Addiction 2



Drug policy and the public good: evidence for effective interventions

John Strang, Thomas Babor, Jonathan Caulkins, Benedikt Fischer, David Foxcroft, Keith Humphreys

Debates about which policy initiatives can prevent or reduce the damage that illicit drugs cause to the public good are rarely informed by scientific evidence. Fortunately, evidence-based interventions are increasingly being identified that are capable of making drugs less available, reducing violence in drug markets, lessening misuse of legal pharmaceuticals, preventing drug use initiation in young people, and reducing drug use and its consequences in established drug users. We review relevant evidence and outline the likely effects of fuller implementation of existing interventions. The reasoning behind the final decisions for action might be of a non-scientific nature, focused more on what the public and policy-makers deem of value. Nevertheless, important opportunities exist for science to inform these deliberations and guide the selection of policies that maximise the public good.

Introduction

Illicit drugs are a substantial threat to the public good, not only because they adversely affect public health, but also because they can generate crime, disorder, family breakdown, and community decay. The diverse policies and programmes to ameliorate these problems vary substantially in their effectiveness. Here we review effective interventions to draw attention to the drug-control policies available to governments, in much the same ways as evidence has contributed to debates about more effective tobacco and alcohol policies.

Building on the first paper in this series,1 which assessed the extent to which illicit drug use contributes to the global burden of disease, we critically assess the scientific basis of interventions intended to prevent or at least minimise the damage that illicit drugs do to the public good. We examine the quality of evidence for different policies, estimate the likely magnitude of their effects, assess potential unintended consequences, and identify promising areas for future investment into research and interventions. We can thus help policy makers make informed decisions about which policy options will maximise the public good. By the public good we refer to social benefits such as better public health, reduced crime, and greater stability and quality of life for families and neighbourhoods. Contemporary drug-related public policy attempts to promote the public good through a broad range of administrative actions designed to prevent the initiation of drug use by non-users, help heavy drug users change their behaviour or reduce the consequences of their drug use, and control the supply of illicit drugs (and the supply of diverted prescription drugs used for non-medical purposes) through laws, regulations, and enforcement.

Much public debate in drug policy is only minimally informed by scientific evidence. Values and political processes (eg, voting) are important drivers of drug policy, but evidence of effectiveness and cost-effectiveness can help the public and policy makers to select policies that best achieve agreed goals.

For the formulation of drug policy, coordination of different methods of study and analysis from different scientific subject areas is needed. Interpretation of this evidence will depend not only on study design and magnitude of effect, but also on the relevance and generalisability of the findings. In addition to the assessment of new interventions and strategies, examination of the costs and benefits of policy measures that might mistakenly be assumed effective is also important.

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See Editorial page 2

See Perspectives pages 20 and 22

This is the second in a **Series** of three papers about addiction

King's College London, National Addiction Centre, London, UK (Prof I Strang MD); Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington, CT, USA (Prof T Babor PhD); Carnegie Mellon University, Heinz College, Pittsburgh, PA, USA, and Qatar Campus, Doha, Qatar (Prof | Caulkins PhD); Centre for Applied Research in Mental **Health and Addictions** (CARMHA), Faculty of Health Sciences, Simon Fraser University, Vancouver, BC, and

Key messages

- Drug policy should aim to promote the public good by improving individual and public health, neighbourhood safety, and community and family cohesion, and by reducing crime.
- The effectiveness of most drug supply control policies is unknown because little
 assessment has been done, and very little evidence exists for the effectiveness of
 alternative development programmes in source countries.
- Supply controls can result in higher drug prices, which can reduce drug initiation and
 use but these changes can be difficult to maintain.
- Wide-scale arrests and imprisonments have restricted effectiveness, but drug testing
 of individuals under criminal justice supervision, accompanied by specific,
 immediate, and brief sentences (eg, overnight), produce substantial reductions in
 drug use and offending.
- Prescription regimens minimise but do not eliminate non-medical use of psychoactive prescription drugs. Prescription monitoring systems can reduce inappropriate prescribing.
- Screening and brief intervention programmes have, on average, only small effects, but
 can be widely applied and are probably cost-effective.
- The collective value of school, family, and community prevention programmes is appraised differently by different stakeholders.
- The provision of opiate substitution therapy for addicted individuals has strong
 evidence of effectiveness, although poor quality of provision reduces benefit.
 Peer-based self-help organisations are strongly championed and widely available, but
 have been poorly researched until the past two decades.
- Health and social services for drug users covering a range of treatments, including needle
 and syringe exchange programmes, improve drug users' health and benefit the broader
 community by reducing transmission of and mortality due to infectious disease.

Centre for Addiction and Mental Health, Toronto, ON, Canada (Prof B Fischer PhD); Oxford Brookes University, Oxford, WK (Prof D Foxcroft PhD); and Department of Veterans Affairs, Stanford University, Palo Alto, CA, USA (Prof K Humphreys PhD)

Correspondence to: Prof J Strang, Addiction Sciences Building, 4 Windsor Walk, Denmark Hill, London, SE5 8BB, UK john.strang@kcl.ac.uk

Search strategy and selection criteria

We used several search strategies with special attention to publicly available reviews of interventions for which sufficient well designed studies have been done to allow rigorous reviews such as by the Cochrane Collaboration or by the National Institute for Health and Clinical Excellence (NICE). We included reviews done for the 2010 report Drug Policy and the Public Good, which used an internal peer-review process to assess the relevance of the work to public policy, and to gauge the scientific strength of the evidence, supplemented by repeat search in June, 2010, of literature databases Medline, PsycINFO, and BioMed Central, as well as specialist databases including the US National Institute of Drug Abuse and England's National Treatment Agency, Drug and Alcohol Findings, and DrugScope, for additional randomised trials. We searched for studies in English; studies in other languages were considered only if identified in our search or if authors were previously aware of them. We used search terms including "prevention", "schools", "policy", "courts", "prison", "detoxification", "maintenance", "methadone", "buprenorphine", "naltrexone", and "prescription". We also requested relevant material from key experts and organisations. Peer-reviewed articles were initially assessed by their titles and abstracts—we reviewed in full all peer-reviewed articles identified as potentially relevant.

We examine evidence of good scientific quality that can inform decision-making about drug policies that can be introduced, modified, expanded, reduced, or stopped. This includes scientific evidence for the likely benefits to the public good. Some of the evidence comes from randomised trials and quasi-experimental designs with similar control conditions.

We also consider other types of evidence when randomised controlled trials could not be implemented or would be politically challenging to implement. This includes natural policy experiments (ie, observational studies done to assess the effect of policy interventions) and time-series analyses. In some policy domains, such studies provide the best available scientific evidence. For each of the five broad policy approaches that we discuss, we first identify the relevant activity, and also the objective (table 1).

Supply control

Illicit drugs are ultimately consumer goods, typically produced and distributed through illegal markets operated by people motivated by profit. The goal of supply control programmes is to reduce access to drugs by interfering with drug suppliers' activities.

The unit of analysis in the assessment of supply control is the market, typically in a city, region, or country. Randomised controlled trials are sometimes possible at the level of neighbourhood markets, but become increasingly impractical for national or regional markets. Most of what is known about supply control comes from natural experiments, case studies, and economic analyses that test theories developed in other contexts, thus limiting the strength of evidence available on the effectiveness of supply-side interventions (table 2).

Ideally, effective supply control would make a drug so scarce that users could not find suppliers without great difficulty or expense. The policy objective in the case of non-users is to reduce exposure to drug sellers, which can be achieved in some circumstances. For most of the 20th century, heroin was largely absent from smaller towns and rural areas in the USA and for whole countries elsewhere in the world. Even at present, cocaine is not readily available in many parts of Asia.

Drug markets are more difficult to suppress when they become established. Drug prices can be kept high (when price takes account of purity as well as volume). Product illegality and law enforcement, even at low levels, increase costs. For example, the illegal shipment of a kilogram of cocaine from Colombia to the USA or Europe costs US\$10 000–15 000, whereas a package delivery service can deliver a kilogram of a legal product for \$50.2

Law enforcement also creates risks for sellers directly (arrest and incarceration) and indirectly (eg, being defrauded without legal recourse for compensation). Drug market operators, therefore, receive far greater

	Targeted policy	Broad policy goals
Supply control	Arrest traffickers and dealers; force suppliers to operate in inefficient ways	Keep prices high; reduce availability
Criminal sanctions	Apply penalties for drug possession and use Deter drug use; prevent normalisation of drug use Identify problem drug users and divert into treatment Success at identification and diversion (overlap with evidence in treatment)	
Controls on prescription drugs	Regulate pharmaceutical companies; restrict pharmacists and physicians to approved treatments	Allow drugs for approved purposes; prevent use for non-approved purposes
Prevention	Drug prevention programmes in schools and mass media campaigns	Improve health knowledge, change attitudes, and prevent drug use
Health and social services for drug users	Attract problem drug users into treatment; enable them to reduce and quit their drug use; and facilitate their recovery and rehabilitation	Stabilise and improve health, reduce overdose deaths, prevent spread of HIV and other infection also reduce crime

monetary compensation than do people engaging in legal markets.³ The distribution system passes these costs on to users via higher drug prices.

Empirical evidence supports five broad conclusions about the effectiveness of supply control in keeping prices high. First, if law enforcement can keep prices high, drug initiation and use will be reduced. Many empirical studies show that indicators of problem drug use, such as records from emergency departments and arrestees' urinalysis results, respond to changes in purity-adjusted prices. Second, illegality and some basic level of enforcement makes illicit drugs far more expensive at retail in developed countries than plausible estimates of the cost of their production and distribution would suggest. Cocaine and heroin are semi-refined agricultural products

that retail for many times their weight in gold—their legal, untaxed price would be like that of coffee.⁵

Third, modelling studies, such as those pioneered at RAND,⁶ have consistently shown that increasing imprisonment is a very expensive way to increase prices in established drug markets—findings from empirical studies are generally not encouraging about the potential success of such control methods. For example, Kuziemko and Levitt⁷ estimate that an increase in the number of prisoners detained on drug-related offences in the USA from 82 000 to 376 000 between 1985 and 1996 increased retail cocaine prices by only 5–15%. Fourth, very little evidence exists for the effectiveness of alternative development programmes in source countries, and no evidence exists that they affect the availability or price of

	Effectiveness	Amount of research support and cross-national testing	Comments
Alternative development in drug-producing countries	No documented correlation with reduced drug use in a final-market country	Programmes in most major source countries have been assessed qualitatively	Alternative development takes time to reduce production, allowing other regions to increase production. Cost is very high
Crop eradication	Typically no recordable effect on downstream markets, but has sometimes created a temporary disruption	Eradication or bans in Mexico, Turkey, and Afghanistan coincident with reductions in downstream supply	Production often shifts to other growing regions. Costs include alienation of farmers whose crops are disrupted
Controls on precursor chemicals	Good evidence for temporary disruption in drug market	Several studies in the USA and Canada	Cheap to initiate through legal statutes but enforcement can be costly. New production materials then used or producers move to other countries
Interdiction	Can disrupt drug market and supply chain, and thus keep retail price of drugs up	Several studies involving the USA and cocaine-producing and transhipment countries	Drug price increases compared with equivalent legal-market prices, suggesting important benefits of small investments but little evidence of a dose-response effect. Interdiction programmes are costly to implement but some aspects have efficiences with other border control efforts
High-level enforcement through criminal investigations	Price mark-ups suggest important benefits of small investments but little evidence of a dose-response effect	Only a few studies have been done	Incarcerating high-level dealers can be more cost-effective than enforcement against retail sellers because retail sellers can easily be replaced, but no head-to-head empirical tests of relative cost-effectiveness exist
Street-level enforcement	Stronger evidence of ability to suppress flagrant use of drugs and market-related harms than to reduce drug use	Only a few studies done outside the USA	Conventional approaches can be very costly to implement and sustain. However, case studies are available of more modern approaches that yield success with far fewer arrests and incarcerations
Imprisonment	Some evidence but diminishing returns from imprisonment beyond specific levels	Only a few investigations done outside the USA or the UK	Expensive to manage prison system and community re-engagement services
Non-criminal penalties imposed for cannabis use and possession	Small or no effect on cannabis use, although reduces adverse consequences for users	Several Australian and US studies	Some benefits to criminal justice system with contested effect on cannabis use and related problems
Reduction of the level of criminal penalties (mainly for cannabis use offences)	Moderate or no effects on cannabis use	Contested evidence from the USA, the Netherlands, and Switzerland	Some benefits to criminal justice system
Diversion to mandated education or treatment	Little effect on cannabis-related problems	Several Portuguese and US studies	Diversion saved money in California, USA
Legalisation (to all intents and purposes) of a controlled retail cannabis market	Circumstantial evidence that the Dutch system might be effective in the separation of cannabis from other drug markets	Several assessment studies in the Netherlands, but no well-controlled research	Effects on cannabis consumption are contested bu Dutch use rates are low compared with other European countries
lo interventions in this table have beer argely on cannabis. Adapted from refer		uch assessments are unlikely to be c	done. Studies of changes in criminal penalties have focus

drugs in final-market countries (although they can possibly trigger a shift in location of production).²

Fifth, supply shocks can substantially reduce drug availability, purity, use, and harms in consumer countries-eg, metamfetamine precursor controls,8 the Taliban opium ban,9 the 1989-90 war on Colombian drug traffickers,10 and the Australian heroin shortage.11 These successes often stem from a convergence of fortuitous circumstances that governments can rarely reproduce by design. Occasionally they follow deliberate actions such as introduction of legislation to regulate precursor chemicals involved in illicit drug preparation,12 although results are not always predictable or simply generalisable.13 However, their success lasts for only as long as it takes the market to adapt. Many attempts to disrupt supply produce no detectable effects.14 Their effects on drug users can sometimes be adverse¹⁵ and sometimes beneficial;16 the difference is probably related to age, regularity, and disadvantage of the users. 11,16 The costeffectiveness of these efforts is not easily assessed.

Distinct from reducing supply, law enforcement can seek to manage the collateral harms from illicit markets, such as drug-selling and violence on street-corners. When police target high-visibility dealing, markets often re-emerge in a different place or form. Such difficulties limit the effect of law enforcement on drug use but can reduce market-related harms.17 Drugs can be distributed by violent gangs that corrupt officials, terrorise neighbours, and employ children as look-outs. They can also be distributed surreptitiously, behind closed doors through social networks. A policy that discourages more socially harmful dealing practices can reduce harm and improve community amenity. This approach has been used to reduce flagrant selling of illicit drugs (eg, in High Point, NC, USA)18 and drug-related violence (eg, in Boston, MA, USA).19

A second additional function of law enforcement is to enforce laws against drug users. Enormous variation exists in how harshly countries apply these laws and to which substances. Some countries have reputations for toughness (Singapore, Saudi Arabia, or China immediately after the 1949 revolution), whereas, in many countries, users are rarely imprisoned for drug use, even when such sentences are allowed in law.

The distinction between drug use and involvement in drug-selling or distribution is often unclear. In the USA, more than 90% of people imprisoned for drug-law violations admit playing some—perhaps minor—part in drug distribution.²⁰ And the law enforcement response also varies greatly, with other sanctions used that do not include imprisonment—namely, arrest, fines, community service, brief incarcerations, and loss of benefits—eg, eligibility for school athletic programmes or public housing.

Drug users' risks of arrest and the consequences of arrest vary substantially between countries. Research on the effect of these variations is sparse and of poor quality. Most studies have been of the effects of cannabis decriminalisation, ²¹ but are methodologically weak, often involving comparisons of prevalence before and after law changes that treat decriminalisation as a binary variable. ²² Interpretations of the evidence are contested, but, evidence that tougher sanctions deter drug use or criminal offending more generally is, at best, weak. ²³

By contrast, increasing evidence shows that specific, immediate, and brief sentences (eg, overnight) for positive drug tests produce substantial reductions in drug use and offending in individuals who are under criminal justice supervision.²⁴ The typical setting for such coerced or mandated abstinence is in offenders on community release (before trial, on probation, or on parole). They are drug tested at least once a week (sometimes once a day or even twice a day), with the typical sanction for a missed or drug-positive test being 24 h in jail.²⁵ Evidence for such mandated abstinence programmes comes from drug and drink-driving offenders on community release^{25,26} and programmes for addicted physicians and airline pilots.²⁷

A fourth function of law enforcement is to encourage drug users to enter and remain in treatment. Drug courts are one approach that can be more effective than suspended sentences or other diversion programmes in keeping clients in treatment.²⁸ However, the scale-up of this approach to community levels has been difficult. Many academics are sceptical about the ability of law enforcement to suppress drug use in established drug markets through supply control or user sanctions. Available evidence is more positive, however, about enforcement's capacity to reduce adverse collateral effects of drug markets, produce abstinence in closely supervised offenders, and improve uptake and retention in treatment (as seen without judicial intervention). See webappendix for further reading.

Prescription regimens to control pharmaceutical drugs

Many illicit drugs were originally created for medical use²⁹ and many are still used as such (eg, opioids). Prescription regimens are a widely used form of drug control in developed countries in which a physician prescribes a drug that is dispensed by a pharmacist. Such regimens are the outcomes of incremental policies first introduced about a century ago. Natural experiments provide useful lessons on the effectiveness of different prescription regimens in the control of psychoactive drugs (table 3).

In the past decade, misuse of sustained and slow-release prescription opioid analgesics (eg, oxycodone, hydrocodone, oral morphine) in the USA and Canada has increased. This change has been accompanied by increased morbidity (eg, emergency room and drug treatment admissions) and mortality (eg, accidental poisonings) since the early 1990s.³⁰⁻³²

Prescription regimens do not eliminate non-medical use of psychoactive prescription drugs. Sourcing of prescription drugs occurs through different forms of diversion—eg, double doctoring, prescription drug

See Online for webappendix

fraud, and thefts and robberies.^{33,34} Family and friends are also a primary source for individuals who use pharmaceuticals non-medically. Such sourcing patterns make the reduction of supply through traditional law enforcement difficult. The emergence of internet-based pharmacy services makes control even more difficult.^{35,36} The high availability and diversion of prescription opioid drugs in North America has led to the prescription of opioid analgesics to replace heroin in many injecting drug users.^{37,38}

Prescription monitoring systems can reduce irregular prescribing practices, but a balance is needed (eg, between the need for access to drugs for legitimate pain relief and the need to restrict access to deter inappropriate non-medicinal use). The introduction of a prescription-monitoring system for barbiturates (1981) and benzo-diazepines (1989) in New York State, USA, greatly reduced excessive prescription of these drugs. ^{39,40} In the UK in the 1970s, barbiturate prescription was reduced by more restrictive professional guidance (the Campaign on the Use and Restriction of Barbiturates initiative). Later, professional guidance to restrict long-term prescription of benzodiazepines led to substantial reduction in overall prescribing.

Monitoring and supervision are usually incorporated as integral elements of the provision of opioid substitution therapies (OSTs), with contingent relaxation of supervision requirements. An increased involvement of prescribed methadone in overdose deaths was recorded in the UK⁴¹ that was postulated to be caused by unsupervised methadone consumption. Supervised consumption was subsequently widely introduced⁴² and the involvement of methadone in overdose deaths reduced substantially thereafter.⁴³

Two caveats of this approach should be noted. First, reduced prescription of some drugs can be followed by increased use of other prescription drugs with similar effects. Second, any effort in this area has the potential to deny needed medications to ill individuals, and this concern should be balanced against concerns about abuse and diversion. See webappendix for further reading.

Prevention

Young people are an obvious and important focus for prevention because the period between being a child and being a young adult is when most people are initially exposed to drugs, and when they are most likely to initiate use. Ideally, preventive interventions should stop young people from starting drug use, but they can also delay initiation of drug use and prevent young people from becoming regular and dependent drug users.

Prevention programmes are often categorised by venue (school, media, community, primary health care, etc), but other categories exist: environmental interventions that limit the availability of dangerous substances, psychosocial developmental interventions, educational interventions

	Effectiveness	Amount of research support and cross-national testing	Comments
Change cost or reimbursement	Some evidence for an effect on drug prescribing	Most studies are from Canada. Single studies in Australia, Germany, Norway, Sweden, and the USA	Some evidence for analgesics when alternative drugs are available
Restrict OTC sales	Conflicting results from studies of overdoses	Three studies from Canada and the UK	No studies of psychoactive substances. Some evidence that OTC restrictions prevent analgesic health problems
Make available only with prescription (vs OTC availability)	Sparse research lends support to some effect	Studies in Sweden, the UK, and the USA of non-psychoactive substances; one study in Chile of a psychoactive substance	Changing a drug between OTC and prescription states has varying effects on sales. In some systems, the consumer pays more for an OTC drug
Authoritative advice to physicians on adverse effects	Some evidence of effects when another drug is available	Six studies from Australia Canada, the UK, and the USA	Some evidence that advice to physicians changes prescribing behaviour, but no studies o psychoactive pharmaceuticals
Prescription restrictions, registers, monitoring	Good evidence that registers and monitoring reduces prescription of targeted drugs and reduces adverse events	Many studies from various European and North American countries	Although prescription of targeted drugs is reduced, there is risk of substitution of drugs that are equally or even more harmful
Restrict list of prescribers	Very little published research	Individual studies in Iran and the UK identified positive effects	In need of further replication studies
Withdraw prescription availability	Good evidence for the reduction of prescribing and use of the drug	Studies from various European countries, Australia, and the USA	Replacement drugs can carry additional risks
Controls on administering OST	Some effects in the reduction of overdoses from supervised OST	Studies in Australia, Denmark, the UK, and the USA	Some evidence for reduced diversion
OST=opioid substitution therapy. OTC=0	over-the-counter. Adapted from reference	22.	

that aim to raise awareness and knowledge of the adverse effects of drugs, and screening and brief intervention programmes in health settings. Psychosocial developmental and educational interventions—approaches aimed at reducing demand—have been a mainstay of national drug prevention policies in many countries for many years. Although evidence is strongest in the context of schoolbased programmes, Cochrane systematic reviews of randomised controlled assessments^{44,45} and other high quality reviews show that psychosocial developmental interventions can be effective, whereas knowledge and awareness are generally ineffective for prevention of use of illicit drugs,^{44,46} tobacco, and alcohol (table 4).

The ineffectiveness of didactic educational tactics is a serious challenge for mass media approaches and also many traditional community and classroom programmes. For example, Drug Abuse Resistance Education (DARE) is a school-based preventive intervention widely adopted in the USA in which police officers provide classroom advice on the dangers of drug use. In many studies it has been shown to neither prevent nor delay drug use. Ikiewise a large-scale assessment of a mass media campaign to prevent cannabis use also showed that it had, at best, no effect, and possibly increased use.

Not all psychosocial interventions fare well in assessments, but findings from a few high quality studies

indicate that some family-based and classroom interventions can reduce drug or alcohol use. These interventions do not focus exclusively or specifically on drug or alcohol use; they aim to develop pro-social behaviour and social skills more generally, and they have benefits beyond the reduction of drug or alcohol misuse, such as the reduction of violence and mental health problems. Three interventions aimed at drug-use prevention for which supportive research evidence exists are the Strengthening Families Programme for young people aged 10-14 years and their parents (SFP10-14), social or life skills training, and the Good Behaviour Game.2 The Good Behaviour Game, a classroom behaviour management approach delivered in some primary and elementary schools in the USA and some countries in Europe when children are aged 5–7 years, has reported positive outcomes 15 years after intervention, when young people were aged 20-21 years.48 There are also tactics, such as correcting young people's misperceptions about how common drug use is, that have been shown to be effective.

Beyond primary prevention,⁴⁹ research from several countries (Australia, Brazil, India, and the USA) has examined the secondary prevention of substance misuse, based on screening and brief intervention in primary care and other settings. Brief intervention in a clinical setting can reduce cocaine and heroin use, even without meaningful contact with the treatment system.⁴⁹

	Effectiveness	Amount of research support and cross-national testing	Comments
Family or parenting programmes	Some studies show effectiveness in the reduction of the onset of drug use	A few studies done in the USA only	Positive findings for the universal Strengthening Families Programme for people aged 10–14 years and their parents with longer-term follow-up and cost-effectiveness analysis. Replication needed. Assessments of other family or parenting programmes have not been as positive
Environmental or classroom management programmes	Some evidence in support of the Good Behaviour Game	A few studies done in the USA, the Netherlands, and Belgium	In one study, the Good Behaviour Game reduced lifetime drug misuse by up to 50% in boys 14 years after the programme, with stronger effects with boys identified when aged 6 years as highly aggressive and disruptive. One US study did not replicate this outcome; Dutch and Belgian studies show promising short-term effects
Social or life skills	Short-term effectiveness is equivocal. Some evidence of positive effect in the medium to longer term	Several high-quality studies done in the USA only	A few assessments have shown positive intervention effects from a small set of prevention programmes for cannabis use and the use of other drugs
Multi-component community	No evidence of effectiveness	Only a few small USA studies	Studies have typically combined school and non-school approaches. Effect sizes tend to be small or negligible
Information about adverse drug effects only	No evidence of effectiveness	A few school-based studies done in the USA	Few well controlled studies—but many uncontrolled assessments—have been done
Mass media	No evidence of effectiveness	Research restricted to a few studies in the USA	Few high-quality scientific assessments
Drug Abuse Resistance Education (DARE)	No evidence of effectiveness	Several well controlled studies and many uncontrolled assessments	Despite DARE's widespread use, meta-analyses show that the programme is ineffective
Adapted from reference 2.			

One session of motivational interviewing with drugtaking college students led to pronounced reductions in their use of cannabis, alcohol, and tobacco. 50 Provision of a self-help booklet and one session of motivational interviewing reduced amphetamine consumption in regular users.⁵¹ Two studies^{52,53} noted that general practitioners can reduce excessive benzodiazepine use in their patients with brief interventions such as letters or consultations. In a large cross-national trial of brief intervention with drug users, Humeniuk and coleagues⁵⁴ recorded substantial reductions in illicit drug use after one brief intervention in primary care settings. With school-age adolescents, screening and personalitytargeted coping skills greatly reduced initiation and the frequency of drug use.55 However, benefits might deteriorate over time⁵⁶ and other investigators have reported negative findings.⁵⁷ Findings from attempts to implement these interventions on a wider scale have been mixed.58-60

Each society needs to make a political judgment about whether the small to medium-sized effects of psychosocial developmental interventions are worth the cost of delivering them. ⁶¹ Economic analyses suggest that these interventions are cost-effective because the lifetime benefits of even slightly lower rates of early drug or alcohol use are substantial. See webappendix for further reading.

Health and social services for drug users

This section covers all interventions designed to change the behaviour of drug users for their benefit and the benefit of others affected by their drug use—ie, family members, neighbours, and colleagues. It includes addiction treatments that enable and support abstinence, health services that aim to reduce the amount and frequency of drug use and the harms arising from it, and interventions to change behaviours that are harmful to the individual and society—eg, behaviours that increase risks of HIV infection, drug overdose, and drug-related crime.

How these interventions are organised and delivered is important. No matter how efficacious a treatment might be, it will produce little benefit to individuals and society if it is inaccessible, or if it is provided in a way that discourages help-seeking behaviour or reduces retention in care. Much better results are achieved by well organised programmes with more comprehensive services. ^{62,63} The difference in benefits between the best and worst programmes can be very large but the reasons for these differences are unclear.

"Treatment works" is an often-quoted mantra intended to alert health professionals and the public to the benefits of addiction treatment. But this is not true of all types of intervention for all problem drug users. The treatment with the strongest evidence of efficacy is substitution treatment for addiction to heroin and other opioids (table 5). Evidence is much weaker for treatment of problem use of other drugs (such as cocaine, crack cocaine, methamfetamine). Some non-pharma-

cological approaches described below have efficacy across different forms of substance abuse.

OSTs are the most extensively studied and controversial forms of treatment.⁶³⁻⁶⁵ They consist of the regular provision of a prescribed replacement supply of opioid drug, usually in longer-acting oral form to avoid swings between intoxication and withdrawal. They are usually taken under direct supervision (especially during the early stages of treatment).

These forms of treatment can enable a person to establish a healthier lifestyle, which, for some individuals, is the main benefit of treatment—for others, having a healthier lifestyle can lead to sustained abstinence from use of illicit drugs. OST has mostly been studied with oral methadone or sublingual buprenorphine,64 although other drugs have been used with benefit, but with a smaller evidence base. 66-69 Attrition and relapse are major challenges. 64,65 Retention in OST is generally better with methadone than it is with buprenorphine, 64,65 whereas drug-free urine (indicating quitting heroin) is generally better with buprenorphine. 64,65 An adaption during the past decade has been a buprenorphine and naloxone combination tablet, which has been developed to reduce potential for intravenous misuse—the extent of extra benefit has not yet been established. These substitution approaches have repeatedly been shown in studies in many countries to produce a wide range of benefits in the reduction of heroin use, overdose mortality, HIV transmission, and crime. 64,70-72 The greatest benefits are seen when treatment is optimised with adequate drug doses and ancillary treatments and support, 62-64,70,72 although some benefit is seen even with low dose and minimum support.62,72

Several other types of medication are available, but do not have the same strength of evidence as OST. Naltrexone (oral) is a highly efficient opioid antagonist that can support abstinence and prevent relapse in the event of further instances of heroin use. However, its use is rare because adherence is often poor,^{73,74} even though better results can be achieved when given under supervision or with behavioural reinforcement.⁷³ Both implantable and injectable sustained-release versions of naltrexone have been developed to circumvent this adherence problem, with positive initial results.

Sustained-release versions of OST have been explored, including long-acting oral levo-alpha-acetylmethadol (subsequently withdrawn after concern about QT prolongation), high-dose sublingual buprenorphine to enable dosing three times a week, and pilot formulations of long-acting depot injection and ultra-long-acting implant of buprenorphine (see webappendix for references on sustained release OST).

A supervised injectable treatment with maintenance doses of supervised diamorphine (pharmaceutical heroin) has been studied in randomised trials in several countries, for the treatment of refractory chronic heroin addicts, with positive findings. ^{68,69}

The provision of emergency naloxone (injection) to prevent heroin overdose death (while waiting for an ambulance) has been introduced in some countries, including the training of users⁷⁵ and families in emergency resuscitation,⁷⁶ but evidence is thus far observational. The prescribing of stimulant substitution treatment for cocaine and amphetamine addiction has been piloted,⁷⁷ but retention has been very poor and reliable evidence of its benefit is scarce. Vaccination against the specific drug has become technically feasible and is being tested against cocaine, but with unclear results thus far.⁷⁸

Behavioural and psychosocial interventions, unlike OST, are not confined to problem users of any particular drug, and include therapeutic communities, contingency management, and brief interventions. Observational evidence shows the effectiveness of residential rehabilitation, with either a 12-step or therapeutic community orientation. The However, few randomised trials have been done. Longer retention in treatment is associated with better outcome but the direction of causality is unclear. No clear evidence exists from randomised trials of a benefit from longer duration of programmmes or from residential versus day care, Linduply a large prospective observational study recorded slightly greater benefit from 12-step versus relapse-prevention cognitive behavioural treatment or eclectic approaches.

	Effectiveness	Amount of research support and cross-national testing	Comments
Methadone or buprenorphine opioid substitution treatment (OST) maintenance	Good evidence for reduced mortality, heroin use, other drug use, crime, HIV infection, and hepatitis	Studies done in many countries, including Australia, China, France, Germany, Indonesia, Italy, Iran, Lithuania, Malaysia, Poland, Spain, Sweden, Switzerland, Thailand, Ukraine, UK, and USA	Appropriate for opiate users only. Combination with psychosocial services enhances outcome. Cost-effectiveness is high relative to other treatme interventions. The evidence-base is slightly strong for methadone. The buprenorphine evidence-base might change after release of a buprenorphine plus naloxone combination formulation
Slow-release oral morphine OST maintenance	Few studies, but produces similar benefit to methadone OST	Trial data mostly from Austria, plus exploratory studies from Australia	In Austria, slow-release oral morphine OST is used well as methadone OST. It might have value for patients for whom methadone OST is not benefic
Heroin (diamorphine) OST maintenance	Evidence of effectiveness in reducing or stopping use of street heroin in individuals who do not respond to oral OST	Demonstration programmes and randomised clinical trials in Switzerland, the Netherlands, Germany, Canada, and the UK	Appropriate for opiate users only. Randomised tria have consistently shown positive results with this population, but heroin OST is the most expensive form of OST and is usually reserved for dependent users who have not responded to oral OST
Oral opiate antagonists (eg, naltrexone) maintenance	Some evidence for reduced opiate use but compliance to treatment is a major limitation	Few studies outside of the USA	Targeted at opiate users, less than 20% of whom a willing to try this treatment. Oral naltrexone studie are of poor methodological quality and do not lensupport to the potential effectiveness of the treatment
Needle exchange programme (NEP)	Observational evidence that NEPs can reduce HIV infections and enable treatment engagement	Most research done in Canada, the UK, Australia, and the USA	Targeted at injecting drug users. Might prevent HIV infections but have no evidence of reducing Hepatitis C infections. NEPs have never been asses by a randomised clinical trial
Psychosocial treatment	Good evidence for reducing drug use, drug-related problems, and criminal activity	Studies in most high-income countries and many low-income and middle-income countries, including India, Mexico, and Peru	Appropriate for individuals using a range of drugs administration routes. Can be combined with pharmaceutical treatment and delivered in outpat and residential settings in group or individual form
Behavioural family-based and couple-based treatment	Several randomised trials show improved retention and benefit during treatment for heroin or cocaine addiction	Research evidence is mostly from the USA	Not widely applied in the USA, not tested in other cultures
Residential drug-free rehabilitation houses	Very few randomised trials. Longer duration of residence associated with better outcome, although randomised trials show equal benefit from shorter programmes with follow-up or with similar day care	Only moderate quantity of good-quality research evidence, despite long history of provision	Extensively provided around the world in different forms, some based on programmatic therapeutic communities, some based on 12-step rehabilitation and recovery, and some based around religious communities
Peer self-help organisations	Good evidence for the reduction of drug use and crime	Evidence available from a range of countries as diverse as the USA, the UK, Iran, and China	Highly cost effective. Probably the most widely available method of treatment globally
Brief interventions in general medical settings	Good evidence for reducing drug use by at-risk drug users	Evidence available from the UK, the USA, South Africa, India, Australia, and Brazil	Evidence available for a variety of substances
dapted from reference 2.			

Contingency management (eg, the use of voucher reinforcement for drug-free urine samples)^{70,86–88} has been shown in many randomised trials (which used specially-trained research therapists and rewards of small monetary value) to substantially increase abstinence, ^{70,86,87} attendance, ^{86,87} and attention to associated health needs. ^{89,90}

Some of these behavioural approaches can be used effectively in combination with drugs to improve adherence and treatment benefits.^{49,60}

In addition to contingency management, several specific forms of psychological intervention have been identified in a review by the UK's National Institute for Health and Clinical Excellence (NICE) as having a robust evidence base.70 Opportunistic brief interventions for drug users with very low or no contact with treatment can increase help-seeking behaviour and stimulate change in drug use behaviour. 50,91,92 Brief motivational techniques applied in primary care or at needle and syringe exchange schemes can affect drug use.93 Behavioural family-based and couples-based interventions in the treatment of heroin or cocaine addiction, usually integrated with drug treatments, produce better abstinence rates both during treatment and at follow-up, and also lessen drug use if it persists.94,95 Synergistic benefits are also seen with active referral to 12-step groups from within treatment programmes with better sustained attendance at self-help groups after intensive referral.96 Cognitive behavioural treatment is of benefit for associated comorbidities, but evidence of a specific benefit in the treatment of drug dependence is unclear.⁷⁰

Needle and syringe programmes provide injecting drug users with sterile needles and syringes, often in exchange for used equipment. These interventions reduce sharing of needles and syringes and infectious disease transmission rather than drug use itself. In some cases, they provide a gateway for drug users to enter addiction treatment and ultimately, cease drug use. Needle and syringe programmes can be incorporated into existing drug treatment services or provided through community pharmacies.

Such programmes have never been the subject of a controlled clinical trial. Nonetheless, findings from a review show strong evidence that syringe exchange programmes reduce injection risk behaviour and suggest that they also reduce HIV transmission. The amount of risk behaviour change induced by needle and syringe programmes does not seem sufficient to protect against hepatitis C, which is much more easily transmitted than HIV.

Peer-led mutual health organisations (such as Narcotics Anonymous, Cocaine Anonymous, and Women for Sobriety) are led by people who are recovering from addiction (Narcotics Anonymous and Cocaine Anonymous are also examples of 12-step programmes). Although self-help is probably the most common type of intervention delivered globally for problem drug use, there were until the past two decades very few scientific studies of its

effectiveness. As with studies of alcohol,¹⁰⁰ evidence now shows that that participation in Narcotics Anonymous is associated with continued abstinence, lower health-care costs, and improvement in other areas of functioning.¹⁰¹⁻¹⁰³

Drug policy to promote the public good

Scientific research can make important contributions to the construction of more effective drug policy, but final resource allocation involves wider public and political processes of priority-setting. ¹⁰⁴ At least three types of benefit can be identified: a substantial benefit to individuals from major changes (eg, OST), widely dispersed benefits from interventions with a small effect on individuals (eg, screening and brief intervention) but substantial population benefit, and indirect benefits to others (eg, reduced HIV transmission and reduced crime from OST).

A conceptual framework is described in the figure, to inform debate and organise the major public policy options. The figure presents a four-tier pyramid that describes potential for the maximisation of the public good as well as individual benefit and can constructively inform the political and economic considerations of different policy initiatives. This model is informed by similar frameworks in tobacco control, communicable disease control, and injury prevention.¹⁰⁵

The bottom tier of the pyramid represents the traditional population-wide (universal) interventions that aim to limit drug supply through interdiction, precursor controls, prescription regimens, and related measures. Although the evidence is mixed, and the quality of the research is poor, supply control can have a substantial population effect, if effective methods are used (as is the case with tobacco and alcohol). The success of such control in the drugs field has been shown in the control of prescription drug epidemics.¹⁰⁶ and the elimination of metamfetamine laboratories.¹⁰⁸

Interventions at the top tiers provide direct help to drug-affected individuals. Individuals (and their carers) typically need to expend much personal effort to receive

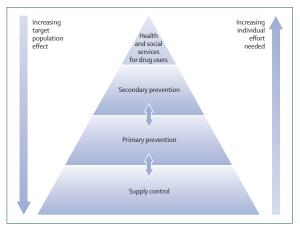


Figure: The effect of drug policy options on the public good and individuals

benefit from these interventions, which can adversely affect adherence. Secondary prevention approaches for problem drug users can prevent deterioration and linked adverse events (eg, HIV, crime) and are included in the second tier because the most effective of these can reach many severely problematic drug users in the community at a time when they are readily accessible. The population-level effect of such services (in the top two tiers) can be further enhanced by increasing availability within the criminal justice system and by use of the leverage of that system to reward behaviour change. Treatment in this setting can be as effective as that in the community when supported by the courts with, for example, diversion into treatment and regular drug testing as an alternative to incarceration.

The second and third tiers represent different types of prevention. These can be either universal—whole population or community efforts—or more selective and indicated forms of secondary prevention targeted at highrisk groups. Although only preliminary evidence exists, screening, brief advice and counselling can potentially reach many at-risk individuals, and aid referral to treatment for those individuals with the most severe drug problems. Some universal prevention programmes—those aimed at the prevention or delay of use of drugs by young people—have evidence of effectiveness, albeit with a small to medium-sized effect. The effective early intervention prevention programmes concentrate on the psychosocial development of young people and also have benefits beyond the prevention of drug misuse.

Between countries and over time, the actual health needs and the extent of public commitment to the provision of interventions will differ. For a society faced with the active spread of HIV through injecting drug use, the priorities will be different from those of a country tackling the continuing addiction problems from a heroin epidemic a decade before.

The interventions themselves vary greatly in relevance. Investments in the strengthening of border security have no relevance to drug problems that involve domestically produced or legal products (such as solvent misuse by adolescents or the misuse of legal pharmaceutical opioids in the USA). The evidence of benefit from OSTs is of little value to a society mainly afflicted by a cocaine or amphetamine problem, as is the situation for most of South and Central America. Similarly, the benefits of needle and syringe programmes will depend on the extent of injecting drug use, sharing of needles, and prevalence of HIV. They are much less relevant to societies where injecting is uncommon, such as those where opioid addiction involves swallowing, smoking, or inhaling the drug (as was previously the case for much of central and southeast Asia). However, the pyramid of policy options outlined above is useful in the identification of interventions, even though the specific problems and the most appropriate type of interventions will vary over time and between societies and geographical locations.

Drug policy has the potential to contribute more to the public good by focusing on interventions with the largest potential population effect, the strongest evidence of effectiveness and cost-effectiveness, and the closest link between the outcomes of the policy and society's idea of the public good. Funders and researchers should pay greater attention to more policy-relevant areas in addiction research study if society's ability to adopt a more evidence-based approach to drug policy is to be improved.

By a shift in focus to maximisation of the public good, greater societal and political support can be generated for evidence-based measures that avoid the detrimental effects of the marginalisation of drug users by, among other strategies, the imposing of severe criminal penalties. Different interventions might be more effective or feasible for different drug problems. A comprehensive public policy approach would implement evidence-based measures at each level of intervention and maximise the synergy between these levelsfor example, through collaboration and coordination between the criminal justice system and treatment providers, which has already been shown in some countries (eg, the USA) to produce synergy between supply control efforts and the health service system. Long-term benefits of these policies would thus increase for whole communities as well as for individuals.

Contributors

All authors contributed to the data collection for and writing of this paper, each leading the writing for areas in which they have expertise.

Conflicts of interest

JS declares that he has worked with UK and international government agencies on treatment guidelines, including chairing UK Department of Health and NICE clinical guidelines committees; has contributed to the work of organisations that review evidence of effectiveness of drug policy; has received research and educational grant support or honoraria, consultancy payments, and travelling, accommodation, or conference expenses from pharmaceutical companies who produce, or have been considering producing, new medicines or new formulations for use in the addiction treatment field, including (past 3 years) Genus (Britannia), Viropharma (Auralis), Martindale (Catalent), Reckitt-Benckiser, Schering-Plough, Lundbeck, UCB, Napp (MundiPharma), Lightlake, and Fidelity International; works within an integrated university and NHS academic health sciences centre (Kings Health Partners AHSC) and is supported by the NIHR Biomedical Research Centre for Mental Health at the Institute of Psychiatry, Kings College London and South London and Maudsley NHS Foundation Trust that provides treatments and undertakes research study; and has close links with various other treatment provider organisations. DF's Department has received funding from the alcohol industry for alcohol education and prevention materials that are being assessed in a randomised controlled trial funded by the Medical Research Council and led by Cardiff University. DF is a Trustee of the UK alcohol education charity, the Drinkaware Trust. BF has consulted for government and non-governmental organisations at national and supranational levels with regard to drug policy and related interventions; travel costs and activity honoraria were received for some of these activities. All other authors declare that they have no conflicts of interest.

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References

- Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet* 2012; 379: 55–70.
- Babor T, Caulkins J, Edwards G, et al. Drug policy and the public good. Oxford: Oxford University Press, 2010.
- 3 Reuter P, Kleiman M. Risks and prices: an economic analysis of drug enforcement. In: Morris N Tonry M, eds. Crime and justice: an annual review of research. London: University of Chicago Press, 1986.
- 4 Dave D. The effects of cocaine and heroin price on drug-related emergency department visits. J Health Econ 2006; 25: 311–33.
- 5 Caulkins JP, Reuter P. How drug enforcement affects drug prices. In: Tonry M, ed. Crime and justice—a review of research, vol 39. Chicago: University of Chicago Press, 2011.
- 6 Rydell CP, Everingham SS. Controlling cocaine: supply versus demand programs. Santa Monica: RAND, 1994.
- 7 Kuziemko I, Levitt SD. An empirical analysis of imprisoning drug offenders. Journal of Public Economics 2004; 88: 2043–66.
- 8 Dobkin C, Nicosia N. The war on drugs: methamphetamine, public health, and crime. Am Econ Rev 2009; 99: 324–49.
- Paoli L, Greenfield V, Reuter P. The world heroin market: can supply be cut? New York: Oxford University Press, 2009.
- 10 Crane BD, Rivolo AR, Comfort GC. An empirical examination of counterdrug interdiction program effectiveness. Alexandria, VA: Institute for Defense Analysis, 1997.
- Degenhardt L, Reuter P, Collins L, Hall W. Evaluating explanations of the Australian heroin drought. Addiction 2005; 100: 459–69.
- 12 Cunningham JK, Liu LM. Impacts of federal precursor chemical regulations on methamphetamine arrests. *Addiction* 2005; 100: 479–88.
- 13 Cunningham JK, Liu LM, Callaghan R. Impact of US and Canadian precursor regulation on methamphetamine purity in the United States. Addiction 2009; 104: 441–53.
- 14 Best D, Strang J, Beswick T, Gossop M. Assessment of a concentrated, high-profile police operation. *British Journal of Criminology* 2001; 41: 738–45.
- 15 Maher L, Dixon D. The cost of crackdowns: policing Cabramatta's heroin market. Current Issues in Criminal Justice 2001; 13: 5–22.
- 16 Day C, Degenhardt L, Hall W. Changes in the initiation of heroin use after a reduction in heroin supply. Drug Alcohol Rev 2006; 25: 307–13.
- 17 Caulkins JP, Reuter P. Toward a harm reduction approach to enforcement. Safer Communities 2009; 8: 9–23.
- 18 Kennedy DM. Deterrence and crime prevention: reconsidering the prospect of sanction. Abingdon, UK and New York, USA: Routledge, 2008.
- 19 Braga AA, Kennedy DM, Waring EJ, Piehl AM. Problem-oriented policing, deterrence, and youth violence: an evaluation of Boston's operation ceasefire. *Journal of Research in Crime and Delinquency* 2001: 38: 195–225
- 20 Sevigny E, Caulkins JP. Kingpins or mules? An analysis of drug offenders incarcerated in federal and state prisons. Criminology and Public Policy 2004; 3: 401–34.
- 21 Room R, Fischer B, Hall W, Lenton S, Reuter P. Cannabis policy: moving beyond stalemate. Oxford, UK: Oxford University Press, 2010.
- 22 Pacula R, MacCoun R. Reuter P, et al. What does it mean to decriminalize marijuana? A cross-national empirical examination. In: Lindgren B, Grossman M, eds. Substance use: individual behaviors, social interactions, markets and politics advances in health economics and health services research, Vol 16. Amsterdam: Elsevier, 2005: 347–70.
- 23 Nagin DS. Deterrence and incapacitation. In: Tonry M, ed. The handbook of crime and punishment. New York: Oxford University Press, 1998.

- 24 Kleiman MAR. When brute force fails: strategy for crime control. Princeton, NJ: Princeton University Press, 2009.
- 25 Voas RB, DuPont RL, Talkins SK, Shea CL. Towards a national model for managing impaired driving offenders. Addiction 2011; 106: 1221–27.
- 26 Caulkins JP, DuPont RL. Is 24/7 sobriety a good goal for repeat DUI offenders? Addiction 2010; 105: 575–77.
- 27 DuPont RL, McLellan AT, White WL, Merlo LJ, Gold MS. Setting the standard for recovery: physicians' health programs. J Subst Abuse Treat 2009; 36: 159–71.
- 28 Eibner C, Morral A, Pacula RL, MacDonald J. Is the drug court model exportable? An examination of the cost-ffectiveness of a Los Angeles-based DUI court. J Subst Abuse Treat 2006; 31: 75–85.
- 29 Courtwright DT. Forces of habit: drugs and the making of the modern world. Cambridge, MA, USA, and London, UK: Harvard University Press, 2001.
- 30 Popova S, Rehm J, Patra J. Illegal drug-attributable mortality and potential years of life lost in Canada 2002: conclusions for prevention and policy. Contemporary Drug Problems 2006; 33: 343–66.
- 31 Fischer B, Gittins J, Rehm J. Characterizing the 'awakening elephant': prescription opioid misuse in North America: epidemiology, harms, interventions. *Contemporary Drug Problems* 2008; 35: 397–426.
- 32 Paulozzi L, Budnitz D, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Saf* 2006; 15: 618–27.
- 33 Fischer B, Bibby M, Bouchard M. Non-medical use and diversion of psychotropic prescription drugs in North America: a review of sourcing routes and control measures. *Addiction* 2010; 105: 2062–70.
- 34 Inciardi J, Surratt HL, Kurtz S, Cicero TJ. Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. *Pain Med* 2007; 8: 171–83.
- 35 McCabe SE, Boyd CJ. Sources of prescription drugs for illicit use. Addict Behav 2005; 30: 1342–50.
- 36 Littlejohn C, Baldacchino A, Schifano F, Deluca P. Internet pharmacies and online prescription drug sales: a cross-sectional study. Drugs: Education, Prevention and Policy 2005; 12: 75–80.
- 37 Fischer B, Rehm J, Patra J, Firestone Cruz M. Changes in illicit opioid use profiles across Canada. CMAJ 2006; 175: 1–3.
- 38 Davis W, Johnson B. Prescription opioid use, misuse, and diversion among street drug users in New York City. *Drug Alcohol Depend* 2008; 92: 267–76.
- 39 Schwartz HI. Negative clinical consequences of triplicate prescription regulation of benzodiazepines. N Y State J Med 1991; 91: 9S–12S.
- 40 Reidenberg MM. Effect of the requirement for triplicate prescriptions for benzodiazepines in New York State. Clin Pharmacol Ther 1991; 50: 129–31.
- 41 Hall W, Lynskey M, Degenhardt L. Trends in opiate-related deaths in the United Kingdom and Australia 1985–1995. Drug Alcohol Depend 2000; 57: 247–54.
- 42 Strang J, Manning V, Mayet S, Ridge G, Best D, Sheridan J. Does prescribing for opiate addiction change after national guidelines? Methadone and buprenorphine prescribing to opiate addicts by general practitioners and hospital doctors in England, 1995–2005. Addiction 2007; 102: 761–70.
- 43 Strang J, Hall W, Hickman M, Bird SM. The impact of supervision of methadone consumption on methadone overdose deaths: analyses using the OD4 Index in England and Scotland. BMJ 2010; 341: c4851.
- 44 Faggiano F, Vigna-Taglianti FD, Versino E, Zambon A, Borraccino A, Lemma P. School-based prevention for illicit drugs' use. Cochrane Database Syst Rev 2005; 2: CD003020.
- 45 Gates S, McCambridge J, Smith LA, Foxcroft DR. Interventions for prevention of drug use by young people delivered in non-school settings. *Cochrane Database Syst Rev* 2006; 1: CD005030.
- 46 Faggiano F, Vigna-Taglianti F, Burkhurt G, et al. The effectiveness of a school-based substance abuse prevention program: 18-month follow-up of the EU-Dap cluster randomized controlled trial. Drug Alcohol Depend 2010; 108: 56–64.

- 47 Ennett ST, Tobler NS, Ringwalt CL, Flewelling RL. How effective is drug abuse resistance education? A meta-analysis of project DARE outcome evaluations. Am J Public Health 1994; 84: 1394–1401.
- 48 Kellam S, Reid J, Balster RL. Effects of a universal classroom behavior program in first and second grades on young adult outcomes. *Drug Alcohol Depend* 2008; 95 (suppl 1): S1–S104.
- 49 Berstein JE, Berstein K, Tassiopoilos T, Huren S, Levenson R, Hingson R. Brief intervention at a clinic visit reduced cocaine and heroin use. *Drug Alcohol Depend* 2005; 77: 49–59.
- McCambridge J, Strang J. The efficacy of single-session motivational interviewing in reducing drug consumption and perceptions of drug-related risk and harm among young people: results from a multi-site cluster randomised trial. Addiction 2004; 99: 39–52.
- 51 Baker A, Lee NK, Claire M, Lewin TJ, Grant T, Pohlman S. Brief cognitive behavioural interventions for regular amphetamine users: a step in the right direction. Addiction 2005; 100: 367–78.
- 52 Cormack MA, Sweeney KG, Hughes-Jones H, Foot GA. Evaluation of an easy, cost-effective strategy for cutting benzodiazepine use in general practice. Br J Gen Pract 1994; 44: 5–8.
- 53 Bashir K, King M, Ashworth M. Controlled evaluation of brief intervention by general practitioners to reduce chronic use of benzodiazepines. Br I Gen Pract 1994: 44: 408–12.
- 54 Humeniuk R, Dennington V, Ali R. The effectiveness of a brief intervention for illicit drugs linked to the alcohol, smoking and substance involvement screening test (ASSIST) in primary health care settings: a technical report of phase III findings of the WHO ASSIST randomized controlled trial. Geneva: World Health Organization, 2008.
- 55 Conrod PJ, Castellanos-Ryan N, Strang J. Brief, personality-targeted coping skills interventions and survival as a non-drug user over a 2-year period during adolescence. Arch Gen Psychiatry 2010; 67: 85–93.
- McCambridge J, Strang J. Deterioration over time in effect of Motivational Interviewing in reducing drug consumption and related risk among young people. Addiction 2005; 100: 470–78.
- 57 Marsden J, Stillwell G, Barlow H, et al. An evaluation of a brief motivational intervention among young ecstasy and cocaine users: no effect on substance and alcohol use outcomes. *Addiction* 2006; 101: 1014–26.
- 58 Gray E, McCambridge J, Strang J. The effectiveness of motivational interviewing delivered by youth workers in reducing drinking, cigarette and cannabis smoking among young people: quasi-experimental pilot study. Alcohol Alcohol 2005; 40: 535–39.
- O'Leary-Barrett M, Mackie C, Castellanos-Ryan N, Al-Khudhairy N, Conrod P. Personality-targeted interventions delay uptake of drinking and decrease risk of alcohol-related problems when delivered by teachers. J Am Acad Child Adolesc Psychiatry 2010; 49: 954–63.
- 60 McCambridge J, Hunt C, Jenkins RJ, Strang J. Cluster randomized trial of the effectiveness of motivational interviewing for universal prevention. *Drug Alcohol Depend* 2011; 114: 177–84.
- 61 Foxcroft DR. The need for values: science and art in alcohol harm reduction. Addiction 2007; 102: 1350–51.
- Kraft MK, Rothbard AB, Hadley TR, McLellan AT, Asch DA. Are supplementary services provided during methadone maintenance really cost-effective? Am J Psychiatry 1997; 154: 1195–97.
- 63 Amato L, Minozzi S, Davoli M, Vecchi S, Ferri M, Mayet S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database Syst Rev 2004; 4: CD004147.
- 64 Connock M, Juarez-Garcia A, Jowett S, et al. Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. *Health Technol Assess* 2007; 11: 1–190.
- 65 Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev 2009; 3: CD002209.
- 66 Eder H, Jagsch R, Kraigher D, Primorac A, Ebner N, Fischer G. Comparative study of the effectiveness of slow-release morphine and methadone for opioid maintenance therapy. *Addiction* 2005; 100: 1101–09.
- 67 Robertson JR, Raab GM, Bruce M, McKenzie JS, Storkey HR, Salter A. Addressing the efficacy of dihydrocodeine versus methadone as an alternative maintenance treatment for opiate dependence: a randomized controlled trial. Addiction 2006; 101: 1752–59.

- 68 Fischer B, Oviedo-Joekes E, Blanken P, et al. Heroin-assisted treatment (HAT) a decade later: a brief update on science and politics. J Urban Health 2007; 84: 552–62.
- 59 Strang J, Metrebian N, Lintzeris N, et al. Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *Lancet* 2010; 375: 1885–95.
- 70 National Institute for Health and Clinical Excellence (NICE). Drug misuse: psychosocial interventions (CG51—Clinical Guideline CG51). London: NICE, 2007.
- 71 Davoli M, Bargagli AM, Perucci CA, et al. Risk of fatal overdose during and after specialist drug treatment: the VEdeTTe study, a national multi-site prospective cohort study. Addiction 2007; 102: 1954–59.
- 72 Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opioid dependence. Cochrane Database Syst Rev 2003; 3: CD002208.
- 73 National Institute for Health and Clinical Excellence (NICE). Naltrexone for prevention of relapse of heroin addiction (technology appraisal TA115). London: NICE, 2007.
- 74 Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev 2011; 16: CD001333.
- 75 Strang J, Manning V, Mayet S, Best D, Titherington E, Santana L. Preventing overdose death through overdose management training and provision of take-home naloxone to opiate users in treatment: prospective cohort study of impact on knowledge, attitudes and behaviour. Addiction 2008; 103: 1648–57.
- 76 Strang J, Manning V, Mayet S, et al. Family carers and the prevention of heroin overdose deaths: unmet training need and overlooked intervention opportunity of resuscitation training and supply of naloxone. *Drugs: Education, Prevention and Policy* 2008; 15: 211–18.
- 77 Grabowski J, Shearer J, Merrill J, Negus SS. Agonist-like, replacement pharmacotherapy for stimulant abuse and dependence. Addict Behav 2004; 29: 1439–64.
- 78 Martell BA, Orson FM, Poling J, et al. Cocaine vaccine for the treatment of cocaine dependence in methadone-maintained patients: a randomized, double-blind, placebo-controlled efficacy trial. Arch Gen Psychiatry 2009; 66: 1116–23.
- 79 De Leon G, Hawke J, Jainchill N, Melnick G. Therapeutic communities. Enhancing retention in treatment using "Senior Professor" staff. J Subst Abuse Treat 2000; 19: 375–82.
- 80 Edelen MO, Tucker JS, Wenzel SL, et al. Treatment process in the therapeutic community: associations with retention and outcomes among adolescent residential clients.

 J. Subst. Abuse Treat 2007; 32: 415–21.
- Miles JN, Wenzel S, Mandell W. The relationship between the dimensions of change instrument and retention in therapeutic community treatment: the moderating influence of time in treatment. Am J Drug Alcohol Abuse 2008; 34: 667–72.
- 82 Bale RN, Van Stone WW, Kuldau JM, Engelsing TM, Elashoff RM, Zarcone VP Jr. Therapeutic communities vs methadone maintenance. A prospective controlled study of narcotic addiction treatment: design and one-year follow-up. Arch Gen Psychiatry 1980; 37: 179–93.
- 83 Nemes S, Wish ED, Messina N. Comparing the impact of standard and abbreviated treatment in a therapeutic community: findings from the district of Columbia treatment initiative experiment. J Subst Abuse Treat 1999; 17: 339–47.
- 84 Greenwood GL, Woods WJ, Guydish J, et al. Relapse outcomes in a randomised trial of residential and day drug abuse treatment. *J Subst Abuse Treat* 2001; **20**: 15–23.
- 85 Finney JW, Noyes CA, Coutts AI, et al. Evaluating substance abuse treatment process models: changes on proximal outcome variables during 12-step and cognitive-behavioral treatment. J Stud Alcohol 1998; 59: 371–80.
- 86 Lussier JP, Heil SH, Mongeon JA, Badger GJ, Higgins ST. A meta-analysis of voucher-based reinforcement therapy for substance use disorders. *Addiction* 2006; 101: 192–203.
- 87 Prendergast ML, Podus D, Finney JW, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: a meta-analysis. Addiction 2006; 101: 1546–60.

- 88 Stitzer M, Petry N. Contingency management for treatment of substance abuse. Annu Rev Clin Psychol 2006; 2: 411–34.
- 89 Sorensen JL, Haug NA, Delucchi KL, et al. Voucher reinforcement improves medication adherence in HIV-positive methadone patients: a randomized trial. *Drug Alcohol Depend* 2007; 88: 54–63.
- 90 Seal KH, Kral AH, Lorvick J, et al. A randomized controlled trial of monetary incentives vs. outreach to enhance adherence to the hepatitis B vaccine series among injection drug users. *Drug Alcohol Depend* 2003; 71: 127–31.
- 91 Humeniuk R, Ali R, Babor T, et al. A randomized controlled trial of a brief intervention for illicit drugs linked to the alcohol, smoking and substance involvement screening test (ASSIST) in clients recruited from primary health care settings in four countries. Addiction (in press).
- 92 Babor TF, McRee BG, Kassebaum PA, Grimaldi PL, Ahmed K, Bray J. Screening, brief intervention, and referral to treatment (SBIRT): toward a public health approach to the management of substance abuse. Subst Abus 2007; 28: 7–30.
- 93 Bernstein J, Bernstein E, Tassiopoulos K, et al. Brief motivational intervention at a clinic visit reduces cocaine and heroin use. Drug Alcohol Depend 2005; 77: 49–59.
- 94 Fals-Stewart W, O'Farrell TJ, Birchler GR. Behavioral couples therapy for male methadone maintenance patients: effects on drug-using behavior and relationship adjustment. *Behav Ther* 2001; 32: 391–411.
- 95 Catalano RF, Gainey RR, Fleming CB, et al. An experimental intervention with families of substance abusers: one-year follow-up of the focus on families project. *Addiction* 1999; 94: 241–54.
- 96 Timko C, Debenedetti A, Billow R. Intensive referral to 12-step self-help groups and 6-month substance use disorder outcomes. Addiction 2006; 101: 678–88.
- 97 Wood E, Tyndall M, Zhang R, et al. Attendance at supervised injecting facilities and use of detoxification services. N Engl J Med 2006; 354: 2512–13.

- 98 Palmateer N, Kimber J, Hickman M, Hutchinson S, Rhodes T, Goldberg D. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews. Addiction 2010; 105: 844–59.
- Pollack HA. Cost-effectiveness of harm reduction in preventing hepatitis C among injection drug users. *Med Decis Making* 2001; 21: 357–67.
- 100 Babor T, Caetano R, Casswell S, et al. Alcohol: no ordinary commodity. Oxford, UK: Oxford University Press, 2010.
- 101 Humphreys K, Moos RH. Can encouraging substance abuse inpatients to participate in self-help groups reduce demand for health care? A quasi-experimental study. Alcohol Clin Exp Res 2001; 25: 711–16.
- 102 Humphreys K. Circles of recovery: self-help organisations for addictions. Cambridge, UK: Cambridge University Press, 2004.
- 103 Gossop M, Stewart D, Marsden J. Attendance at Narcotics Anonymous and Alcoholics Anonymous meetings, frequency of attendance and substance use outcomes after residential treatment for drug dependence: a 5-year follow-up study. Addiction 2008; 103: 119–25.
- 104 Room R, Reuter P. How well do international drug conventions protect public health? *Lancet* 2012; 379: 84–91.
- 105 Frieden TR. A framework for public health action: the health impact pyramid. Am J Public Health 2010; 100: 590–95.
- 106 Brill H, Hirose T. The rise and fall of an amphetamine epidemic: Japan 1945–1955. Semin Psychiatry 1969; 1: 179–94.
- 107 Fountain J, Griffiths P, Farrell M, Gossop M, Strang J. Benzodiazepines in polydrug-using repertoires: the impact of the decreased availability of temazepam gel-filled capsules. Drugs: Education, Prevention and Policy 1999; 6: 61–69.
- 108 Cunningham JK, Liu L-M. Impacts of federal ephedrine and pseudoephedrine regulations on methamphetamine-related hospital admissions. Addiction 2003; 98: 1229–37.