Chapter 16
Current and future perspectives on harm reduction in the European Union

Marina Davoli, Roland Simon and Paul Griffiths

The drift to evidence-based European drug policies

Over the last 20 years, whether as an overarching concept, or as shorthand for specific interventions, 'harm reduction' has changed the way we think about and respond to drug problems in Europe. Debates continue today about what sort of interventions legitimately fall under the heading of harm reduction, and what value they bring. However, measures that reduce harm, but do not specifically attempt to reduce drug use, are an important element in a drug strategy and harm reduction is now a largely uncontested component of European drug policy. Indeed, practice is ahead of political rhetoric in this respect, with governments sometimes being more cautious in their public pronouncements than they are in their actions.

How Europe got to today's pragmatic approach, where the balance is tipped to what can be *shown to work*, rather than what policymakers might *wish would work,* is addressed by many of the contributors to this monograph. It would be naive to suggest that modern drug policies are solely directed by a cold assessment of the scientific evidence for effectiveness. Many examples can be cited to demonstrate that this is not the case — for instance, the investment of large sums of money in anti-drug mass media campaigns where there is growing evidence that this approach is at best ineffective, and at worst counter-productive. Drug policies, like other social policies, are shaped by many factors, and Herring and colleagues' (2010) statement on alcohol is true for other substances as well: 'Evaluation and research findings are only one element in decisions to adapt or reject harm reduction as a legitimate goal for policy'.

Nonetheless, the development of harm reduction as a mainstream concept in Europe does demonstrate that over time, and when faced with a serious public health threat, evidence-based argument can result in the adoption of policy options that are initially viewed as controversial. It is beyond the scope of this chapter to discuss how the mainstreaming of harm reduction into drug policy was possible in the European Union (EU) and some other countries, whilst in other parts of both the developed and developing world harm reduction has remained largely outside of the mainstream. The diffusion of harm reduction in Europe was brought about initially by public health concerns related to HIV. It seems likely it has also been facilitated by structural factors, including a strong public health ethos, a culture of independence within the medical and health professions, activism and user involvement, and advocacy by affected individuals and communities. At the EU level, a growing political culture of sharing experiences of what works and moving towards common positions may have also played a part and, importantly, removed some of the anxiety felt by policymakers that they were moving alone into uncharted waters. It is interesting to note that many of the Member States joining the EU in 2004 very rapidly adopted relatively sophisticated drug policies that reflected Community norms, and in which harm

reduction was a component. Arguably, a key factor contributing to these countries' avoidance of major HIV epidemics among their injecting populations is their rapid adoption of the European model in which HIV prevention was an integral element.

The question of definition

Interventions towards substance use and dependence have always been topics of discussion well beyond the public health arena. Ethical issues relating to the use of drugs have influenced the objectives and aims of interventions, both preventive and therapeutic. Indeed, the historical development of drug policy is often represented as an ongoing debate between a *moral position* in which drug use is portrayed as 'criminal' and 'deviant' and a *public health position* where drug users are seen as in need of treatment and help. Harm reduction gives clear primacy to a public health perspective in which the imperative is to reduce immediate harms, and the question of long-term abstinence from drug use is either unaddressed or left open. Moreover, many of those who advocate for a harm reduction approach also point out that the regulatory control system itself can contribute to harm, and some regard it as a major contributing factor. Furthermore, some, on both sides of the drugs debate, would equate harm reduction as running in close parallel to an anti-prohibitionist perspective. However, it is important to note that the mainstreaming of harm reduction within political policy debate at the European level has taken place overwhelmingly within a context of concern about the health of the public and has not be linked with the issue of drug prohibition.

From a European policy perspective, where Member States' domestic policies differ, the question of definition is an important one; or conversely, an important area for flexibility in interpretation. A fundamental position of current European drug policy is support for the international drug control conventions, and no European country would regard its policies as out of step with the leeway given to States to interpret their obligations in this respect. Harm reduction as mainstream in Europe is therefore viewed by policymakers as compatible with a balanced approach, which also includes support for vigorous supply reduction measures. This is not to say that policymakers have ignored the argument that harms can result from the drug control system. Recognition of this fact can be seen, for instance, in a shift in emphasis in which a distinction is now commonly made between those who traffic and trade in drugs, and those who consume them. It is reflected in policies that attempt to divert those with drug problems from the criminal justice system towards treatment or that introduce more lenient penalties for the personal use of drugs. These developments have, however, largely taken place within a policy debate on how the costs of drug control can be minimised and the benefits maximised. The reduction of harm is clearly part of this agenda, but this is usually implicit rather than explicit and harm reduction is most commonly discussed in the context of HIV risk reduction, not criminal justice policies. A strong argument can be made that the absence of an explicit common definition of what constitutes 'harm reduction' at the EU level has facilitated the mainstreaming of the concept against a background where there is considerable diversity in respect to national and local policies and actions. And when events have forced the adoption of a working definition the approach has usually been a relatively restricted one: for example, explicitly listing measures targeting HIV risk behaviour among drug injectors.

The question of evidence

The mantra for the European approach to drugs is for comprehensive, balanced and evidence-based policies. The importance given to evidence in this perspective can be contrasted with policies that are more ideologically driven. This raises two important questions. First, what constitutes sufficient evidence for policy formation? And second, to what extent are policies skewed towards the easily measurable, at the expense of the potentially most desirable?

It is probably fair to say that in many areas of drug policy the evidence base for supporting current approaches is often weak, and where evidence does exist it is rarely unequivocal. That said, the situation is considerably better than it once was and research and evaluation studies provide a growing base of evidence for informing policy decisions. It is understandable that policymakers will be more concerned with the quality and availability of evidence for politically controversial measures than they are for actions that have broad-based support. This is likely to be why harm reduction has come under greater scrutiny than many other areas of drug policy, although this is arguably changing in light of a more generic concern to fund only interventions that can be shown to be effective.

Appraisal of the available evidence for an intervention is a complex process requiring methodological rigour, particularly in conducting a comprehensive search of the literature, evaluating quality of primary studies and summarising the results (Higgins and Green, 2008). The credibility of this process depends on a rigorous approach to the evaluation exercise. The gold standard for the evaluation of medical research is the randomised control trial (RCT). This model is often applied to drug interventions, especially in the more medically orientated areas such as treatment. Interventions can be considered effective if there is evidence deriving from multiple well-conducted studies. In the last 15 years, considerable efforts have been made to ensure that all conducted RCTs are registered and their findings made accessible. This is not the case for most other types of research and comprehensively auditing and accessing the evidence base for other types of study design is consequently more difficult. The efforts made to improve the quality of reporting for RCTs has also to some extent resulted in an improvement in quality of the studies published in the scientific literature (Moher et al., 2001; Plint et al., 2006). Only recently have guidelines for reporting results of study designs other than RCTs also been published (von Elm et al., 2007).

For good reason, RCTs therefore represent a gold standard for research evidence as, when replicated and properly applied, they provide a robust evidence base for demonstrating with a high probability of certainty that a given intervention has resulted in a measurable effect. They do, however, have some obvious weaknesses that have important implications for their use in the drugs field. RCTs work best with simple study designs and where extraneous variables can easily be controlled for. This model fits well for testing the effectiveness of a new medicine where the condition to be treated is well described and the desired action of the drug can be easily measured. However, harm reduction interventions usually take place in real world settings, in which other interventions may also be taking place. Furthermore, confounding variables are difficult to control for, subject characteristics are often highly heterogeneous, and outcomes may be complex to interpret and difficult to measure. Practical,

methodological and ethical challenges exist to developing convincing RCT study designs that are applicable to many areas of social policy evaluation. This is a particular problem for controversial social policy options as it may be in practice very difficult using other study designs to provide policymakers with the high level of certainty that properly conducted RCTs can provide. The number of RCT study designs in the harm reduction area is growing but remains limited. Not surprisingly RCTs are most commonly found in the treatment area, as this setting is most amenable to this kind of approach. In considering other areas, the evidence is largely drawn from more observational studies and ecological ones. Such studies provide a weaker evidence base for drawing conclusions and can be more challenging to interpret. These kind of studies are probably also at higher risk of publication bias, where there is a greater likelihood of getting positive rather than negative results published, although RCTs are not immune to this problem.

This monograph has provided the reader with a systematic review of the evidence regarding harm reduction among injecting opiate users. In other areas, the lack of studies makes a systematic appraisal more difficult but the contributions elaborate the evidence that exists. In order to consider future priorities for the European research agenda, we provide below an overview, using strict assessment criteria, of the current state of the art with respect to the evidence for effectiveness of harm reduction activities. The reader should note that lack of robust evidence means that the research conducted so far is not sufficient to make confident judgements, negative or positive, on the effectiveness of the intervention in question.

Harm reduction among injecting drug users

There is sufficient evidence to support the role of opioid substitution treatment (OST) in reducing HIV transmission, while the evidence in support of needle and syringe distribution programmes is more tentative, and the evidence that drug consumption reduces transmission is insufficient at present. All three interventions appear to reduce self-reported injecting risk behaviour. The evidence on the impact of drug consumption rooms and peer naloxone distribution in reducing overdose deaths at the community level remains insufficient, although the studies that have been conducted suggest the potential that these approaches may have and therefore both interventions remain important areas for further study. No strong evidence exists to support the concern that any of these interventions, when well managed, leads to increased harms for those using them, or encourages drug use in the wider community. However, a problem with the diversion of drugs from substitution treatment into the illicit market has been reported in some countries.

In terms of research priorities, methodologically robust primary studies on the impact of harm reduction interventions on the incidence of HIV and HCV are needed as are studies on what measures may reduce drug overdose deaths. In the EU, drug overdose now represents the major cause of avoidable morbidity associated with illegal drug use and therefore must be regarded as a priority area for the identification of effective interventions. In general, future studies of interventions designed to reduce drug-related infectious diseases would be wise to focus on primary biological outcomes rather than behavioural ones, as this is a key weakness in current evidence. Where possible, randomised designs should be employed and compare

the impact of additional or increased intensity of interventions against current or low level of activity. A number of studies have suggested that the impact of interventions may be enhanced by, or even dependent upon, providing the target population with a package of different services. This implies the need to research how different interventions work together to provide benefit. Although this approach is analogous to some standard medical research questions — the provision of multi-drug therapy, for example — for interventions conducted in the real world settings, in which most harm reduction approaches are employed, such research questions pose real methodological challenges. More innovative approaches, including natural experiments, large-scale modelling and carefully evaluated case studies, may prove to be the way forward here.

Harm reduction policies for cocaine and other stimulants

There is now greater understanding of the mental and physical health consequences associated with the use of cocaine and other stimulants. However, to date, most harm reduction interventions have largely focused on risks related to infectious diseases transmission and assumptions are built largely on the evidence of HIV prevention among heroin injectors.

Although some studies have looked at crack cocaine users overall, there is little evidence from published studies on the effectiveness of harm reduction interventions among users of cocaine or other stimulants. This population is often considered a subset of a study, rather than the target population, and most research has exclusively focused on intravenous drug use. Interventions for crack users have been developed based on the assumption that providing material for safer crack smoking will reduce the risk of viral transmission, but these have not yet been systematically evaluated.

No convincing evaluations, and very limited service development, has targeted the majority of stimulant users who neither inject nor smoke their drugs. Some limited experimentation with pill testing initiatives has been conducted in some countries, but it has not been systematically evaluated, and recently the limited support for this kind of programme appears to be waning further.

'Safer dancing' programmes have looked at environmental risks such as fire safety and drinking water availability along with information-giving. Impact evaluations are not available in this area but as these measures are not viewed as particularly controversial and generally considered to represent sensible public health and safety measures, this may not be a priority as long as investment in researching more controversial measures is lacking.

In terms of research priorities, the extent of stimulant-related harm in Europe remains largely unmeasured. Around 400 deaths per year are thought to be associated with cocaine use but this may be an underestimate, as the extent to which cocaine use is an aggravating factor in deaths related to cardiovascular problems remains unknown. Treatment demands for stimulants are growing however, and some countries have long-established amphetamine injection populations that are probably not directly comparable to opioid injectors.

The pattern of polydrug use consumption, especially the co-use of alcohol, is also likely to be a major issue both for assessing the harm of different consumption patterns and for targeting interventions. Put simply, despite the growing importance of stimulant use with the European drug field, there is very little research evidence to permit an informed analysis of the effectiveness of harm reduction interventions and therefore even informed speculation on what approaches might prove successful currently remains difficult.

Harm reduction policies for cannabis

Despite a growing interest in, and evidence base for, harms attributed to cannabis use there is very limited evidence of effectiveness of the proposed harm reduction strategies in this area. There is not sufficient evidence that roadside drug-testing reduces mortality due to car crashes. Screening and brief interventions for excessive cannabis users have been proposed as adaptations of similar interventions for alcohol abuse, but no sufficient evidence is available yet on their effects. Vaporisers and other developing technology may reduce the risks associated with smoking cannabis products but the extent to which this is so remains unclear. The question also remains open on the extent to which vaporisers are likely to be viewed by consumers as acceptable alternatives to current modes, especially given the link between tobacco smoking and cannabis use that exists in Europe. There is therefore a wide range of important questions to be addressed by well-constructed primary research in this area. These include, but are not limited to: the extent to which roadside testing would reduce motor vehicle accident fatalities; whether informing cannabis users about related harms can reduce the actual levels of problems experienced; to what extent brief interventions can reduce harm; and how new technologies, or behavioral changes, reduce risks associated with smoking.

Harm reduction policies for tobacco

There is good evidence that public smoking bans and mandatory reduced ignition propensity standards for cigarettes reduce tobacco-related harms to non-smokers and improve health at the population level. There is no evidence that modified smoked tobacco products and cigarette-like devices substantially reduce harm, and limited evidence that pharmaceutical nicotine or low nitrosamine smokeless tobacco products might reduce tobacco-related harm in those who are unable or unwilling to quit but are willing to switch to such products. Nonetheless, given the high probability of health damage for those who continue to smoke there remains a considerable need for primary research into the extent to which innovative new products would be attractive to current smokers and to what extent they can reduce harm to users who are unable to quit. A parallel research question would be the extent to which 'safer smoking technologies', should they become available, would undermine smoking reduction policies at the population level. This is, however, an area in which multi-site RCTs to evaluate both benefits and risks of new products are clearly feasible. Studies in this area will need to identify biomarkers that are sensitive to short-term changes in smoking behaviour and are also predictive of long-term harm.

Alcohol harm reduction

There is sufficient evidence on the effectiveness for some outcome measures of a total ban on sales, minimum legal purchase age, government monopoly and restrictions of retail sales, alcohol taxes, lowered limits of blood alcohol concentration (BAC) for car drivers and low BAC limits for young drivers. There are several studies on public service messages and alcohol education in school but no evidence of effectiveness. There are too few studies in the areas of voluntary codes of bar practice, promoting alcohol-free activities, warning labels, college student education, designated drivers and ride services to allow comment on their effectiveness, although all these areas appear interesting topics for further research. In general there is a growing interest in interventions that can reduce the harm accruing from alcohol use, and across Europe alcohol problems are becoming an area of greater policy concern. As drugs and alcohol are often consumed together in recreational settings the challenge will be to develop research designs that are adequate to the complexities of assessing interventions targeting poly substance consumption patterns. Finally, in this area a clear need exists for a thorough systematic review to identify the key gaps in the current knowledge base and provide a better road map for setting future research priorities.

Pragmatism, policy and the evidence base

The value of taking a strict approach to assessing the quality of evidence concerning the impact of harm reduction interventions is that it allows policymakers to make decisions with greater certainty. The problem, however, is that this may set the bar too high, given that in the 'real world' there are practical, methodological and ethical reasons that mean that it may be extremely difficult or even impossible to generate such a high level of evidence. Moreover, if RCT designs are employed it may be necessary to control the parameters of the study so strictly that any findings may have limited applicability to the real world setting in which harm reduction interventions typically take place. This problem is not restricted to harm reduction but is common to many areas of social policy. Models are being developed that try to incorporate the available evidence to inform policy formation even if this has to be based on a lower level of certainty.

An interesting development in this field is the guidelines produced by the GRADE method group (Guyatt et al., 2008). This approach clearly opens the way towards considering other study designs in appraising the evidence. An example of this can be found in the recently published WHO guidelines for substitution treatment, which used non-randomised studies to evaluate the evidence supporting recommendations for the use of substitution treatment in reducing HIV infection and mortality (WHO, 2009).

In reality, policymakers are often faced with making choices in areas in which a high level of certainty is lacking and pragmatic choices are required. But how can pragmatic policy choice be supported? Evidence that interventions are not producing harm to those that receive them or to the wider community is likely to be important. As is evidence that they are reaching their intended recipients, who are appearing to benefit from well-constructed measures. If there is no evidence of harm, and some evidence of benefit, it can help to provide sufficient justification for pragmatic policy choices to be made, even when clear evidence of effectiveness is lacking.

This can be seen in the area of needle and syringe exchange where the evidence can still be regarded as tentative in respect of demonstrating that HIV transmission is reduced. However, numerous studies do show that reported risk behaviour is lowered and/or are suggestive that provision of syringe exchange can be associated with low, or reduced, rates of new HIV infections at the population level. Moreover, no strong evidence exists that this type of intervention delivers harm, although this concern has been repeatedly raised by those who were hostile to the development of this kind of service.

When faced with this evidence policymakers in Europe have made a pragmatic choice that there is sufficient data to include this sort of provision in a comprehensive package of services for drug injectors, even if it is still not possible to show conclusively that such services reduce by themselves rates of new infections. In practice needle and syringe programmes (NSPs) are usually not isolated services, but are typically implemented by agencies who offer a range of other services, operate in a variety of settings, and in the context of diverse epidemic and behavioral scenario. A multitude of mediating factors therefore have to be accounted for when assessing their impact, which complicate both the collection and interpretation of evidence.

Future perspectives: harm reduction and contemporary patterns of drug use in Europe

This monograph has provided a state-of-the-art reflection on the development of harm reduction services in Europe and considered what we know about their effectiveness. It has provided historical context and an analytical framework for understanding how harm reduction approaches have moved into the mainstream in Europe. It has also launched a discussion on the potential role for harm reduction in addressing the problems caused by the consumption of alcohol and tobacco. The EMCDDA's role is to monitor and report on drug use in Europe and the policies and responses Member States have developed to respond to the drug situation. It is from this perspective that we offer some concluding remarks on the future challenges that changing patterns of drug use will bring to the debate in Europe on how best to reduce the harm associated with drug consumption.

Drug policy at the European level is not only concerned with understanding the situation within the EU. An explicit element of the EU drug strategy and accompanying action plans is to enable the EU to have a strong and united voice in the international debate on drugs. This is important for many reasons, not least because the future drug problem faced by the EU will be influenced by the situation and policies of other countries. Drug problems transcend national boarders and are becoming increasingly global in nature. In this context, the situation in countries bordering the EU is clearly an important factor for consideration.

The issues for the diffusion of harm reduction practice look somewhat different when looking out from Europe rather than within. In many non-EU countries HIV epidemics among injectors appear to be a growing problem, the availability of services of all types is often limited, and considerable political and professional resistance can exist to introducing harm reduction approaches, even where the evidence base is robust. In international debates and in funding

for development programmes, Europe has supported the role of harm reduction as an important part of a comprehensive HIV prevention strategy. This battle is far from won. Globally the problem of HIV infections acquired through drug injection remains a critically important public health issue and one in which Europe is likely to want to remain a strong advocate for evidence-based approaches.

Within the EU, preventing HIV infections related to drug injection remains an important objective for drug policies and there is a need to develop services and responses further. However, it no longer has the primacy it once had. Overall, the long-term trend appears to be for a stabilisation, or fall, in both levels of injecting, and opiate use, and despite some localised problems the assessment of the situation in respect to drug related HIV infections is generally a positive one (EMCDDA, 2009). Despite this, morbidity and mortality associated with drug injecting remains considerable. There is a need to develop treatment regimes that are attractive to those that are currently hard to treat. There is a need to develop effective approaches to HCV infection — which is found virtually universally at high prevalence among drug injectors across Europe. Finally, there is a pressing need to find effective measures to address opioid-associated drug overdose. This is now the major avoidable cause of morbidity amongst injectors. To date, in each of these areas some innovative harm reduction approaches have been developed, but the evidence base for informing policymakers remains inadequate.

At points throughout this monograph it has been argued that harm reduction interventions may sometimes be most effective when provided as part of a 'package' of care, rather than as a stand-alone approach. If this is the case, a challenge for the future will be to develop research and evaluation designs that are adequate to the task of exploring the impact of programmes delivered consequently, and across different levels of intensity. Methodologically this is no trivial task. Nonetheless, progress in this direction is required to gain a more holistic understanding of how interventions work in order to inform spending choices on what sort of programme mixes are likely to be most appropriate.

During the 1980s, and 1990s, the concept of problem drug use in Europe was virtually synonymous with opioid use and drug injection. It was recognised that some, mainly Nordic, countries had long-established amphetamine injecting populations, that smoking was becoming a common mode of administration among some heroin using groups, and that drugs like ecstasy were becoming more important on the recreational drug scene. However, the focus for discussions on drug problems remained very much on the chronic use of heroin usually by injection. The perspective today looks very different. Heroin and injecting problems remain with us, but policymakers are equally concerned by what can be seen as a broader, more complex and faster moving drug situation.

Today's concerns are as likely to focus on the widespread use of cocaine and other stimulants, the misuse of medicinal products, polydrug use including the use of licit substances or even intensive cannabis use, as they are to focus on heroin injecting. To some extent the harm reduction agenda has failed to keep pace with the political one in this respect. A challenge for the future growth of harm reduction services in Europe will be to develop intervention models that address the harms associated with a broader set of consumption

patterns. This monograph helps to chart where developments are needed in these areas. Here, the boundaries between drug prevention, drug treatment and harm reduction become increasingly fluid. This can be seen at the service level, for example in brief interventions for cannabis users, and at the individual level, for example where practitioners develop client care plans that include prevention, treatment and harm reduction services simultaneously.

Finally, this monograph has concentrated on the topic of evidence and how it should be assessed. Yet it is important to remind ourselves that the absence of evidence does not necessarily justify the absence of action. As Fry (2010) argues in his discussion on the ethical aspects of harm reduction, 'values' have to be taken into account, especially when disputes and uncertainty about 'facts' exist. In this policy field, 'evidence' can be a precious commodity. The challenge for the research community is to provide policymakers with a higher degree of certainty that the policies and actions they pursue are more likely to reduce rather than augment harm.

References

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) (2009), *Annual report 2009: the state of the drugs problem in Europe*, Publications Office of the European Union, Luxembourg.

European Union (2008), 'EU drugs action plan for 2009–2012', 2008/C 326/09, *Official Journal of the European Union*, 20 December, C326/7–25.

Fry, C. (2010), 'Harm reduction: an "ethical" perspective', in Chapter 4, 'Perspectives on harm reduction: what experts have to say', in European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), *Harm reduction: evidence, impacts and challenges*, Rhodes, T. and Hedrich, D. (eds), Scientific Monograph Series No. 10, Publications Office of the European Union, Luxembourg.

Guyatt, G. H., Oxman, A. D., Kunz, R., et al. for the GRADE Working Group (2008), 'Going from evidence to recommendations, *BMJ* 10 May, 336 (7652), pp. 1049–51.

Herring, R., Thom, B., Beccaria, F., Kolind, T. and Moskalewicz, J. (2010), 'Alcohol harm reduction in Europe', in European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), *Harm reduction: evidence, impacts and challenges*, Rhodes, T. and Hedrich, D. (eds), Scientific Monograph Series No. 10, Publications Office of the European Union, Luxembourg.

Higgins, J. P. T. and Green, S. (eds) (2008), *Cochrane handbook for systematic reviews of interventions*, version 5.0.1 (updated September 2008), The Cochrane Collaboration. Available at www.cochrane-handbook.org.

Moher, D., Schulz, K. F. and Altman, D. G. (2001), 'The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials', *Lancet* 357 (9263), pp. 1191–4.

Plint, A. C., Moher, D., Morrison, A., et al. (2006), 'Does the CONSORT checklist improve the quality of reports of randomised controlled trials? A systematic review', *Medical Journal of Australia* 185 (5), pp. 263–7.

von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C. and Vandenbroucke, J. P. (2007), 'STROBE initiative: the strengthening the reporting of observational studies in epidemiology (STROBE) statement — guidelines for reporting observational studies', *Lancet* 20 October, 370 (9596), pp. 1453–7.

WHO (World Health Organization) (2009), *Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence*, WHO, Geneva. Available at http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf.