpose to illicit use; can be done with criminal intent
Misuse	Inappropriate use of a drug, whether deliberate or unintentional
Physical dependence	Condition in which ongoing use of a drug causes increased tolerance and abrupt termination causes a withdrawal syndrome
Pseudo-addiction	Condition characterized by behaviors, such as drug hoarding or demand for painkillers, that outwardly mimic addiction but is actually driven by a desire for pain relief due to undertreated pain
Self-medication	Use of a drug without consulting a health care professional to alleviate stress, depression, or anxiety
Substance abuse	Maladaptive pattern of substance use leading to considerable impairment or distress
Tolerance	Phenomenon in which pain relief or other effects of the opioid drug decrease as the body grows accustomed to a given dosage of a drug

(Passik 2009)

response to the chronic use of the medication, just as suddenly stopping a blood pressure medicine can cause hypertension, heart attack, or stroke (Lessenger and Feinberg 2008). Likewise, both an opioid abuser and a person with chronic pain that is not sufficiently treated may doctor-shop, attempt to pressure a physician into prescribing opioids (or a higher dose of an opioid), and appear to be drug seeking. Another unfortunate scenario involves a person with a history of addiction, or a person in recovery from addiction, who is experiencing significant pain and is unable to obtain appropriate medication and adequate pain relief because of a physician's fear of triggering a relapse or of being sued. If the patient's pain is under-treated, a syndrome of pseudo-addiction may occur, in which the person engages in drug-seeking behavior simply to obtain a therapeutic and effective dosage level of a pain reliever (Lessenger and Feinberg 2008). Many people in recovery from addiction describe requiring higher-than-normal levels of opioid pain medication to receive pain relief. This has not been confirmed by medical research, but altered opioid receptors could account for this form of lasting tolerance.

### Mortality

In recent years, the dramatic increases in the nonmedical use of prescribed opioids have been followed by equally dramatic rises in morbidity and mortality from prescription opioids, especially in accidental overdoses and death (Streltzer, Ziegler, and Johnson 2009).

Deaths involving the use of prescription painkillers increased substantially from 2001 through 2005. The number of accidental deaths in the United States involving prescription opioids increased 114%, from approximately 3,994 in 2001 to 8,541 in 2005. Unintentional overdose deaths in which methadone was mentioned increased 220% in this time frame, from 1,158 in 2001 to 3,701 in 2005. This was primarily due to methadone used for the treatment of pain, not for maintenance treatment of heroin addiction. Also, the number of accidental deaths from prescription opioids surpassed the number of accidental deaths from cocaine and heroin throughout this period (NDIC 2009).

Six states (Maine, New Hampshire, Vermont, Maryland, Utah, and New Mexico) participate in the mortality component of the Drug Abuse Warning Network (DAWN). Among these states, the death rates from opioid-related drug misuse in 2003 ranged from 7.2 per 100,000 population in New Hampshire to 11.6 per 100,000 population in New Mexico. In all six of these states, most deaths related to opioid abuse involved multiple drugs. In five of the six states, adults age 35 to 54 had the highest rates of opioid misuse deaths. In the remaining state (Maine), the highest rate was for adults age 21 to 34 (SAMHSA 2006b).

Fatalities associated with prescription opioid use are strongly linked to the simultaneous use of multiple substances. An examination of 2,024 opiate-related deaths in England examined the factors associated with the deaths of both non-addicts and addicts in the group. The non-addicts tended to be older than 45 and died as a result of intentional overdose, while the addicts tended to be young males and victims of accidental overdose. In 93% of the deaths, opioids were used in combination with another substance. Among the non-addicts, alcohol was used most often in accidental deaths and antidepressants were typically used in the intentional deaths. Likewise, illicit drugs and hypnotics/sedatives were typically reported in the accidental deaths among the addicts (Schifano et al. 2006).

A national epidemic of drug-related deaths in the United States began in the 1990s, coinciding with the increased prescribing of opioid painkillers. National figures from the Centers for Disease Control and prescription painkiller sales data from the DEA found that unintentional drug overdose mortality rates increased an average of 5.3% per year from 1979 to 1990, and 18.1% per year from 1990 to 2002. The rapid increase during the 1990s reflects the rising number of deaths attributed to opioids and unspecified drugs. Between 1999 and 2002, the number of prescription opioid overdoses, or poisonings, that were indicated on death certificates increased by 91.2%, while heroin and cocaine poisonings increased 12.4% and 22.8%, respectively. By 2002, prescription opioid poisoning was listed in 5,528 deaths—more than either heroin or cocaine. The increase in deaths generally matched the increase in sales for each type of prescription opioid, and the increase in deaths involving methadone paralleled the

increase in methadone used as a painkiller rather than methadone used in narcotic treatment programs (Paulozzi, Budnitz, and Xi 2006).

Some regions of the United States have been especially hard hit by the increase in prescription opioid-related overdose deaths. In rural Virginia, drug overdose deaths increased 300% from 1997 to 2003, with 58% of these deaths due to the use of multiple drugs. Prescription opioids (74.0%), antidepressants (49.0%), and benzodiazepines (39.3%) were found more often among the deceased than illicit drugs. Two-thirds of the deceased were 35 to 54 years old and 37% were female (Wunsch et al. 2009).

### **Methadone-related Mortality**

Methadone is a safe and effective drug when it is properly used for pain or as treatment for opioid addiction, but it can be deadly when it is prescribed by those unfamiliar with its use, or is misused or abused, particularly when taken with other prescription drugs, street drugs, or alcohol. Although much concern has been raised over methadone clinics being the primary source of abused methadone, most methadone-related deaths involve the abuse or misuse of methadone originating from hospitals, pharmacies, practitioners, and pain management physicians. From 1999 to 2005, the number of methadone-related deaths increased more than fivefold, from 786 to 4,462, a rate higher than overdose deaths associated with other prescription opioids such as oxycodone, hydrocodone, and fentanyl (U.S. General Accounting Office [USGAO] 2009). By comparison, deaths associated with other prescription opioids such as oxycodone, morphine, hydromorphone, and hydrocodone increased 90% from 1999 to 2004 (table 1.3) (NDIC 2007).

In 2004, the Substance Abuse and Mental Health Services Administration (SAMHSA) performed a national assessment to help understand the causes of this increase in methadone-related deaths. The report concluded that most deaths involved one of three scenarios:

- the accumulation of toxic levels of methadone during the initiation phase of methadone maintenance treatment, or from methadone prescribed for pain management that was due to a combination of overestimating the ability of the patient to tolerate methadone and methadone's long and variable half-life
- the misuse of diverted methadone by individuals with little or

Table 1.3

**Deaths Associated with Methadone versus  
Other Opioids, 1999–2004**

Year	Methadone	Other prescription opioids
1999	786	2,757
2000	988	2,932
2001	1,456	3,484
2002	2,360	4,431
2003	2,974	4,877
2004	3,849	5,242
<b>Change from 1999 to 2004</b>	390%	90%

*(NDIC 2007)*

no opioid tolerance who may have taken excessive doses in an attempt to achieve euphoria

- the additive or synergistic effects of methadone in combination with other central nervous system depressants (alcohol, benzodiazepines, or other prescription opioids) among individuals with little or no tolerance to opiates

Medwatch, the Food and Drug Administration's safety information and adverse event reporting program, reported that seizures of methadone tablets (prescribed to treat pain) increased 133% between 2001 and 2002, in contrast to seizures of liquid methadone (dispensed to treat opioid addiction), which increased 11% during the same period (Center for



Substance Abuse Treatment [CSAT] 2004b). From 1994 to 2001, DAWN reported substantial increases in drug-related emergency department visits for several prescription painkillers, including 352% for oxycodone, 230% for methadone, and 131% for hydrocodone (SAMHSA 2004; Manchikanti 2006).

Methadone is more likely to cause overdose because of the slow rate at which it is broken down in the body. This can contribute to increased blood levels, increased toxicity, and respiratory depression, which can cause death. Methadone prescriptions for pain management grew from about 531,000 in 1998 to about 4.1 million in 2006, an increase of almost 700% (USGAO 2009), and since the late 1990s, methadone has been increasingly prescribed by practitioners to treat pain. It is a relatively inexpensive, long-lasting pain medication, therefore very useful. Using methadone to treat pain is very different from using it to treat opioid addiction. While a single dose of methadone suppresses opioid withdrawal symptoms for a day or more, it generally relieves pain for only four to eight hours despite remaining in the body much longer. It may also take three to five days to achieve full pain relief, so dosage increases must be done more slowly than with other opioids. As a result, patients may take too much methadone before the previous dose has left the body. However, if taken too often, in too high a dose, or with certain other medicines or supplements, it may build up in the body to a toxic level. Variability in methadone's absorption, metabolism, and relative pain-relief potency among patients requires a highly individualized approach to prescribing by an experienced physician (USGAO 2009).

From 2002 to 2007, the distribution of methadone to businesses associated with pain management such as pharmacies and practitioners almost tripled, increasing from about 2.3 millions grams to about 6.5 million grams. In contrast, distribution to methadone clinics increased more slowly, from about 5.3 million grams to about 6.5 million grams (USGAO 2009). Although the distribution of methadone for pain management is largely responsible for the increases in methadone-related deaths, methadone clinics do contribute to a fair amount of diversion and a significant proportion of the deaths. Perhaps the biggest reason underlying these increases in deaths among methadone clinic patients has to do with methadone clinics offering methadone maintenance therapy to anyone who meets a

loose criteria of opioid dependence. In this respect, many of the patients are very different from the traditional methadone clinic patient who has a history of chronic heroin addiction and a correspondingly high tolerance to opioid drugs. Methadone clinics usually escalate the dose of methadone during the induction phase of therapy, and the majority of the rare methadone clinic-associated fatalities occur during this induction phase of treatment. Methadone clinic personnel may overestimate the degree of opioid tolerance in the patient, or a patient may use other opioids or CNS depressant drugs in addition to the prescribed methadone (CSAT 2004b; Manchikanti 2006). Table 1.4 summarizes the increases in the legitimate distribution of methadone from 2001 to 2006.

Table 1.4

## Legitimate Methadone Distribution, in Grams, 2001–2006

Year	Practitioners	Pharmacists	Hospitals
2001	6,250	1,660,432	225,368
2002	10,381	2,328,287	310,027
2003	15,113	3,274,059	393,957
2004	35,466	4,228,660	466,028
2005	43,199	4,810,467	509,138
2006	51,046	5,986,488	584,144
<b>Change from 2001 to 2006</b>	715%	261%	159%

(NDIC 2007)



## The History of Opioids

**T**he current epidemic in nonmedical use of prescription opioids is actually part of a recurring pattern, and we can learn valuable lessons by studying the history of these drugs. The extensive consumption of opioids, including morphine and heroin, as well as the massive consumption of cocaine, which occurred before World War I, are now all but forgotten. We assume that recent epidemics—heroin in the 1960s and 1970s, cocaine in the 1980s, or prescription painkillers today—are new phenomena. The history of attempts at legislative control in the United States, and their successes and failures, suggests that devising and implementing a rational approach for the current problem is more likely to occur if we consider these earlier efforts at narcotic regulation (Musto 1999).

### Opioid Use throughout History

Opium is derived from the juices of the poppy plant *Papaver somniferum*. The word *opium* comes from *opos*, the Greek word for *juice*. Opioid is used as an umbrella term for all the natural and synthetic (humanmade) medicines that are derived from or based on opium. Opiate, a more commonly used term, applies only to those medicines that specifically use opium or thebaine, the natural products of the opium poppy—they are the

“natural” opioids. The natural medications and the synthetics act the same way in the brain.

The medicinal and recreational use of opium dates back to antiquity. Evidence of poppy plant use from preserved remains of cultivated poppy seeds and pods dates back to the fourth millennium BCE (Booth 1996). The Sumerians (4000 BCE) and the Egyptians (2000 BCE) knew of the pain-relieving and euphoric effects of the poppy plant (Rehman 2001). Opium was proposed as a remedy for numerous ailments in the Ebers papyrus, an ancient Egyptian medical document, dating from about 1550 BCE. The recreational use of opium in ancient central Asia was mentioned by the Greek historian Herodotus in the fifth century BCE, when he observed that the Massagets (a people who inhabited the northern coast of the Caspian Sea) inhaled the smoke from burnt poppy heads to induce euphoria (Ulyankina 1987; Smith 2008).

In 1732, British physician Thomas Dover developed “Dover’s Powder,” a formula that combined opium with ipecacuanha (known today as ipecac), which induces vomiting. The result was a pain-reducing potion that could cause euphoria but could not be ingested in large quantities because of its emetic properties. It was taken as a nonprescription medicine for more than 200 years and was also prescribed by physicians until the early 1900s when its addictive properties were realized (Boyes 1931).

The publication of Thomas de Quincey’s *Confessions of an English Opium-Eater* (1821–1822) brought the addictive potential of opioids (which was already known) into the spotlight (Smith 2008).

### **Enter Morphine**

Drugs have been used for millennia in their natural form. Coca leaves and poppy plants were chewed, dissolved in alcoholic beverages, or taken in some way that diluted the impact of the active agent (Musto 1991). Advances in chemistry in the nineteenth century spawned the modern pharmaceutical industry, and this industry quickly turned its attention to the old botanical products already in wide use. These agents were reprocessed and made more widely available in highly refined and far more potent forms—among them morphine and heroin (refined from opium poppies) and cocaine (from coca leaves) (Drucker 2000).

## ABOUT THE AUTHORS

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Marvin Seppala is chief medical officer at Hazelden, and serves as adjunct assistant professor at the Hazelden Graduate School of Addiction Studies. His responsibilities include overseeing all interdisciplinary clinical practices at Hazelden, maintaining and improving standards for evidence-based practices, and supporting growth strategies for Hazelden's residential and nonresidential addiction treatment programs and services throughout the country.

Dr. Seppala attended St. Olaf College in Northfield, Minnesota, and is a graduate of Drake University in Des Moines, Iowa. He obtained his M.D. at Mayo Medical School in Rochester, Minnesota, serving his residency in psychiatry and a fellowship in addiction at University of Minnesota Hospitals in Minneapolis.

Dr. Seppala is the author of *Clinician's Guide to the Twelve Step Principles* and coauthor of *When Painkillers Become Dangerous* and *Pain-Free Living for Drug-Free People*.

Dr. Seppala served as a board member of the American Society of Addiction Medicine (ASAM) for several years and is a national expert on addiction treatment. He has appeared as a guest on the CBS-TV "Early Show" and on National Public Radio. He has been quoted in the *New York Times*, the *Washington Post*, *USA Today*, *Newsweek*, and the *Wall Street Journal*.

### **Mark E. Rose**

Mark Rose has been extensively involved in the field of addiction for more than fifteen years as a licensed psychologist, researcher, and owner of a biomedical communications business. He has authored scientific papers published in peer-reviewed psychiatry and addiction journals, written continuing education courses on addiction for physician audiences, testified in criminal trials as a court-validated expert in addiction, conducted research studies investigating processes related to addiction and recovery, and performed numerous psychological evaluations of criminal defendants and disability claimants when substance use was an issue.

**Hazelden**, a national nonprofit organization founded in 1949, helps people reclaim their lives from the disease of addiction. Built on decades of knowledge and experience, Hazelden offers a comprehensive approach to addiction that addresses the full range of patient, family, and professional needs, including treatment and continuing care for youth and adults, research, higher learning, public education and advocacy, and publishing.

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*Prescription Painkillers* offers current, comprehensive information on the history, social impact, pharmacology, and addiction treatment for commonly abused, highly addictive opioid prescription painkillers.

Marvin D. Seppala, M.D., provides context for understanding the current drug abuse problem by tracing the history of opioids and the varying patterns of use over time. He then offers an in-depth study of controversial issues surrounding these readily available drugs, including over-prescription by physicians and adolescent abuse. Also included is a straightforward look at the leading treatment protocols based on current research.



**Marvin D. Seppala, M.D.**, chief medical officer at Hazelden, is the author of *Clinician's Guide to the Twelve Step Principles* and coauthor of *When Painkillers Become Dangerous* and *Pain-Free Living for Drug-Free People*. He is a board member of the American Society of Addiction Medicine.

Written for professionals and serious lay readers by nationally recognized experts, the books in the **Library of Addictive Drugs** series feature in-depth, comprehensive, and up-to-date information on the most commonly abused mood-altering substances. Other titles include *Methamphetamine*, *Heroin*, and *Alcohol*.

Cover design: Theresa Jaeger Gedig

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