

Heroin Dependence

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ABSTRACT

Heroin use, particularly injection use, is a problem of great public health importance. The risks associated with heroin dependence, such as HIV and viral hepatitis, and the social costs due to associated crime and poverty exceed those of most other drugs of abuse. Increasing purity and decreasing cost of heroin likely contribute to trends of decreasing age at first use and an increasing rate of initiation into regular use in the United States. Effective treatment is available for heroin dependence, so primary care providers should screen patients for this disorder. This article reviews the epidemiology of heroin use and dependence in the United States and outlines what is known regarding risk factors for initiation of heroin use and for heroin dependence.

INTRODUCTION

Heroin, originally developed by the Bayer Pharmaceutical Company as a cough suppressant in 1895, is derived from the opium poppy, placing it in the class of chemicals known as opiates.¹ Opiates have been used for centuries for their pain relieving and euphorogenic properties. (Other modern opioids include morphine, oxycodone, hydrocodone, codeine, hydromorphone, and methadone.) Although they possess several beneficial properties, including vasodilatory action and unmatched analgesic effectiveness, the positive reinforcing (euphorogenic) properties of opiates, particularly heroin, create the potential for addiction (and/or dependence). In fact, 53% of individuals who have ever used heroin become dependent, as opposed to 11% of alcohol users and 15% of marijuana users.²

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What is Dependence (or Addiction)?

Opioid dependence is a chronic relapsing condition characterized by compulsive self-administration of opioids despite adverse consequences. The most widely cited sets of criteria for a diagnosis of opioid dependence come from The World Health Organization's *ICD-10, Classification of Mental and Behavioral Disorders*³ and the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)*.⁴ The ICD-10 defines a dependence syndrome as "a cluster of physiological, behavioral, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviors that once had greater value." According to the ICD-10, drug dependence manifests in compulsive substance use despite evidence of harm due to use, the presence of characteristic withdrawal phenomena upon discontinuation or drastic reduction of use, development of tolerance to the effects of the substance, and dysfunction in other life areas due to use and/or preoccupation with use. DSM-IV criteria differ slightly and are outlined in Table 1.

The term "addiction" is often used among specialists in addiction medicine to refer to the syndrome involving the combination of physical and psychological dependence, as defined in the DSM-IV. The term "addiction," however, is not explicitly used in the DSM-IV or ICD-10.

The Impact of Heroin Dependence

Heroin use, particularly injection use, is a problem of major public health importance. The risks associated with heroin dependence, such as HIV and viral hepatitis, and the social costs due to associated crime and poverty exceed those of most other drugs.⁵ Though more difficult to measure objectively, familial dysfunction and disruption are also significant consequences of heroin dependence. Children of opiate dependent parents appear to be at increased risk of certain forms of psychopathology (particularly attention deficit disorders, anxiety, and depression) and future substance use disorders.⁶

Survey data from the Substance Abuse and Mental Health Services Administration indicate that heroin use and dependence are on the rise. During the latter half of the 1990s, the annual number of heroin initiates rose to a level not reached since the late 1970s. In 1974, there were an estimated 246,000 heroin initiates. Between 1988 and 1994, the annual number of new users ranged from 28,000 to 80,000. Between 1995 and 2001, the number of new heroin users was consistently greater than 100,000.³ The increased purity and reduced cost of heroin in recent years is thought to contribute to this overall increase in use. From the late 1980s to the late 1990s heroin purity increased from 10% to between 40% and 60% while cost decreased by two-thirds. (Purity has increased to a greater degree and cost decreased to a greater degree on the US East Coast, where South American sources predominate, as opposed to the West Coast, where Mexican heroin is more commonplace.)⁷ Individuals who might have previously been intimidated by the need to inject heroin to experience euphoria are now able to smoke (“chase the dragon”) or use it intranasally to achieve desired effects. In addition, increased purity and decreased cost likely contribute to the decreasing age of initiation into heroin use from a mean of 27 years in 1988 to a mean of 19 years in 1995.⁸

Heroin dependence exacts significant costs to society via medical care, crime, social welfare, and lost productivity. The estimated cost of heroin addiction in the United States was \$21.9 billion in 1996. Of these costs, productivity losses accounted for approximately \$11.5 billion (53%), criminal activities \$5.2 billion (24%), medical care \$5 billion (23%), and social welfare \$0.1 billion (0.5%).⁵

Heroin users have a death rate 13-17 times that of their age-matched peers, and a 14-fold risk of suicide.⁹⁻¹² Between 10% and 35% of deaths in heroin-dependent individuals are due to suicide.¹² Overdose and suicide result in a significant loss of life years, as these deaths typically occur during the 3rd and 4th decades of life.^{10,11}

Etiology of Opiate Dependence

Existing literature supports a complex etiology for drug dependence with genetic,¹³⁻¹⁶ physiologic/neurochemical,¹⁷⁻²⁰ psychological,²¹⁻²⁴ and social²⁵⁻²⁷ contributing factors. A final common biological pathway in opiate dependence appears to be the upregulation of cyclic AMP at the level of individual neurons in the central nervous system, particularly in the region known as the locus caeruleus. This occurs as an adaptation to chronic inhibition of cyclic AMP by opiates. This phenomenon likely at least partially explains the

Table 1. DSM-IV¹ Criteria for Opiate Dependence

A maladaptive pattern of use, leading to clinically significant impairment or distress, as manifested by 3 (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:
 - a. need for markedly increased amounts of opiate to achieve intoxication or desired effect
 - b. markedly diminished effect with continued use of the same amount of opiate
2. Withdrawal, as manifested by either of the following:
 - a. the characteristic withdrawal syndrome for opiates (3 of: dysphoric mood, nausea or vomiting, muscle aches, lacrimation or rhinorrhea, diarrhea, yawning, fever, insomnia, gooseflesh, sweating)
 - b. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3. Opiates taken in larger amounts over a longer time period than intended
4. Persistent desire or unsuccessful attempts to cut down or control opiate use
5. Great deal of time spent in activities necessary to obtain or use opiates or to recover from their effects
6. Important social, occupational, or recreational activities are given up or reduced because of opiate use
7. Opiate use continues despite knowledge of having a persistent or recurrent physical or psychological problem that is likely caused or exacerbated by opiates

phenomena of tolerance and withdrawal (see Table 1) occurring with the long-term use of opiates.²⁸

DESCRIPTIVE EPIDEMIOLOGY

Obtaining accurate estimates of the prevalence of heroin dependence is difficult. Given an estimated prevalence of approximately 1%, very large samples would need to be surveyed to obtain adequate information for analysis. In existing surveys, the stigma attached to illicit drug use likely leads to underestimation of prevalence due to concealment.²⁹ Additionally, populations at particular risk for opiate dependence (homeless and institutionalized populations) are underrepresented in household surveys. Finally, heroin use and addiction is often concentrated within relatively circumscribed groups or areas, and, thus, is not detectable in aggregated data covering the general population. However, given the strong association between any heroin use and the development of dependence, estimates of heroin use provide important information regarding populations at risk for future dependence and the need for addiction treatment.³⁰

There are an estimated 800,000-1 million opiate-dependent individuals in the United States.^{4,31-33} Increasing purity of the heroin supply has led to an increase in intranasal (snorting) and smoking over inject-

Table 2. Characteristics of Major Epidemiologic Studies of Heroin Dependence

| Study | Year Examined | Method | Population | N |
|-----------------------------|---------------|---|---|---------|
| NSDUH | 1999 | Computer-assisted interview | Independent multi-stage area probability sample of US households | 68,126 |
| DAWN | 1999 | Passive surveillance | Patients of emergency departments in 21 US metropolitan areas | 554,570 |
| MTF | 1999 | Self-administered questionnaire in random samples of classrooms established through 3-stage (geographic area, school, classroom) stratification process | US 8th, 10th, and 12th graders | 43,700 |
| Dorus & Senay ³⁸ | 1980 | Interview and questionnaires | Opioid-dependent individuals entering 1 of 30 Chicago treatment centers | 432 |

NSDUH = National Survey on Drug Use and Health (formerly National Household Survey on Drug Abuse); DAWN = Drug Abuse Warning Network; MTF = Monitoring the Future Study

tion use, since, with heroin of higher purity, these routes of use yield highly euphoric effects not possible with the less pure heroin supplies of the past. This has likely directly affected the demographic characteristics of the heroin using and dependent population. Individuals previously intimidated by the injection route of drug use may be willing to attempt smoking or intranasal use. This is thought to have made heroin use less intimidating to adolescents and to have contributed to the increase in heroin use and a younger heroin-using population in the United States in recent years.³⁴⁻³⁶ However, 37% of new heroin users have injected.^{32,37}

Three major data sources exist for estimates of the prevalence of heroin use in the United States: the National Household Survey on Drug Abuse (NHSDA),³² the Monitoring the Future Study (MTF),³⁸ and the Drug Abuse Warning Network (DAWN).³⁷ The populations studied and methods used vary significantly between these databases. The characteristics of these surveys and an additional study on demographics of heroin users in a Chicago treatment program and 1 United Kingdom study are presented in Table 2. The demographic characteristics of the populations surveyed in these studies are presented in Table 3.

The NHSDA, through face-to-face surveys of randomly selected households in all 50 states, reports on the use of illicit drugs by individuals age 12 and older. The lifetime prevalence (at least 1 use in a person's lifetime) for heroin for those age 12 and older was 1.4%. The NHSDA also found a higher rate of heroin dependence in urban areas (particularly in New York where the prevalence is 2500-3000 per 100,000) and in the Northeast and on the West Coast.

According to the 1999 MTF, a national survey involving randomly selected US classrooms of 8th, 10th, and 12th graders, rates of heroin use remained relatively stable from the late 1970s through the early 1990s. After 1991, however, use began to rise among 10th and 12th graders, and after 1993, among 8th graders. In 1999, prevalence of heroin use was comparable for all 3 grade levels. Past year prevalence rates for heroin use in 1999 were about 2 to 3 times higher than those reported in 1991.

DAWN presents data regarding drug-related emergency room visits to emergency departments in 21 US metropolitan areas. Rates of emergency department visits precipitated by heroin use remained statistically stable from 2000 to 2002 at 36 per 100,000 population (93,519 ER visits, or 14% of drug-related ER visits) in the 21 metropolitan areas included in the surveillance. However, mentions of heroin use in ER visit records, where the ER visit was not directly due to heroin use, have increased by 35% since 1995. The highest rates of heroin use mentions per 100,000 population occur in the 25-34 year old age range, and occur for men 2 to 4 times as frequently as women.³⁷

Of patients entering treatment for heroin dependence in 1998, 50% were non-Hispanic white, 25% were Hispanic, and 22% were non-Hispanic black. Van Etten and Anthony³⁹ also found strong associations between black or Hispanic ethnicity and rates of heroin dependence.

Hickman et al³⁰ and Dorus et al⁴⁰ found similar demographic risk factors with male heroin users outnumbering female users by 2:1, young adulthood (early to late 20s) being the age of greatest representation, and with black ethnicity being disproportionately represented.

Table 3. Demographic Characteristics of Study Samples in Major Epidemiologic Studies of Heroin Dependence

| Study | Year | N | Gender | | Age Range | Race | | | | | |
|---------------|------|---------|---------|---------|-----------|---------|---------|-----|-------|--------|--------|
| | | | M | F | | W | AA | NA | As | H | O |
| NHSDA | 1999 | 68,126 | 32,092 | 34,614 | 12 | 46,054 | 7,982 | 739 | 2,146 | 8,481 | 1,072 |
| DAWN | 1999 | 554,570 | 291,943 | 257,860 | 6 | 309,910 | 132,900 | NR | NR | 56,783 | 54,977 |
| MTF | 1999 | 43,700 | 6,410* | 6,901* | 13-19 | 9,180** | 1,793** | NR | NR | NR | 745** |
| Dorus & Senay | 1980 | 432 | 289 | 143 | 18 | 155 | 277** | NR | NR | NR | NR |

NSDUH = National Survey on Drug Use and Health (formerly National Household Survey on Drug Abuse); DAWN = Drug Abuse Warning Network; MTF = Monitoring the Future Study

W = White; AA = African American; NA = Native American; As = Asian; H = Hispanic; O = multi-racial or unknown; NR = not reported

*Demographic characteristics readily available only for subjects in 12th grade.

**The only racial groups reported in Dorus & Senay were "white" and "black." Which ethnicities are included in these categories is unclear. Similarly, in MTF, subjects were restricted to "white, black, or Hispanic" ethnic categories.

The limitations of available data make inference regarding a general estimate of the prevalence of heroin dependence in the United States difficult. However, certain statements are supported by the available literature. Male gender and young adult age range (26-34 years) appear to be primary demographic risk factors for heroin dependence. Black and Hispanic ethnic groups are also disproportionately represented. Urban living area is also strongly associated with prevalence of heroin dependence. Examination of other risk factors lends further insight into the multifaceted etiology of heroin dependence.

RISK FACTORS

Many social, behavioral, and psychological factors are strongly associated with heroin dependence. Indicators of a low socioeconomic status (SES) have consistently been associated with heroin use and dependence.^{27,35,36,41} Investigations have included measurements of individual income and occupation as well as neighborhood-level indicators of SES. Unskilled occupation,⁴² as opposed to business or professional occupation, and unemployed versus employed status^{30,32,43-45} are strongly predictive of heroin use and dependence. Using multiple regression modeling, Latkin et al⁴¹ found associations between individual heroin dependence and neighborhood indicators such as percent of households with income <50% of poverty (odds ratio 1.37), percent of males unemployed (odds ratio 2.34), and percent of houses that were boarded up in the community (odds ratio 5.88).

Educational status is also a strong predictor of heroin use and dependence.^{46,47} In one study of heroin users seeking treatment, 62% had less than a 12th grade education, a rate far in excess of the general population.³³

More complicated social factors have also been

found to be significantly associated with heroin use and dependence. Continued social contact with illicit drug users is predictive of ongoing heroin use,⁴⁴ as is parental absence during childhood.⁴⁷ Immediate social contact with active heroin users is more strongly associated with ongoing heroin use than is the prevalence of heroin use in an individual's neighborhood of residence.⁴⁴ The presence of a specific spiritual or religious practice during childhood may be protective, even in families with parents who use heroin.⁴⁸

Children of parents with opiate dependence are at increased risk of other major psychopathology (particularly attention and anxiety disorders and depression), as well as decreased academic, family, and social functioning.⁶ Childhood psychopathology (primarily attention disorders, anxiety, and depression) has also been associated with the later development of substance use disorders, including opiate dependence.⁴⁹

Suicide risk is increased among individuals with opiate dependence. The presence of other psychopathology or a history of childhood abuse increases this risk.⁵⁰

TREATMENT

Methadone maintenance is the most widespread and extensively researched treatment for opioid addiction. Methadone maintenance has been shown to reduce the frequency of opiate use,⁵¹⁻⁵⁴ reduce mortality,^{51,55-57} reduce the transmission of HIV^{53,58,59} and viral hepatitis,⁶⁰ improve employment status,^{57,61} and reduce the frequency of criminal behavior.⁶²⁻⁶⁴ Many of these positive effects are strongly associated with higher daily methadone dose and with increasing duration of treatment.⁶⁵⁻⁶⁸ Current US federal and state policies, however, restrict the supervision of this modality to federally licensed methadone treatment facilities.

Buprenorphine, a Drug Enforcement Agency

Schedule III partial opioid agonist, provides another option for the detoxification or maintenance of opioid-dependent individuals. With the appropriate training (certification in addiction medicine or addiction psychiatry, or an 8-hour training course for those not specializing in addiction medicine), physicians may prescribe buprenorphine in the outpatient clinic setting. Buprenorphine has been shown to reduce opioid use,⁶⁹⁻⁷² reduce craving for opioids,⁶⁹ and to lead to greater retention in addiction treatment.^{71,73,74}

SUMMARY

The social characteristics of populations at highest risk for heroin dependence often make detailed study difficult. Populations commonly neglected in large studies include the homeless and the institutionalized. Studies of individuals already engaged in substance abuse treatment, though providing greater power for detecting trends of significance, may not provide the basis for extrapolation to the general population of heroin addicts. Prospective study of at-risk populations would allow for a greater ability to detect significant correlates of future heroin use and dependence, and is an important area for future epidemiological research.

Current literature, though limited somewhat by these considerations, directs health care providers and communities to screen and monitor young men particularly. Available information also indicates that groups at increased risk include certain minority groups (particularly blacks and Hispanics), individuals of lower SES (50% or less of poverty), individuals living in neighborhoods of low mean SES, individuals with lower educational attainment (9th grade or lower, in particular), individuals living in urban centers (particularly New York), and children and adolescents with a history of psychopathology (particularly attention deficit disorders, anxiety, and depression). Families and health care providers should also be concerned when the academic performance of an adolescent (particularly a male age 12-17) drops sharply.

Targeting these populations for further study and intervention will allow for more accurate estimations of the prevalence of heroin use and dependence, and more precise knowledge regarding significant risk factors for the development of heroin addiction.

REFERENCES

1. The ICD-10 Classification of Mental and Behavioral Disorders. Clinical Descriptions and Diagnostic Guidelines. Geneva: World Health Organization; 1992.
2. Diagnostic and Statistical Manual of Mental Disorders. 4 ed. Washington, D.C.: American Psychiatric Association; 1994.
3. Available at <http://www.pbs.org/wgbh/pages/frontline/shows/heroin/etc/history.html>. Accessed June 2, 2004.
4. Results from the 2002 National Survey on Drug Use and Health: National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2002. Publication SMA 03-3836.
5. Mark TL, Woody GE, Juday T, Kleber HD. The economic costs of heroin addiction in the United States. *Drug Alcohol Depend.* 2001;61(2):195-206.
6. Wilens T, Biederman J, Bredin E, et al. A family study of the high-risk children of opioid- and alcohol-dependent parents. *Am J Addict.* 2002;11:41-51.
7. 2001 Domestic Monitor Program. Washington D.C.: Office of Strategic Intelligence, Drug Enforcement Agency; 2002. Publication DEA-03023.
8. Substance Abuse Report [Newsletter] 1997;23(2):2.
9. Hickman M, Carnwath Z, Madden P, et al. Drug-Related Mortality and Fatal Overdose Risk: Pilot Cohort Study of Heroin Users Recruited From Specialist Drug Treatment Sites in London. *J Urban Health.* 2003;80(2):274-287.
10. Sporer KA. Acute heroin overdose. *Ann Intern Med.* 1999;130(7):584-590.
11. Lind J, Oyefeso A, Pollard M, Baldacchino A, Ghodse H. Death rate from use of ecstasy or heroin.[comment]. *Lancet.* 1999;354(9196):2167.
12. Darke S, Ross J. Suicide among heroin users: rates, risk factors and methods. *Addiction.* 2002;97(11):1383-1394.
13. Croughan J. The contributions of family studies to understanding drug abuse. In: LN R, editor. *Studying Drug Abuse*. New Brunswick, NJ: Rutgers University Press; 1985:240-264.
14. Mirin S, Weiss R, Sollogub A, Michael J. Psychopathology in families of drug abusers. In: SM M, editor. *Substance Abuse and Psychopathology*. Washington, DC: American Psychiatric Association Press; 1984:79-106.
15. Rounsaville B, Kosten T, Weissman M, et al. Psychiatric disorders in relatives of probands with opiate addiction. *Arch Gen Psychiatry.* 1991;48:33-42.
16. Dinwiddie S, Reich T. Genetic and family studies in psychiatric illness and alcohol and drug dependence. *J Addict Dis.* 1993;12:17-27.
17. Robbins T, Everitt B. Limbic-striatal memory systems and drug addiction. *Neurobiol Learn Mem.* 2002;78:625-636.
18. Volkow N, Fowler J, Wang G. The addicted human brain: insights from imaging studies. *J Clin Invest.* 2003;111:1444-1451.
19. Winder D, Egli R, Schramm N, Matthews R. Synaptic plasticity in drug reward circuitry. *Curr Mol Med.* 2002;2:667-676.
20. DiLeone R, Georgescu D, Nestler E. Lateral hypothalamic neuropeptides in reward and drug addiction. *Life Sci.* 2003;73:759-768.
21. Turner R. The pursuit of socially modifiable contingencies in mental health. *J Health Soc Behav.* 2003;44:1-17.
22. Acton G. Measurement of impulsivity in a hierarchical model of personality traits: implications for substance use. *Subst Use Misuse.* 2003;38:67-83.
23. Rosen C, Ouimette P, Sheikh J, Gregg J, Moos R. Physical and sexual abuse history and addiction treatment outcomes. *J Stud Alcohol.* 2002;63:683-687.
24. Stevens S, Murphy B, McKnight K. Traumatic stress and gender differences in relationship to substance abuse, mental health, physical health, and HIV risk behavior in a sample of adolescents enrolled in drug treatment. *Child Maltreat.* 2003;8:46-57.

25. Best D, Hernando R, Gossop M, Sidwell C, Strang J. Getting by with a little help from your friends: the impact of peer networks on criminality in a cohort of treatment-seeking drug users. *Addict Behav.* 2003;28:597-603.
26. Musher-Eizenman D, Holub S, Arnett M. Attitude and peer influences on adolescent substance use: the moderating effect of age, sex, and substance. *J Drug Educ.* 2003;33:1-23.
27. Walton M, Blow F, Bingham C, Chermack S. Individual and social/environmental predictors of alcohol and drug use 2 years following substance abuse treatment. *Addict Behav.* 2003;28:627-642.
28. Nestler E. Molecular mechanisms of opiate and cocaine addiction. *Curr Opin Neurobiol.* 1997;7:713-719.
29. Morral AR, McCaffrey D, Iguchi MY. Hardcore drug users claim to be occasional users: drug use frequency underreporting. *Drug Alcohol Depend.* 2000;57(3):193-202.
30. Hickman M, Seaman S, de Angelis D. Estimating the relative incidence of heroin use: application of a method for adjusting observed reports of first visits to specialized drug treatment agencies. *Am J Epidemiol.* 2001;153(7):632-641.
31. National Consensus Panel on Effective Medical Treatment of Opiate Addiction: Effective medical treatment of opiate addiction. *JAMA.* 1998;280:1936-1943.
32. National Household Survey on Drug Abuse. Rockville, MD: Substance Abuse and Mental Health Services Administration;1999 2001.
33. Treatment episode data set. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2000 1993-1998.
34. Tarabar AF, Nelson LS. The resurgence and abuse of heroin by children in the United States. *Curr Opin Pediatr.* 2003;15(2):210-215.
35. Hopfer CJ, Khuri E, Crowley TJ, Hooks S. Adolescent heroin use: a review of the descriptive and treatment literature. *J Subst Abuse Treat.* 2002;23(3):231-237.
36. Hopfer CJ, Mikulich SK, Crowley TJ. Heroin use among adolescents in treatment for substance use disorders. *J Am Acad Child Adolesc Psychiatry.* 2000;39(10):1316-1323.
37. Year-end 2000 emergency department data from the Drug Abuse Warning Network. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2001 2000.
38. Johnston L, O'Malley P, Bachman J. *Monitoring the Future National Survey Results on Drug Use, 1975-2002.* Ann Arbor, MI: University of Michigan Institute for Social Research; 2003.
39. Van Etten ML, Anthony JC. Comparative epidemiology of initial drug opportunities and transitions to first use: marijuana, cocaine, hallucinogens and heroin. *Drug Alcohol Depend.* 1999;54(2):117-125.
40. Dorus W, Senay E. Depression, demographic dimensions, and drug abuse. *Am J Psychiatry.* 1980;137:699-704.
41. Latkin C, Glass G, Duncan T. Using geographic information systems to assess spatial patterns of drug use, selection bias, and attrition among a sample of injection drug users. *Drug Alcohol Depend.* 1998;50:167-175.
42. Dorus W, Senay E. Depression, demographic dimensions, and drug abuse. *Am J Psychiatry.* 137:699-704.
43. Anonymous. Heroin addicts in the long run. *Harvard Mental Health Letter.* 2001;18(5):8.
44. Schroeder JR, Latkin CA, Hoover DR, Curry AD, Knowlton AR, Celentano DD. Illicit drug use in one's social network and in one's neighborhood predicts individual heroin and cocaine use. *Ann Epidemiol.* 2001;11(6):389-394.
45. Neaigus A, Miller M, Friedman SR, Hagen DL, Sifaneck SJ, Ildefonso G, et al. Potential risk factors for the transition to injecting among non-injecting heroin users: a comparison of former injectors and never injectors. *Addiction.* 2001;96(6): 847-860.
46. Backmund M, Meyer K, Eichenlaub D, Schutz C. Predictors for completing an inpatient detoxification program among intravenous heroin users, methadone substituted, and codeine substituted patients. *Drug Alcohol Depend.* 2001;64:173-180.
47. Schwartz R. Adolescent heroin use. *Pediatrics.* 1998;102: 1461-1465.
48. Miller L, Wiessman M, Gur M, Adams P. Religiousness and substance use in children of opiate addicts. *J Subst Abuse Treat.* 2001;13:323-326.
49. Haheisy A, Wilens T, Biederman J, Van Patten S, Spencer T. Temporal association between childhood psychopathology and substance use disorders: Findings from a sample of adults with opioid or alcohol dependency. *Psychiatry Res.* 2002;109:245-253.
50. Roy A. Characteristics of opiate dependent patients who attempt suicide. *J Clin Psychiatry.* 2002;63:493-497.
51. Langendam M, van Brussel G, Coutinho R, van Ameijden E. The impact of harm-reduction-based methadone treatment on mortality among heroin users. *Am J Public Health.* 2001;91:774-780.
52. Newman R, Whitehill W. Double-blind comparison of methadone and placebo maintenance treatments of narcotic addicts in Hong Kong. *Lancet.* 1979;2(8141):485-488.
53. Gunne L, Gronbladh L. The Swedish methadone maintenance program: A controlled study. *Drug Alcohol Depend.* 1981;7:249-256.
54. Ling W. Methadyl acetate and methadone as maintenance treatments for heroin addicts. *Arch Genl Psychiatry.* 1976;33(6):709-720.
55. Fugelstad A, Rajs J, Bottiger M, Gerhardsson de Verdier M. Mortality among HIV-infected intravenous drug addicts in Stockholm in relation to methadone treatment. *Addiction.* 1995;90:711-716.
56. Stenbacka M, Leifman A, Romelsjo A. The impact of methadone on consumption of inpatient care and mortality with special reference to HIV status. *Subst Use Misuse.* 1998;33(14):2819-2834.
57. Ward J, Malrick R, Hall W. The effectiveness of methadone maintenance treatment: an overview. *Drug Alcohol Rev.* 1994;13:327-336.
58. Des Jarlais D, Marmor M, Paone D, et al. HIV incidence among injecting drug users in New York City syringe-exchange programmes. *Lancet.* 1996;348(9033):987-991.
59. Ball J, Lange W, Myers C, Friedman S. Reducing the risk of AIDS through methadone maintenance treatment. *J Health Soc Behav.* 1988;29:214-226.
60. Hagan H, Des Jarlais D, Friedman S, Purchase D, Alter M. Reduced risk of hepatitis B and hepatitis C among injection drug users in the Tacoma syringe exchange program.[comment]. *Am J Public Health.* 1995;85(11):1531-1537.
61. Hser Y, Anglin D, Powers K. A 24-year follow-up of California narcotics addicts. *Arch Gen Psychiatry.* 1993;50:577-584.
62. Dole V, Joseph H. Long-term outcome of patients treated with methadone maintenance. *Ann N Y Acad Sci.* 1978;311:181-189.
63. Bell J, Hall W, Byth K. Changes in criminal activity after entering methadone maintenance. *British Journal of Addiction.* 1992;87:251-258.
64. McGlothlin W, Anglin M. Long-term follow-up of clients of high- and low-dose methadone programs. *Arch Gen Psychiatry.* 1981;38:1055-1063.

65. Strain E, Stitzer M, Liebson I, Bigelow G. Dose-response effects of methadone in the treatment of opioid dependence. *Ann Intern Med.* 1993;119(1):23-27.
66. Simpson D. The relation of time spent in drug abuse treatment to posttreatment outcome. *Am J Psychiatry.* 1979;136:1449-1453.
67. Caplehorn J, Bell J, Kleinbaum D, Gebiski V. Methadone dose and heroin use during maintenance treatment. *Addiction.* 1993;88:119-124.
68. Strain E, Bigelow G, Liebson I, Stitzer M. Moderate- vs high-dose methadone in the treatment of opioid dependence: A randomized trial. *JAMA.* 1999;281(11):1000-1005.
69. Fudala PJ, Bridge TP, Herbert S, et al. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *N Engl J Med.* 2003;349(10):949-958.
70. Montoya ID, Gorelick DA, Preston KL, et al. Randomized trial of buprenorphine for treatment of concurrent opiate and cocaine dependence. *Clin Pharmacol Ther.* 2004;75(1):34-48.
71. Mattick RP, Kimber J, Breen C, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence.[update of Cochrane Database Syst Rev. 2002;(4):CD002207; PMID: 12519569]. *Cochrane Database of Systematic Reviews.* 2003(2):CD002207.
72. Giacomuzzi SM, Riemer Y, Ertl M, et al. Buprenorphine versus methadone maintenance treatment in an ambulant setting: a health-related quality of life assessment. *Addiction.* 2003;98(5):693-702.
73. Mattick RP, Ali R, White JM, O'Brien S, Wolk S, Danz C. Buprenorphine versus methadone maintenance therapy: a randomized double-blind trial with 405 opioid-dependent patients.[see comment]. *Addiction.* 2003;98(4):441-452.
74. Ahmadi J. Methadone versus buprenorphine maintenance for the treatment of heroin-dependent outpatients. *J Subst Abuse Treat.* 2003;24(3):217-220.

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