Chapter 6

Illicit Drug Dependence

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INTRODUCTION

In 2012, by various estimates, 165 million to 315 million people ages 15–64 years worldwide used illicit drugs, including those in the following categories (UNODC 2013):[1]

- *Cannabis products.* Marijuana, hashish, and bhang are the most widely used drugs, with an estimated 181 million users (129 million to 230 million) constituting 3.9 percent of the global population ages 15–64 years.
- *Amphetamine-type stimulants (ATSs).* The next most widely used illicit drugs are stimulants such as cocaine; methamphetamine; drugs with stimulant and hallucinogenic properties, such as MDMA (3,4-methylenedioxy-N-methylamphetamine), or ecstasy; and novel psychoactive substances,[2] with an estimated 34 million users worldwide (14 million to 53 million), including 17 million cocaine users (14 million to 21 million), and 20 million MDMA users (10 million to 29 million).
- *Illicit opioids.* An estimated 17 million persons use heroin or opium; 32 million use any illicit opioid, including diverted pharmaceutical opioids, such as methadone or morphine (28 million to 36 million).

Scope of the Chapter

This chapter is concerned with cannabis, amphetamine, and opioid dependence. The chapter identifies disease control priorities for illicit drug dependence in low- and middle-income countries (LMICs). First, we describe patterns of dependence and the disease burden (mortality, morbidity, and societal economic costs) attributable to dependence, by global region. Second, we summarize evidence on the effectiveness of interventions to reduce illicit drug dependence and the harm caused by such dependence. Finally, we consider the extent to which research on illicit drug dependence in high-income countries (HICs) is relevant to disease control priorities in LMICs.

In undertaking the reviews for this chapter, we relied on previous systematic reviews of the epidemiology of drug use, dependence, and health consequences (Degenhardt and Hall 2012), many of which were conducted for the Global Burden of Disease (GBD) 2010 study (Degenhardt, Whiteford, and others 2013). Our review of interventions drew heavily on our previous work reviewing effective interventions for illicit drug use and dependence (Strang and others 2012). We updated these with a review-of-reviews approach, whereby we conducted a systematic review of reviews of interventions to address illicit drug use and dependence.

Definition of Illicit Drug Dependence

The health risks of illicit drug use increase with the frequency and quantity of use and route of administration. The International Classification of Diseases (ICD) defines *harmful use* if there is evidence that substance use is causing physical or psychological harm; it defines

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drug dependence if three or more indicators of dependence are present for at least one month within the past year (WHO 1993).

The *Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-4)* used a similar classification for *substance abuse* and *substance dependence* (APA 2000). However, the fifth edition *(DSM-5)* defines a *substance use disorder* if two of 11 criteria grouped under impaired control, social impairment, risky use, and pharmacological dependence are present; it categorizes the severity along a continuum of mild, moderate, and severe disorders, based on the number of criteria present (APA 2013).

NATURAL HISTORY OF DEPENDENCE

Onset of illicit drug use typically occurs in the mid- to late teens and peaks in the early to late 20s; few users continue beyond age 40 years (Degenhardt, Whiteford, and others 2013). The percentage of illicit drug users who transit from use to dependence ranges from 9 percent for cannabis to 20–25 percent for users of psychostimulants and heroin (Lopez-Quintero and others 2011). Cannabis use accounts for 80 percent of illicit drug use worldwide; the dependence risk is lower, and the morbidity attributable to its use is smaller, than for other drugs (Degenhardt, Whiteford, and others 2013).

The lag time from illicit drug use to dependence is shorter than that observed for substances such as nicotine and alcohol (Behrendt and others 2009). Dependence can occur within 1.5–2 years of cocaine and opioid use and within three years of cannabis use (Florez-Salamanca and others 2013; Wu and others 2011).

The 2010 rates of cannabis and opioid dependence were higher in HICs than LMICs; cocaine use and dependence rates were highest in North America and tropical and southern Latin America (Degenhardt, Bucello, Calabria, and others 2011). Amphetamine dependence rates, however, appear to be highest in Southeast Asia and Australasia (Degenhardt, Baxter, and others 2014).

Risk Factors

Risk factors often coexist and are similar across the different categories of illicit drugs, as well as across global regions (Degenhardt and others 2010):

- *Social and contextual factors:* low socioeconomic status, early substance-use onset, and social norms that are tolerant of alcohol and other drug use
- *Family factors:* poor quality of parent-child interaction and relationships, parental conflict, and parental and sibling drug use
- *Individual factors:* male gender; having an externalizing disorder, such as attention-deficit hyperactivity disorder or conduct disorders in early childhood; sensation- and novelty-seeking personality traits; and low education levels
- *Peer group factors:* association with antisocial or drug-dependent peers, which is one of the strongest risk factors for illicit drug dependence in adolescence and which operates independently of social, contextual, family, and individual factors.

Consequences

Mortality

Mortality rates for heavy users of opioids, amphetamines, and cocaine are 3–14 times higher across the lifespan than for the general population (Degenhardt, Bucello, Mathers, and others 2011; Stenbacka, Leifman, and Romelsjo 2010). In 2011, an estimated 211,000 people died from drug-related causes, mostly younger users whose deaths were primarily preventable (UNODC 2013).

Based on the type of drug dependence, studies have found the following risk correlations:

- *Heroin.* Long-term heroin users have a substantially increased risk of premature death from drug overdose, violence, suicide, and alcohol-related causes (Degenhardt, Charlson, and others 2014).
- *Amphetamines.* Amphetamine-related deaths typically are associated with cardiac failure and cerebral vascular accidents (Darke and others 2008).
- *Cocaine.* Cocaine dependence is associated with elevated risks of intentional and accidental injuries (Blow and others 2011). Cocaine-related deaths are usually related to cardiovascular complications, brain hemorrhage, stroke, and kidney failure (Restrepo and others 2009).
- *Cannabis.* Cannabis dependence is associated with significant disability burden, including the precipitation of psychosis in vulnerable people (Bloomfield and others 2013).

HIV and Hepatitis Infection

In 2010, injecting drug use accounted for almost two million years of life lost (YLLs) globally as a risk from HIV infection (Degenhardt, Whiteford, and others 2013). Injecting drug use has been a major driver of HIV epidemics in LMICs (Mathers and others 2010).

Hepatitis B and C infection is highly prevalent globally among people who inject drugs (Nelson and others 2011). Chronic infection occurs in 75 percent of infections, and 3–11 percent of chronic hepatitis C virus (HCV) carriers develop liver cirrhosis within 20 years. The risk of HIV and hepatitis C infection is elevated among non-injecting drug users; psychostimulants such as crack cocaine and amphetamine disinhibit users and facilitate riskier sexual activity and increase the risk of HIV infection (Volkow and others 2007). Among men who have sex with men, amphetamines (specifically, crystal methamphetamine) may be used to enhance sexual encounters, increasing the risk of HIV infection from unprotected anal intercourse (Rajasingham and others 2012).

Criminal Activity

The relatively few adults who become dependent on heroin have a disproportionate criminal impact on their communities. The average heroin user engages in criminal behavior 40–60 percent of the time that he or she is not incarcerated or in treatment (Ball, Shaffer, and Nurco 1983); the most common offenses include drug dealing and property crimes (Degenhardt, Larney, and others 2013).

Economic Losses

The production, distribution, and consumption of illicit drugs result in significant economic costs affecting consumers, families, industries, societies, and governments. For example, there is a strong correlation between unemployment and drug use in HICs and LMICs. Illicit drug use limits the affected individuals' chances of entering or remaining in the workforce and is linked to low productivity and accidents. Drug-taking employees in the United States are absent three times more often, are three to four times more likely to be involved in a workplace accident, and file approximately five times more workers' compensation claims than non-drug-taking employees (UNDCP 1998). There are opportunity costs of the expenditures used to treat illicit drug dependence, prevent crime, enforce laws, and process drug-dependent offenders in the judicial system. For example, the economic cost of drug abuse was estimated at 2 percent of gross domestic product in Australia (Collins and Lapsley 2007).

Trends

Global trends are difficult to estimate because drug use is routinely tracked only in a minority of HICs; assessments of trends in other countries often rely on indirect indicators, such as law enforcement data on drug seizures, demand for treatment, and overdose deaths.

Consumption Trends

Despite reported increases in the global number of illicit substance users, other indicators such as area under drug cultivation, production, manufacture, and seizures suggest that consumption (about 167 million to 315 million users) has remained relatively stable since 2010 (UNODC 2013). The illicit market for ATSs appears to be growing, with global increases in seizures, particularly in Africa and Mexico (see UNODC 2013). Cocaine markets appear to be shifting from the United States and Western Europe to Asia. Heroin availability, use, and overdose also appear to be increasing in Asia and East and West Africa and the United States. Afghanistan saw large increases in heroin availability and an increased net cultivation of 36 percent from 2012 to 2013, and a 140 percent increase in estimated regular users from 2005 to 2009 (UNODC 2009).

Of particular concern is the large increase in dependence on pharmaceutical opioids, such as oxycodone, methadone, hydrocodone, and fentanyl. In the United States, the annual incidence of pharmaceutical opioid abuse rose by almost 300 percent from 1990 (628,000 initiates) to 2001 (2.4 million) (U.S. Department of Health and Human Services 2012); treatment admissions and death rates due to overdose increased from 1999 to 2008 (CDC 2012). Similarly large increases in pharmaceutical opioid prescriptions and abuse have been reported in Australia, Estonia, Finland, and New Zealand (UNODC 2013).

Burden of Disease Trends

The GBD 2010 study found that disability-adjusted life years (DALYs) from drug use disorders rose 52 percent, from 13.1 million in 1990 to 20.0 million in 2010 (Degenhardt, Whiteford, and others 2013). Population growth accounted for 28 percent and increased prevalence for 22 percent of the increase in this period. The overall opioid dependence burden increased by 74 percent from 1990 to 2010, amounting to almost four million additional DALYs in 2010 (Degenhardt, Charlson, and others 2014). Much of the drug-related increase in DALYs can be attributed to population growth; one exception is opioid dependence, in which 56 percent of the total increase in DALYs was attributable to increased prevalence.

INTERVENTIONS AND POLICIES: EFFECTIVENESS AND COVERAGE

Research on the effectiveness and cost-effectiveness of policies and interventions for control of illicit drug use has varied in quantity and quality and largely comes from a few HICs, although recent research has assessed these interventions in LMICs.

Population Platform Interventions

Interventions to reduce the availability of illicit drugs and discourage their use include legal and regulatory approaches, such as prohibitions on the manufacture, sale, and use of opioid drugs for nonmedical purposes; law enforcement of these sanctions through fines and imprisonment; and restricted availability of medically prescribed drugs, such as opioids, to prevent their diversion to the black market. Interventions to increase public health and awareness include educational campaigns, delivered via the mass media or school-based drug education programs, about the health risks of drug use (table 6.1).

Control of the Supply of Illicit Drugs

Precursor Chemical Control. Precursor chemical regulation has produced some major supply interruptions (Cunningham, Liu, and Callaghan 2013).[3] However, the impacts are not always predictable, and drug supply interruptions have been relatively short lived (ONDCP 2008).

Law Enforcement. The most popular interventions in many countries have been law enforcement approaches focusing on drug interdiction and enforcement of sanctions against the possession, use, and sale of illicit drugs (Strang and others 2012). Although there is limited evidence on the effectiveness of these expensive strategies (Kuziemko and Levitt 2004), these interventions work to reduce drug use and harm, including fatal and nonfatal heroin overdoses (Day and others 2004), as well as drug-related emergency room visits (Dave 2006), by increasing the price of illicit drugs. Alternative development programs in source countries do not seem to reduce availability or increase prices in destination countries (Babor and others 2010).

However, supply interruptions often arise from a convergence of circumstances that is difficult to reproduce by design in different regions and drug markets. Accordingly, it is difficult to assess the cost-effectiveness of supply reduction via expensive, high-level law enforcement strategies (Shanahan, Degenhardt, and Hall 2004). Nor have street-level law enforcement activities proven effective in the long run, as the markets are usually displaced elsewhere, causing more harm to some groups of drug users. For example, heroin shortages have been linked with marked increases in cocaine and amphetamine injection and incident HCV infection (Strang and others 2012).

Prescription Monitoring Programs. The evidence on control of pharmaceutical opioid misuse has been dominated by HICs. Control of pharmaceutical opioid misuse

Table 6.1 Summary of Population Platforms and Recommended Interventions for Illicit Drug Dependence

Universal prevention and health promotion	Evidence level	CEA available?	Notes
Legislation and regulation			
Precursor chemical control	May be effective	No	Some impact, short-term; some consequences difficult to predict
High-level law enforcement	May be effective	No	Difficult to know if or when effect will occur; may be short-lived
Street-level law enforcement	Inconclusive	No	May have short-term, localized effect but leads to compensatory increases elsewhere
Prescription monitoring programs	May be effective	No	Poorly studied to date; may have some impact, although misuse of other medications may occur
Information and awareness			
Mass media campaigns	Inconclusive	No	Limited research with inconsistent results, with some showing negative and others positive impacts on drug attitudes and use
Intersector collaboration			
Imprisonment	Inconclusive	No	No evidence suggesting drug use is reduced on release, although decreased use during imprisonment
Drug testing for offenders	May be effective	No	Encouraging observational evidence from U.S. states where this has been introduced
Court-mandated treatment	Inconclusive	No	Includes mandated treatment and drug courts

Note: CEA = cost-effectiveness analysis.

likely differs in LMICs, where opioids such as morphine are less readily available because of excessive enforcement of regulations to prevent their misuse. HICs have attempted to reduce increases in the use, misuse, and diversion of pharmaceutical opioids by implementing controlled-substance laws, prescription monitoring systems, and clinical guidelines against overprescribing (Compton and Volkow 2006).

However, extramedical users may obtain pharmaceutical opioids in several ways, for example, doctor shopping, informal sharing and trading of medications between peers and family members (Fischer, Bibby, and Bouchard 2010), larger-scale diversion via thefts (Inciardi and others 2007), and proliferation of online pharmacies (Littlejohn and others 2005) that limit the beneficial effects of prescription systems. Restrictions on one class of prescription drug may increase the use of another class; these measures can also restrict access by those who have a legitimate medical need for them (Strang and others 2012).

Public Awareness Campaigns

Populationwide mass media campaigns to deliver information and expand public awareness have not had consistent impacts on use (Ferri and others 2013; Wakefield, Loken, and Hornik 2010).

Criminal Justice Platforms

Imprisonment. One consequence of the focus on law enforcement is that imprisonment for drug or property offenses is the most common intervention (Strang and others 2012). Although imprisonment is not an effective way to reduce drug dependence (Manski, Pepper, and Petrie 2001), constructive health interventions, such as hepatitis B vaccinations, can be provided in this setting (Farrell, Strang, and Stover 2010).

Studies examining the effect of cannabis decriminalization (Room and others 2010) have been methodologically weak, often simply comparing the prevalence of cannabis use before and after changes in the law. This area remains controversial; only weak evidence exists that tougher sanctions reduce either criminal offending in general or drug use in particular (Strang and others 2012).

Drug Testing of Offenders. Research has yielded increasing evidence that sure, immediate, and modest sanctions for positive drug tests substantially reduce drug use among individuals under criminal justice supervision (Kleiman 2009), but controlled evaluations have been limited. Typically, this evidence applies to offenders who have been released into the community before trial or who are on probation or parole, and sanctions can include 24 hours of imprisonment.

Court-Mandated Treatment. Court-mandated treatment refers to treatment entered under legal coercion by persons who have been charged with or convicted of an offense to which their drug dependence has contributed. Such treatment is most often provided as an alternative to imprisonment—and usually with the threat of imprisonment if the person fails to comply with treatment (Hall, Farrell, and Carter 2014).

Research into the effectiveness of court-mandated treatment is largely limited to observational studies in the United States of offenders entering treatment under various forms of legal coercion, including methadone maintenance treatment (MMT). Early evidence of the effectiveness of such treatment comes from a study in the United States that showed that among illicit drug offenders, a much greater reduction in heroin use and substantially lower incarceration rates were found among those enrolled in opioid substitution therapy (OST) in the year after release from prison (Dole and others 1969). Some more recent observational studies support these findings (Anglin 1988; Young, Fluellen, and Belenko 2004), but others do not (Klag, O'Callaghan, and Creed 2005).

Formal drug courts are another alternative to suspended sentences or diversion programs; in the short term, they can reduce future criminal offending and drug use more than conventional courts. However, few randomized controlled trials have been conducted to evaluate these (Brown 2010), and there are few studies of the costs and cost-effectiveness of any of these criminal justice interventions. Of the 69 relevant studies conducted in Australia and the United States between 1980 and 2004 (Perry and others 2009), only one reported cost-effectiveness data (Schoenwald and others 1996), suggesting that the cost of treatment was nearly offset by the savings incurred by reducing days incarcerated.

Community Platform Interventions

Workplace Drug Testing

Drug testing has been increasingly used in workplace settings, such as athletics, criminal justice, mining, the military, government agencies, and health services. Urine sampling is considered the gold standard (Phan and others 2012) because of the accuracy, speed, ease of administration, and limited invasiveness required. There have been limited evaluations of the impact of mandatory drug testing in the workplace; some supportive

evidence is available from programs in the United States that have used drug testing with doctors and airline pilots (DuPont and others 2009).

School-Based Prevention Programs

Schools provide a popular setting for prevention programs, because of the ready access to young adults and the ease of intervention delivery. Evidence of the effectiveness of school-based interventions varies widely. Reviews of randomized controlled evaluations suggest that psychosocial interventions may have some benefit (Faggiano and others 2014), but no evidence indicates that interventions that only target knowledge and awareness of negative consequences of illicit drug use are effective (Strang and others 2012).

Drug Education. An example of a widely used but ineffective drug education program in the United States was the Drug Abuse Resistance Education (DARE) program, in which police officers gave classroom advice on the dangers of drug use. Rigorous study showed that DARE neither prevented nor delayed drug use (Ennett and others 1994). Similarly, evaluation of a populationwide mass media campaign targeted at youths ages 9–18 years to prevent cannabis use also showed that it had no effect and possibly increased use (Hornik and others 2008).

Skills Training. School-based interventions targeting social skills are effective in reducing drug use and have positive effects in other domains, including reducing internalizing and externalizing disorders.[4] The Strengthening Families Program, targeting youths ages 10–14 years and their parents, is an evidence-based family skills training program that has been shown to reduce drug abuse and other problem behaviors (Strang and others 2012). The Good Behavior Game, a classroom behavior management approach for children ages 5–7 years that originated in the United States and that has been tested worldwide, has shown positive outcomes up to 15 years after the intervention (Kellam, Reid, and Balster 2008). Economic analyses suggest that these early-age interventions are cost-effective because substantial lifetime benefits are realized from even modestly lower rates of early drug or alcohol use (Caulkins and others 2002).

Early Intervention with At-Risk Youth. There is limited, low-quality, and inconsistent evidence about the effectiveness of school-based drug testing among high school students (Shek 2010). The evidence on the impact of psychosocial interventions for young people using substances or at risk of doing so is limited and inconsistent (Strang and others 2012).

Self-Help and Mutual Aid Groups

Self-help and mutual aid groups are run by recovering drug users, typically using adaptations of the 12-step principles of Alcoholics Anonymous. The groups include Narcotics Anonymous, Cocaine Anonymous, and Marijuana Anonymous. A mutual aid approach called Self-Management and Recovery Training (SMART Recovery) offers an alternative choice for group-based rehabilitation without the 12-step approach, especially for those who are either unwilling or unable to use 12-step groups (Horvath 2000).

Some individuals use these groups as their sole support for abstinence; others use them in combination with professional counseling and other strategies (Freimuth 2000). Although self-help is probably the most common type of intervention delivered globally for drug abuse, until recently there have been few scientific studies of its effectiveness. Observational and quasi-experimental evidence suggests that participation in Narcotics Anonymous is associated with continued abstinence, lower health care costs, and improvement in other areas of functioning (Gossop, Stewart, and Marsden 2008; Strang and others 2012) (table 6.2).

Health Care Platform Interventions

Community-Level Care

Community-based strategies can potentially reduce harms related to illicit drug use, especially blood-borne virus (BBV) transmission and opioid overdoses. These strategies include OST, overdose prevention education, emergency response education, and supervised injecting facilities (SIFs) (table 6.3).

Access to Treatment. Consistent evidence from observational studies and randomized trials shows that the risk of death from overdose is substantially reduced in individuals while they receive OST compared with their risk when not receiving OST (Degenhardt, Bucello, Mathers, and others 2011). Maximizing OST provision to drug users in the community, in prison (Larney, Gisev, and others 2014), and after release from prison (Degenhardt, Larney, and others 2014) will have demonstrable population-level effects on overdose mortality.

Overdose Prevention Education. Polydrug use increases the chances of fatal overdose, particularly the concurrent use of opioids and other drugs that depress the central nervous system, like benzodiazepine and alcohol (Warner-Smith and others 2001). Educating people who use opioids, particularly by injection, about these dangers and the risks of injecting alone or on the

Table 6.2 Summary of Community Platforms and Recommended Interventions for Illicit Drug Dependence

Selective prevention and health promotion, by platform	Evidence level	CEA available?	Notes
Workplaces			
Drug testing	Limited	No	Evidence from programs for employees with identified substance use problems
Schools			
Drug testing	Inconclusive	No	Inconsistent, poor evidence
Drug education	Sufficient	No	Not effective; substance use possibly even increased
Skills and psychosocial interventions with primary school children	Sufficient	Yes	Strengthening Families Program
			Good Behavior Game: long-term effects up to 15 years post-intervention
Skills training with adolescents	Inconclusive	No	Short-term effects at best; no effect found by some studies
Early intervention with at-risk youth	Limited	No	Limited, low-quality evidence with inconsistent findings; small, short-term effects found by some studies, but no effects found by others
Community			
Self-help groups	Limited	No	Narcotics Anonymous, Cocaine Anonymous, Marijuana Anonymous, SMART Recovery (amphetamines): limited RCT evidence and selection bias likely in observational studies

Note: CEA = cost-effectiveness analysis; RCT = randomized controlled trial; SMART Recovery = Self-Management and Recovery Training.

streets, where assistance in case of overdose is limited, might reduce the risk of overdose (McGregor and others 2001).[5] However, the effectiveness of these strategies has not been rigorously evaluated.

Naloxone and Other Emergency Responses. Another strategy is to improve bystander responses to opioid overdoses by encouraging drug users who witness overdoses to seek medical assistance and use simple but effective resuscitation techniques until help arrives (Wagner and others 2010). This approach includes the distribution of naloxone to opioid injectors and their peers. Naloxone is a narcotic antagonist that rapidly reverses the effects of acute narcosis, including respiratory depression, sedation, and hypotension.[6] An increasing number of jurisdictions have been implementing such programs, although evaluations have largely been observational (Tobin and others 2009).

Supervised Injecting Facilities. SIFs are located in areas where injecting drug users are concentrated, typically in areas with large, open drug markets. The goal is to reduce drug overdose deaths and BBV infections among injectors who inject in public places. SIFs have potential community impact but exist in a limited number of locations, only 61 cities in eight countries (Hedrich, Kerr, and Dubois-Arber 2010; Kerr and others 2007). Although models differ, all SIFs provide sterile injecting equipment and a hygienic environment where pre-obtained drugs can be injected.

Observational evaluations in Vancouver and Sydney have suggested that SIFs attract risky injectors, facilitate safe-injection education, reduce syringe sharing, and increase referral and entry into withdrawal management and drug treatment. Although reviews suggest that drug use does not change among clients or among drug injectors in the areas where SIFs are located (Kerr and others 2007; MSIC Evaluation Committee 2003), the evidence of their impact on HIV transmission is uncertain (Kimber and others 2010). However, reducing the risk among the most vulnerable injecting drug users may increase the effectiveness of other interventions.

Primary Health Care

Screening and Brief Intervention. Some evidence suggests that a single brief intervention in a clinical setting can reduce illicit drug use (Baker and others 2005; Humeniuk and others 2012), although a recent systematic review concluded that further studies were needed (Young and others 2014). Brief interventions from prescribers, such as tailored written letters to patients or consultations, reduced heavy benzodiazepine use up to six months after intervention (Mugunthan, McGuire, and Glasziou 2011).

Table 6.3 Summary of Health and Social Care Interventions and Recommendations for Illicit Drug Dependence

Intervention, by platform	Evidence level	CEA available?	Notes
Community-based care			
Emergency naloxone provision (opioid overdose)	Limited	No	Becoming increasingly implemented, but evidence limited to observational evaluation
Supervised injecting facilities	Limited	No	No clear impact on drug use per se (not the intent)
Primary health care			
Screening and brief intervention	Limited	No	Some evidence of short-term reduction in drug use, but further studies needed
Specialist health care			
Detoxification and withdrawal	Limited	No	Not effective as stand-alone postwithdrawal treatment
Naltrexone-accelerated withdrawal alone	Limited	No	Not effective as stand-alone postwithdrawal treatment
Medication for cannabis withdrawal alone	Limited	No	Reduces withdrawal symptoms; no difference in long-term reduction in cannabis use
Residential rehabilitation	Limited	No	Some level II and III studies[a]
Brief psychological intervention			
CBT for cannabis dependence	Sufficient	No	Short-term, modest impact
CBT for opioid dependence	Sufficient	No	As an adjunct to OST
CBT for psychostimulant dependence	Sufficient	No	Short-term, modest impact
Acupuncture	Inconclusive	No	Low-quality studies; no clear evidence of effect (cocaine and opioid dependence)
Medications for heroin and other opioid dependence			
BMT	Sufficient	Yes	Reduces risk of overdose and opioid use
MMT	Sufficient	Yes	Reduces risk of overdose and opioid use
HMT	Sufficient	No	Expensive; not first-line OST
Oral naltrexone	Sufficient	No	Effectiveness limited by poor adherence
Implant or sustained-release naltrexone	Limited	No	Potential for improved adherence, but insufficient evidence
Medications for cannabis dependence	Limited	No	Some limited benefits identified with symptomatic medications; preliminary evidence for cannabis antagonists
Medications for cocaine dependence	Sufficient	No	Not efficacious
Medications for psychostimulant dependence	Sufficient	No	Weak efficacy in trials; no evidence of effectiveness

Note: BMT = buprenorphine maintenance treatment; CBT = cognitive behavioral therapy; CEA = cost-effectiveness analysis; HMT = supervised injectable heroin maintenance treatment; MMT = methadone maintenance treatment; OST = opioid substitution therapy.
a. Level II studies refer to randomized controlled trials; level III studies refer to well-designed, pseudo-randomized controlled trials, cohort studies, case-control studies, or interrupted time-series studies.

Specialist Health Care

Detoxification and Withdrawal. Detoxification centers provide supervised withdrawal from a drug of dependence with the aim of minimizing the severity of withdrawal symptoms. Detoxification is not a treatment, but it is the intervention that dependent users seek most often. It provides users with a respite from use, an occasion to reconsider their drug use, and a potential prelude to abstinence-based treatment. Detoxification has minimal, if any, enduring impact on dependence on its own (Mattick and Hall 1996).

Residential Rehabilitation. Residential rehabilitation can be a therapeutic community (TC) model that typically involves residency for six months and a 12-step approach, often after 28 days of residential treatment followed by community engagement in a network of 12-step groups or a faith-based approach (for example, Christian rehabilitation houses), with the aim of abstinence from all opioid and other illicit drugs. These approaches often encourage patients to become involved in self-help groups, such as Narcotics Anonymous. They use group and psychological interventions to help users remain abstinent.

There have been few successful randomized controlled trials for TCs or outpatient drug counseling (Vanderplasschen and others 2013). TCs are more demanding of drug users and are less successful than OST in attracting and retaining drug users in treatment. Nevertheless, TCs substantially reduce drug use and crime in those who remain in treatment for at least three months (Smith, Gates, and Foxcroft 2006). TCs may be more effective if they are used in combination with legal coercion to ensure that drug users stay in treatment long enough to benefit from it (Gerstein and Harwood 1990).

Psychosocial Interventions.

Brief Intervention. Brief interventions have been found to be effective when provided through outreach services, such as needle and syringe programs. Behavioral family- and couple-based interventions have produced better abstinence rates in treatment and at follow-up (Strang and others 2012).

Cognitive Behavioral Therapy. Cognitive behavioral therapy, particularly short-term treatments provided in three to six outpatient sessions, have resulted in modest abstinence rates of 20–40 percent at the end of treatment, but high relapse rates and more modest abstinence rates after 12 months. Psychosocial treatments for cocaine and amphetamine dependence have limited effectiveness and high rates of relapse after treatment (NICE 2007; Strang and others 2012).

Contingency Management. Contingency management is a behavioral reinforcement approach that uses incentives, such as vouchers or clinic benefits, to improve adherence to treatment and duration of abstinence (Budney and others 2006). The benefits of treatment depend on the magnitude of reward. This form of intervention may work best for people with more severe dependence on cocaine (Petry and others 2004). Contingency management also improves completion of hepatitis B vaccination among opioid-dependent people (Weaver and others 2014).

Medications for Heroin and Other Opioid Dependence.

Methadone Maintenance. Once-daily oral MMT is the most common form of drug substitution worldwide that is more effective than a placebo (Mattick and others 2014). Large observational studies have found that patients in MMT decreased their heroin use and criminal activity while in treatment. MMT substantially reduces HIV transmission through needle sharing, and it is the best-supported form of OST in terms of retention in treatment and reduction of heroin use (Gowing, Hickman, and Degenhardt 2013; Mattick and others 2014).

Buprenorphine Maintenance. Buprenorphine is a mixed agonist-antagonist opioid receptor modulator that has partial agonist effects similar to those of morphine while also blocking the effects of pure agonists like heroin. In high doses, its effects can last up to three days, and its antagonist effects substantially reduce the risk of overdose and abuse. Meta-analyses of controlled trials of buprenorphine have found it to be effective in the treatment of heroin dependence (Mattick and others 2014).

Morphine Maintenance. Other opioid medications have been used as OST medications with success, such as supervised OST with long-acting morphine (Mathers and others 2010).

Supervised Injectable Heroin Maintenance. Supervised injectable heroin maintenance treatment (HMT) has been evaluated in a series of trials as a second-line treatment for chronic heroin users who have repeatedly failed to respond to oral forms of opioid maintenance. Reviews suggest that HMT can increase well-being and reduce heroin use and criminal activity; it may potentially reduce mortality. The risk of serious adverse events, however, means that HMT should be reserved for those who have failed in other treatments and should be provided under medical supervision (Ferri, Davoli, and Perucci 2011).

Naltrexone Maintenance. Naltrexone completely blocks the effects of any opiate, such as heroin. From a clinical perspective, however, oral naltrexone has been disappointing because of patient nonadherence (Minozzi and others 2011). This finding has led to two very different approaches to improving adherence: (a) behavioral strategies to improve adherence and the use of contingency management strategies, such as rewards for adherence, and (b) the development of long-acting naltrexone formulations (implant or slow-release injection). The evidence for the effectiveness of these approaches remains limited (Larney, Gowing, and others 2014).

Medications for Cannabis Dependence. No effective maintenance pharmacotherapies exist for cannabis dependence (Danovitch and Gorelick 2012); no pharmacotherapies have been approved for cannabis withdrawal. Only limited benefits are documented from trials of symptomatic medications, including antidepressants (Carpenter and others 2009); mood stabilizers, including lithium (Winstock, Lea, and Copeland 2009); and the α_2-adrenergic agonist lofexidine (Haney and others 2008).

Oral delivery of synthetic delta-9-tetrahydrocannabinol reduced a subset of cannabis withdrawal symptoms in laboratory (Haney and others 2004) and outpatient settings (Vandrey and others 2013). Nabiximols (Sativex), a cannabis agonist, has been found in a randomized controlled trial to significantly reduce the severity of cannabis withdrawal-related effects, including irritability, depression, and cannabis cravings, compared with a placebo (Allsop and others 2014).

Medications for Psychostimulant Dependence. Despite substantial investment in research, no effective pharmacological treatments have emerged for cocaine dependence (Amato and others 2011) or for amphetamine or methamphetamine dependence (Brensilver, Heinzerling, and Shoptaw 2013). Weak evidence indicates the efficacy of oral dexamphetamine maintenance (Galloway and others 2011; Longo and others 2010).

COST-EFFECTIVENESS OF INTERVENTIONS FOR ILLICIT DRUG DISORDERS

There is evidence of the cost-effectiveness of a few interventions (tables 6.1–6.3), but there is a paucity of information to support resource allocation to different drug policies. This lack of evidence can be attributed in part to challenges in identifying and measuring the costs and effects of supply-side strategies or policies, such as the high-level enforcement of sanctions against illicit drug possession, use, and sale (Shanahan, Degenhardt, and Hall 2004), or criminal justice interventions (NICE 2007). The paucity of information also mirrors the modest level of evidence on the cost-effectiveness of many of the interventions reviewed in this chapter. A final reason is the shortage of technical capacity to undertake these studies, particularly in LMICs.

Cost-effectiveness evidence is mainly available for substitution or maintenance treatment of opioid dependence using methadone or buprenorphine (Simoens and others 2006). One or two studies have also assessed the costs and consequences of school-based life skills programs on future illicit drug use (see, for example, Caulkins and others 1999). Since these economic analyses have been conducted almost exclusively in HICs, their relevance to lower-resource contexts is limited. Nevertheless, the studies have demonstrated that these interventions represent reasonable value for money in these settings. In Australia, for example, MMT and buprenorphine maintenance treatment (BMT) were shown to produce increases in heroin-free days at an acceptable and not significantly different level of cost-effectiveness (Doran 2005; Harris, Gospodarevskaya, and Ritter 2005).

A cost-effectiveness analysis of MMT and BMT was conducted in LMICs as part of the second edition of *Disease Control Priorities in Developing Countries* (Hall and others 2006). This analysis found that MMT was a more cost-effective option than BMT, with a year of healthy life generated for less than US$1,000 in the lower prevalence settings (including Sub-Saharan Africa) and for US$1,000–US$10,000 elsewhere. In LMICs, where HIV is being spread by injecting drug users, MMT programs can be an effective and cost-effective strategy for prevention, as indicated in a study in Belarus, where the average cost per HIV infection averted was less than US$500 (Kumaranayake and others 2004).

IMPLICATIONS FOR LOW- AND MIDDLE-INCOME COUNTRIES

Most of the research on drug dependence, its disease burden, and its societal harm has been conducted in HICs. To translate these findings into disease control priorities for LMICs, we examine three sets of issues: country-specific variations in illicit drug use and disease burden, countries' health care infrastructure and capacity, and varying cultural attitudes toward drug problems and treatments.

Issues for Assessment

Illicit Drug Use and Disease Burden

Countries differ in the scale of illicit drug use and the disease burden. This variation may reflect differences in the prevalence of injecting versus non-injecting opioid and stimulant use; users' access to health services for treating overdoses, BBVs, and other complications of drug use; access to preventive interventions for HIV and other BBV infections, such as needle and syringe programs (Mathers and others 2010); and the extent to which illicit drug use is concentrated in socially disadvantaged groups. Many LMICs lack the research infrastructure to assess the use of illicit drugs and its harm and to evaluate the effectiveness of interventions.

Health Care Infrastructure and Capacity

Societal wealth and the extent of health care infrastructure affect the capacity of countries to respond to illicit drug dependence. For example, a country's capacity to provide OST is affected by the cost of opioid drugs and the nonexistence of infrastructure to deliver OST effectively and safely. This infrastructure would include, for example, specialist drug treatment centers; trained medical, nursing, and pharmacy staff; and a drug regulatory system. In HICs, the treatment delivery infrastructure includes medically trained staff and community-based pharmacists to prescribe and dispense these drugs and control systems for the distribution of substitute opioids that minimize diversion and illicit use. There is little evidence to suggest the level of minimal infrastructure necessary to deliver these treatments safely and effectively is available in LMICs.

Medical versus Moral Models of Addiction

A society's response to illicit drug use is affected by cultural attitudes and beliefs, including the dominant views on illicit drug use and the governing cultural images of drug dependence (Gerstein and Harwood 1990). A critical determinant is the relative dominance of moral and medical understandings of drug dependence.

A moral model of addiction sees drug use as largely voluntary and addiction as an excuse for bad behavior that allows drug users to continue without assuming responsibility for their conduct (Szasz 2003). According to the moral view, drug users who offend against the criminal code should be imprisoned (Szasz 2003). A medical model of addiction recognizes that some users lose control over their use and develop a mental or physical disorder—an addiction—that requires specific treatment to become and remain abstinent (Leshner 1997).

The competition between the medical and moral perspectives is not resolved in either HICs or LMICs. These competing views affect the societal preference for and acceptability of certain interventions, especially OST and abstinence-oriented approaches (Cohen 2003).

Research Needs

HICs and LMICs need better estimates of the prevalence of dependence. LMICs, in particular, need well-designed prospective studies of mortality and morbidity among illicit drug users, especially in countries with high rates of HIV infection and recent substantial increases in drug-related problems.

LMICs also need randomized controlled trials and economic and outcome evaluations of treatments for illicit drug dependence. Comparative data on efficacy and cost-effectiveness are essential to judge the applicability of findings in HICs to LMICs. The research needs to include LMIC-specific evaluation of a range of interventions, including self-help, abstinence-based approaches, and oral OST.

It is particularly important to assess the effectiveness and safety of treatment delivery modifications in LMICs that lack the quality of health care infrastructure found in HICs. Such studies may also identify novel and cheaper ways to deliver these treatments in lower-resource settings.

Potential New Treatments

New treatments and improved forms of existing treatments could improve the modest outcomes of treatment for illicit drug dependence. Technological advances are enabling researchers to develop ultra-long-acting implants or injectable depot formulations of drugs. These might overcome, at least in part, the major problem of poor medication adherence and dropout.

OST trials are exploring the potential for greater therapeutic gain using depot buprenorphine lasting at least a month, implant buprenorphine lasting at least six months, and ultra-long-lasting formulations of the opiate antagonist naltrexone as either depot injections (lasting a month) or implant (lasting several months).

Additional benefit might come from exploring existing medications or new formulations that are not yet widely considered in the addiction treatment field. For example, several European countries have prescribed slow-release morphine as an alternative opioid maintenance treatment.

Finally, health care providers could deliver existing treatments less expensively, thereby reaching a larger proportion of opioid-dependent people. Buprenorphine maintenance treatment is equally effective whether given in a first-level facility or a third-level facility in Australia (Gibson and others 2003).

CONCLUSIONS AND RECOMMENDATIONS

Illicit drug use contributes to premature mortality and morbidity on a global scale. The substantial economic costs include the health care costs of managing dependence; treating drug overdoses; and addressing the complications of BBV infections, such as HIV and hepatitis C. Illicit drug dependence also generates substantial externalities that the burden of disease estimates do not include, principally, high law enforcement costs in dealing with drug dealing, property crime, and loss of public amenities (such as clean, pleasant, and quality public infrastructure and environments).

The most popular interventions in HICs have involved law enforcement to interdict drug supply and arrest individuals for the possession, use, and sale of opioid drugs. Consequently, imprisonment for drug or property offenses is the primary intervention for most users. Treatment interventions hold the greatest promise for long-term effectiveness.

The most commonly available interventions for dependence have been medically supervised detoxification and drug-free (abstinence) approaches. OST is available in many countries, but coverage is typically poor (Mathers and others 2010). Opioid antagonists have a niche role in the maintenance treatment of opioid dependence, but suffer from poor compliance and probably increase the risk of overdose on return to heroin use. Their efficacy may improve with the development of long-acting depot formulations, but the evidence remains limited (Larney, Gowing, and others 2014; Lobmaier and others 2008).

Most of the limited research on the effectiveness and cost-effectiveness of interventions for illicit opioid dependence has been conducted in HICs. Three broad sets of issues affect the way in which these findings can be translated into disease control priorities in LMICs:

- Countries will differ in the scale of illicit drug use and the burden that it causes.
- Societal wealth and health care infrastructure will affect the capacity of LMIC societies to respond to illicit drug dependence.
- Countries' responses will be affected by cultural preferences for moral and medical understandings of drug dependence.

Multiple interventions have been shown to have an impact on illicit drug use and dependence, ranging from preventive interventions with young people to medication-assisted interventions with people who are opioid dependent. The challenge is to ensure that these efficacious interventions are delivered to scale, while minimizing the use of interventions that are not effective.

NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  a) Lower-middle-income = US$1,046 to US$4,125
  b) Upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

1. Illicit drugs are defined as those covered by international drug control treaties such as the Single Convention on Narcotic Drugs (United Nations General Assembly 1972).
2. "Novel psychoactive substances" refer to psychoactive substances not under international control that pose a health threat. They include substances such as ketamine, synthetic cannabinoids in various herbal mixtures, piperazines (such as N-benzylpiperazine [BZP]), products marketed as "bath salts" (cathinone-type substances such as mephedrone and methylenedioxypyrovalerone [MDPV]), and various phenethlamines (UNODC 2013).
3. "Precursor chemicals" refer to chemicals that are used in the manufacture of illicit drugs such as cocaine (for example, potassium permanganate, ethyl ether, and hydrochloric acid), heroin (acetic anhydride, ammonium chloride, ergot alkaloids, and lysergic acid), and ATSs (ephedrine and pseudoephedrine). Control measures for such chemicals typically involve regulations on their sale and distribution domestically and internationally, often requiring chemical producers to register with drug enforcement agencies and keep records of sales and customers. Communication and intelligence-gathering platforms (such as the Precursors Incident Communication System) are also used to alert governments of suspicious shipments, seizures, and actual and attempted diversions of precursors, and to identify emerging precursors (INCB 2014).
4. "Internalizing disorders" are mental disorders where the persons suffering from the disorder keep the problem to themselves, or "internalize it." Common examples include depression, withdrawal, and anxiety. "Externalizing disorders" are mental disorders that comprise negative behaviors that are directed toward the external environment (such as aggression and violence), including attention-deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder (APA 2000).
5. "Polydrug use" refers to the use of more than one drug or type of drug by an individual, consumed at the same time or sequentially. Polydrug use has several functions, including maximizing drug effects, balancing or controlling negative effects, and substituting the sought-after effects of a primary drug when supply is low (WHO 1993).
6. A narcotic antagonist is a receptor antagonist that binds to narcotic receptors, effectively preventing the body from responding to narcotics.

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