



European Monitoring Centre
for Drugs and Drug Addiction



ECDC AND EMCDDA **GUIDANCE**

Prevention and control of infectious diseases among people who inject drugs

www.ecdc.europa.eu
www.emcdda.europa.eu

ECDC AND EMCDDA GUIDANCE

Prevention and control of infectious diseases among people who inject drugs



European Monitoring Centre
for Drugs and Drug Addiction

The content of this joint guidance was developed by the European Centre for Disease Prevention and Control (ECDC) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) with the support of a technical advisory group composed of policy makers, service providers, civil society representatives and preventative health experts from throughout the EU/EEA.

The guidance was written by Mika Salminen, Anastasia Pharris and Andreas Sandgren from ECDC and by Dagmar Hedrich and Lucas Wiessing from the EMCDDA. The text box on *Minors' access to needle and syringe programmes* was produced by Anna Tarján and Robert Csák, the box on *Scaling up coverage of services* by Kristi Rüütel, and the one on *Point-of-care testing* was produced by Henrikki Brummer-Korvenkontio. Hans Blystad substantially contributed to the section on tuberculosis screening, testing and treatment. Tuukka Tammi contributed to the evidence base for the section on core values. Additional comments were provided by Frode Forland, Erika Duffel, Giedrius Likatavicius, Teymur Noori and Marita van de Laar at ECDC, and Alessandro Pirona, Marica Ferri, Teodora Groshkova and Roland Simon at the EMCDDA.

A framework for the guidance and review of part of the evidence concerning needle and syringe programmes and other services was produced under contract ECDC/10/2246 by Eva van Velzen and Sharon Hutchinson (University of Strathclyde/Health Protection Scotland); Norah Palmateer, Kirsty Roy, Alex Sánchez-Vivar, David Goldberg (Health Protection Scotland); Matt Hickman (University of Bristol); Avril Taylor (University of West of Scotland); Jennifer Kelly and John Campbell (Glasgow Addiction Services); and Vivian Hope (London School of Hygiene and Tropical Medicine). An additional review of the evidence regarding drug treatment was produced under EMCDDA contract CC.10.RES.011 by Georgie MacArthur and Matt Hickman (University of Bristol).

This Guidance is also published 'In brief' and accompanied by two Technical Reports: 'Evidence for the effectiveness of interventions to prevent infections among people who inject drugs. Part 1: Needle and syringe programmes and other interventions for preventing hepatitis C, HIV and injecting risk behaviour' and 'Part 2: Drug treatment for preventing hepatitis C, HIV and injecting risk behaviour'.

We would like to thank the following members of the ECDC/EMCDDA Technical Advisory Group for their valuable input:

- Henrique Barros, National AIDS Coordination, Portuguese Ministry of Health; University of Porto Medical School, Portugal
- Hans Blystad, Norwegian Institute of Public Health, Department of Infectious Disease Epidemiology, Norway
- Grazyna Cholewinska, Warsaw Hospital for Infectious Diseases, Poland
- Hans Haltmayer, Verein Wiener Sozialprojekte, Vienna, Austria
- Niklas Karlsson, National Institute for Communicable Disease Control, Sweden
- Astrid Leicht, Fixpunkt Berlin, Germany
- Xavier Majó i Roca, Programme on Substance Abuse, Department of Health, Catalonia, Spain
- Luis Mendão, EU Civil Society Forum
- Viktor Mravcik, National Monitoring Centre for Drugs and Drug Addiction, Czech Republic
- Anne Ovaska, A-Clinic Foundation, Finland
- Maria Prins, Amsterdam Municipal Health Services, Netherlands
- Kristi Rüütel, Estonian National Institute for Health Development, Department of Infectious Diseases and Drug Abuse Prevention, Estonia
- Ioana Tomus, Romanian Harm Reduction Network, Romania

Suggested citation: European Centre for Disease Prevention and Control and European Monitoring Centre for Drugs and Drug Addiction. Prevention and control of infectious diseases among people who inject drugs. Stockholm: ECDC; 2011.

Stockholm, October 2011

ISBN 978-92-9193-313-6

doi 10.2900/58565

© European Centre for Disease Prevention and Control, 2011

© European Monitoring Centre for Drugs and Drug Addiction, 2011

Reproduction is authorised, provided the source is acknowledged.

Contents

Acronyms and glossary	iv
Executive summary	1
Seven recommended key interventions	1
Achieve synergy: combine key interventions.....	2
Target audience	2
Evidence-based public health guidance	2
National coordination	2
Tailor measures to the national situation.....	2
Introduction.....	3
Infections among people who inject drugs	3
Why is this important?	6
Aims, objectives and methodology	6
Scope	7
Target readership	8
Core values of prevention of infections among people who inject drugs.....	9
Principles of prevention	9
Principles of service provision.....	10
Recommended interventions for the prevention of infections among people who inject drugs	12
Key intervention components.....	12
Combine key interventions to achieve synergy.....	13
Developing and providing programmes for infectious disease prevention and control among people who inject drugs	14
Cooperation and coordination	14
Seven recommended key interventions	15
Injection equipment.....	15
Vaccination	17
Drug dependence treatment.....	18
Testing	21
Infectious disease treatment.....	23
Health promotion.....	24
Targeted delivery of services	26
Knowing and understanding the national situation.....	32
Monitoring problem drug use and responses	32
Surveillance of infections	32
Monitoring and evaluation of programmes	33
Setting targets for intervention coverage	33
Annex A. Epidemiology of injecting drug use and major infections among people who inject drugs in the EU/EEA	35
Injecting drug use	35
HIV	35
Hepatitis B and C.....	35
Tuberculosis.....	36
Hepatitis A virus	36
Bacterial skin and systemic infections	37
Sexually transmitted infections.....	37
Human T-lymphotropic virus type II (HTLV-II)	37
Annex B. Key interventions to prevent infections among people who inject drugs.....	38
Annex C. Additional guidance and technical guidelines.....	42
References.....	44

Acronyms and glossary

ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFTA	European Free Trade Association
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
European neighbourhood	EU Member States and their geographical land neighbours, EU candidate and potential candidate countries, EFTA and EEA countries
EU	European Union
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
Health promotion	Health promotion is the process of enabling people to increase control over, and to improve, their health. Health promotion includes not only information giving and support, but also risk-reduction counselling.
IGRA	Interferon-gamma release assays, a blood test for tuberculosis
Low-threshold services	Low-threshold services are social and health services for people who use drugs; they typically offer a place to be, health education and counselling, needle and syringe programmes, referral to drug treatment, and sometimes overnight shelter. The low-threshold approach aims to reach more users with problematic use patterns earlier and to remain in contact with them in order to prevent health damage while not requesting abstinence.
NSP	Needle and syringe programmes
OST	Opioid substitution treatment
Problem drug use	Injecting drug use or long-duration/regular use of opioids, cocaine and/or amphetamines
Secondary needle exchange	The distribution of sterile injecting equipment to one service user, who then redistributes it to others in his or her social network. This is referred to as 'peer distribution' in some settings.
STI	Sexually transmitted infection
TB	Tuberculosis
TST	Tuberculin skin testing
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Executive summary

Since the emergence of the HIV epidemic among people who inject drugs in the mid-1980s, many European countries have achieved substantial progress in implementing evidence-based measures to prevent and control infectious diseases among this group. In the 1990s, EU countries started to develop common prevention policies both in the fields of HIV/AIDS and drugs and drug addiction, which included the establishment of EU agencies to monitor the drug situation (the EMCDDA in 1993) and to prevent and control infections (ECDC in 2005). In the past two decades, prevention and treatment interventions have been expanded and brought to scale. According to reports for the year 2009, more than half of the estimated population of problem opioid users received substitution treatment, and many countries have established needle and syringe programmes with increasing coverage among people who inject drugs. Data from countries with well-established surveillance systems suggest that the number of new HIV infections among people who inject drugs has decreased considerably in most, but not all, EU countries during the last decade.

In the European neighbourhood, injecting drug use remains a major factor of vulnerability for acquiring blood-borne and other infectious diseases, including HIV, hepatitis B and C, tuberculosis, bacterial skin and soft tissue infections, and systemic infections. Estimates of the number of people who inject drugs suggest that there are significant populations at-risk for these infections in all European countries. Unaddressed, these infections result in a large burden on European health systems, significant individual suffering, as well as high treatment costs.

It has been shown that a pragmatic public health prevention approach can have a strong effect on reducing the spread of blood-borne and other infections among people who inject drugs. Prevention is feasible and effective, if properly implemented.

Seven recommended key interventions

This evidence-based joint guidance by ECDC and the EMCDDA identifies good practice for prevention and control of infectious diseases among people who inject drugs.

Based on the most robust evidence available, expert opinion, and best practice within the EU/EEA, the following key intervention components should be applied and, if possible, combined to achieve the maximum prevention effect through synergy:

Key intervention components

Injection equipment: Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes free of charge, as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes.

Vaccination: Hepatitis A and B, tetanus, influenza vaccines, and, in particular for HIV-positive individuals, pneumococcal vaccine.

Drug dependence treatment: Opioid substitution treatment and other effective forms of drug dependence treatment.

Testing: Voluntary and confidential testing with informed consent for HIV, HCV (HBV for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment.

Infectious disease treatment: Antiviral treatment based on clinical indications for those who are HIV, HBV or HCV infected. Anti-tuberculosis treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated.

Health promotion: Health promotion focused on safer injecting behaviour; sexual health, including condom use; and disease prevention, testing and treatment.

Targeted delivery of services: Services should be combined and organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.

Achieve synergy: combine key interventions

Recent studies and experience from successful prevention programmes document the added value of offering a range of effective intervention measures in the same venues, and of providing a combination of interventions according to clients' needs, to achieve the maximum effect in preventing infections.

Target audience

This guidance aims to support policy makers in Europe to plan adequate, evidence-based, pragmatic, and rationally designed public health responses for the prevention and control of infections among people who inject drugs. It aims at public health programme planners and decision makers working in the fields of infectious diseases, general public health, addiction and mental healthcare, social services, and drug control at national and regional levels.

The guidance is coherent with and supports existing EU-wide policies in the field of drug control and infectious diseases and aims to give a comprehensive overview of the best current knowledge in the field, expanding previous work to include combinations of key interventions. It also relies on a foundation of core values derived from public health and human rights principles, which should guide prevention and service provision.

Evidence-based public health guidance

Research results relevant to the guidance have been reviewed and assessed using evidence-based medicine (EBM) principles adapted within a public health framework. To produce the guidance, high-level scientific evidence has been comprehensively reviewed, and the results were combined with expert knowledge and advice on benefits and harms. Best practices as well as user preferences have contributed to the development of key interventions suggested in this document.

National coordination

A prerequisite to the effective delivery of the key interventions is national and local cooperation, and coordination between sectors. National consensus building and mutually respected objectives are essential when it comes to the successful implementation of interventions. Objectives should be agreed on by actors across all sectors, particularly those that engage with people who inject drugs.

Tailor measures to the national situation

In order to ensure that interventions best serve the population of people who inject drugs, as well as prevent and control infectious diseases, there must be sufficient surveillance of problem drug use and infections on national and sub-national levels. Measures taken should be continuously monitored and evaluated in terms of response, impact, relevance and scale of coverage. Investment in adequate surveillance systems of both drug use and infectious disease is necessary and cost-effective.

Evidence suggests that higher levels of coverage of needle and syringe programmes and opioid substitution treatment per drug injector are more effective than lower levels of coverage. The goal should be to ensure that the services offered meet local needs and demand. Unmet demand for needle and syringe exchange services or waiting times for drug treatment indicate inefficiency in prevention.

Introduction

Infections among people who inject drugs

Since the emergence of the HIV epidemic among people who inject drugs in the mid-1980s, many European countries have achieved substantial progress in implementing evidence-based measures to prevent and control infectious diseases among this group. In the 1990s, EU countries started developing common prevention policies in the fields of HIV/AIDS and drugs and drug addiction, which included the establishment of EU monitoring agencies on drugs (in 1993) and infections (in 2005) (3). During subsequent decades, interventions were brought to scale: for example, around 700 000 opioid substitution treatments were reported in 2009, more than half of the estimated population of problem opioid users (4). The proportion of people who inject drugs among new HIV infections and the number of infections in this group decreased considerably in many EU countries. However, in the European neighbourhood, injecting drug use remains a major factor of vulnerability for acquiring blood-borne and other infectious diseases. Estimates of the number of people who inject drugs suggest that there are significant populations at-risk in all European countries (5). Patterns of injection use vary across the region, with opioid injection prevalent in all countries and a significant proportion of stimulant (mainly amphetamine) injection in the northern and eastern parts of Europe. Poly-drug use further complicates the pattern (5).

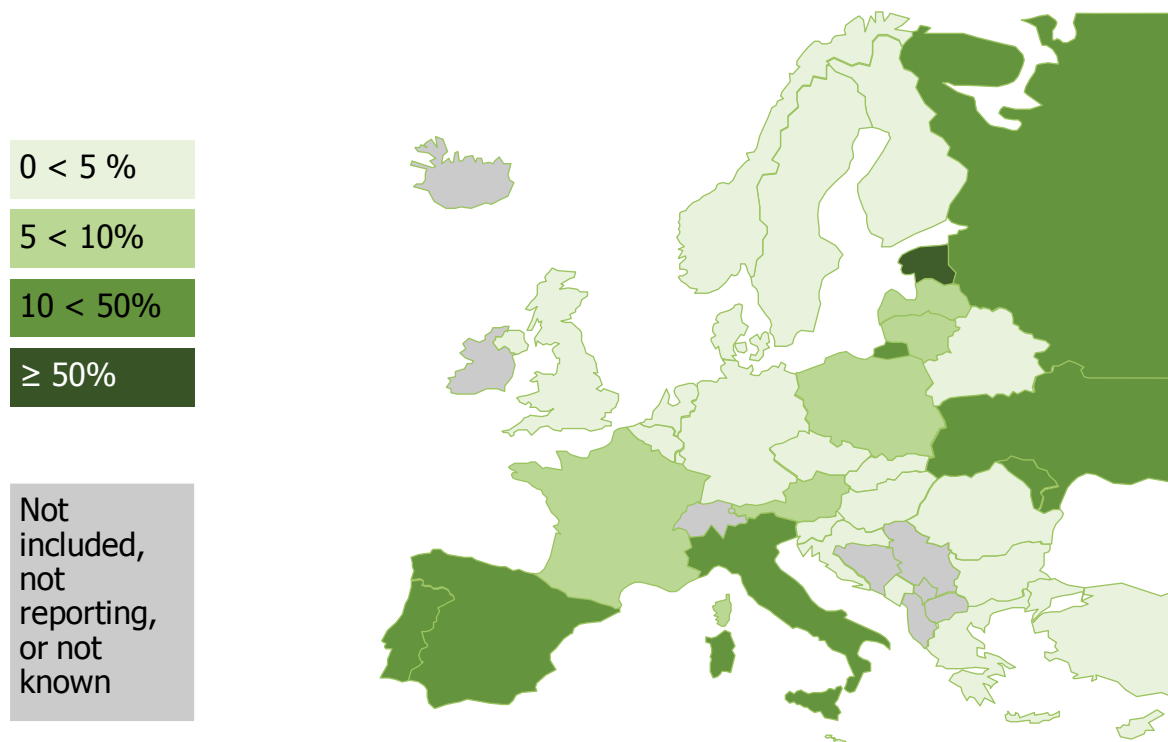
Infections for which people who inject drugs may be at increased risk:

- HIV infection;
- hepatitis A;
- hepatitis B (HBV);
- hepatitis C (HCV);
- hepatitis D;
- tuberculosis (TB)
- skin and soft tissue infections caused by *Staphylococcus aureus* (including methicillin-resistant *Staphylococcus aureus*, MRSA) and streptococcal infections (e.g. endocarditis, necrotising fasciitis);
- severe systemic sepsis (e.g. infections with *Clostridium novyi*, *Bacillus anthracis*);
- STIs other than HIV infection or hepatitis (e.g. chlamydia infection, syphilis and gonorrhoea);
- respiratory infections such as pneumonia, diphtheria and influenza;
- wound botulism;
- tetanus;
- human T-cell lymphotropic virus (HTLV) infections.

Common blood-borne infections in this group include human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV). The main mechanism of transmission for these infections is the sharing of injection equipment among users, such as syringes, needles, drug mixing vessels and other drug preparation paraphernalia. In addition to spread through shared injection equipment, there is sexual transmission of HIV and HBV, both within the population of people who inject drugs and from current or former injectors to their sexual partners or clients. While all of the above viral infections are easily transmitted through sharing of used injection equipment, transmission risks vary. Compared to HIV infection, hepatitis C infection is characterised by relatively high concentrations of virus in the blood, not only during the primary infection phase, but also in those who become chronically infected. This is thought to lead to high transmission rates upon exposure to HCV when infected and non-infected individuals share needles, syringes or other drug preparation equipment. Hepatitis C prevalence normally exceeds HIV prevalence in user communities, and hepatitis C epidemics often precede HIV epidemics among people who inject drugs. The higher transmission risk may also explain why HCV is more difficult to limit through the application of single interventions, and why higher intervention coverage may be needed to reduce HCV rates at population level.

While the most recently available European surveillance data suggests that the incidence of HIV infection has dropped considerably over the past decade and is further decreasing among people who inject drugs, there are clear differences between regions of Europe (6). Many EU Member States experienced large outbreaks of HIV infection among people who inject drugs in the 1980s and 1990s, while most countries in the eastern part of the European region, including some EU Member States, experienced major outbreaks in the early 2000s. This has led to the establishment of high HIV prevalence among active and former drug injectors in several countries within the EU. Some east European countries which border the EU have been particularly heavily affected by the rapid spread of HIV infections among people who inject drugs. Some EU countries, as well as some neighbouring countries, report a high prevalence of co-infection with HIV and tuberculosis among people who inject drugs.

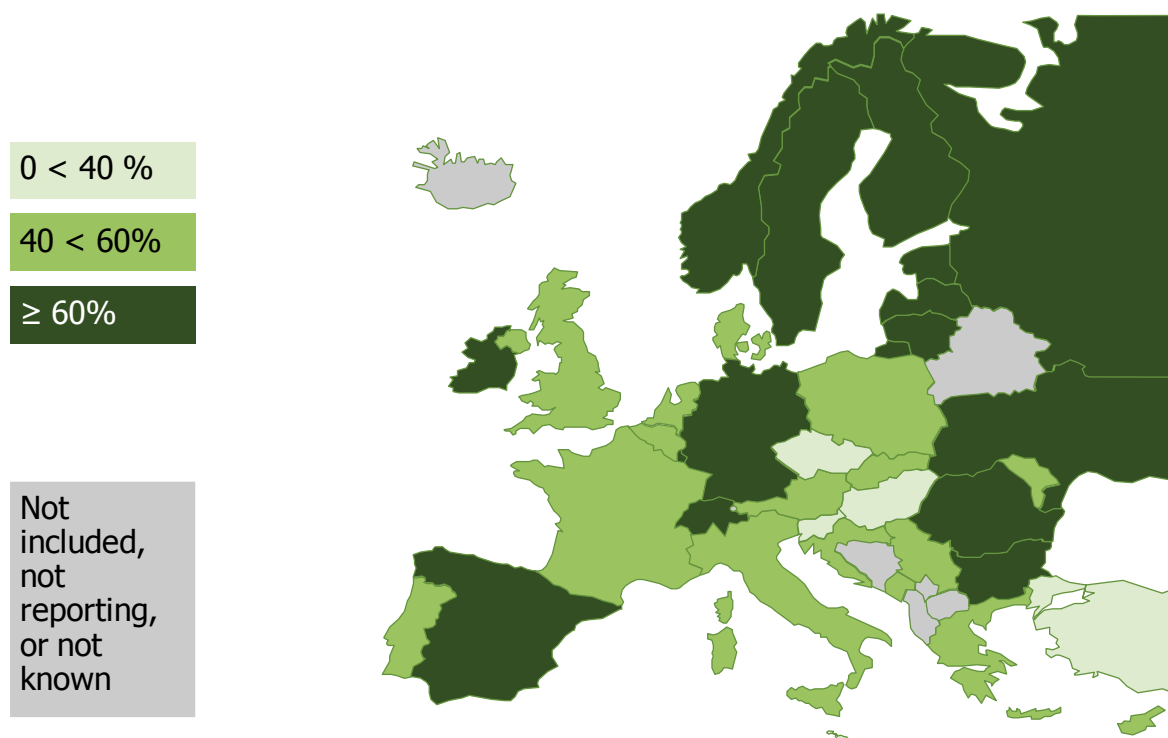
Figure 1: HIV prevalence among people who inject drugs; Europe, 2008–2009



Source: The EMCDDA and Reitox National Focal Points (EMCDDA countries: EU, Croatia, Turkey and Norway); Mathers et al., Lancet 2008 (other countries). Colour indicates midpoint of national data, or if not available, of local data. For EMCDDA countries data are mostly from 2008–2009. When 2008–2009 data were unavailable, older data were used. The EMCDDA data are sub-national for Croatia, Netherlands, Turkey, Sweden, United Kingdom, Belgium, Bulgaria, Lithuania, France, Estonia, Ireland; for non-EMCDDA countries this information is not available.

Hepatitis B and C virus infections are common in active and former injectors, and a history of injecting drug use is the most frequent risk factor in Europe, particularly for hepatitis C infection. The timing of the introduction of hepatitis C infection in this population is less well understood, but the virus is likely to have preceded HIV by a few decades. European surveillance data on incidence of new infections are poorly standardised, making it difficult to determine trends across the region (7). However, targeted prevalence studies have found high prevalence and evidence for frequent outbreaks among users in almost all geographic areas studied (5,8-9). More importantly, there is a strong association between the duration of injection drug use and hepatitis C infection (10). Co-infection with more than one type of hepatitis, or co-infection with HIV and hepatitis C present growing clinical and prevention challenges in many parts of Europe (1).

Figure 2: Prevalence of hepatitis C virus antibodies among people who inject drugs; Europe, 2008–2009



Source: The EMCDDA and Reitox National Focal Points (EMCDDA countries: EU, Croatia, Turkey and Norway); Nelson et al., *Lancet* 2011; IHRA, EHRN and WHO Regional Office for Europe (other countries). Colour indicates midpoint of national data, or if not available, local data. Data for EMCDDA countries are mostly from 2008–2009. When 2008–2009 data were unavailable, older data were used. The EMCDDA data are sub-national for Turkey, UK, France, Slovakia, Netherlands, Belgium, Poland, Bulgaria, Spain, Sweden, Ireland, Latvia, Germany, Lithuania, Romania, Estonia. For non-EMCDDA countries, this information is not available.

In addition to HIV and hepatitis B and C, infections caused by human T-lymphotropic virus type II (HTLV-II) have been shown to have spread among people who inject drugs as early as the 1970s (11). There have been reports of outbreaks of hepatitis A within the EU in groups of people who inject drugs, although isolating the injection risk from other risk factors such as poor hygiene is challenging (12–15).

People who inject drugs, especially those who are socially marginalised, are not only vulnerable to infections from blood-borne viruses, but also to other infections. A list of some of these infections is provided in the text box on page 3 (16), and additional information on the epidemiology of these diseases is presented in Annex A. These include localised bacterial wound and injection site infections, systemic infections, sexually transmitted infections and respiratory infections, such as tuberculosis. Cases of tetanus are reported among people who inject drugs. In some settings, persons with a history of drug injection comprise about half of the reported tetanus cases (17). Outbreaks of tetanus have been documented in drug user populations, particularly among users who report subcutaneous injection of heroin and have a history of no or partial immunisation (18–19).

The spread of infections that are associated with injecting drug use have been controlled during the last decade in some European countries, and infection rates are falling (8). This has most likely been due to a combination of behaviour change in user populations, scaling-up of prevention services, and treatment of disease and vaccination. Despite these positive developments, there is no room for complacency as blood-borne infections can spread very rapidly among people who inject drugs, unless injection-driven infection risks can be continuously controlled. Several studies of HIV outbreaks among people who inject drugs document an almost exponential spread in the early stages and the rapid establishment of high HIV prevalence levels (20–21). The same has been demonstrated for hepatitis C, where a combination of low infection dose, extended length of viral survival outside of the body, and continuously high blood virus load in chronic infection may result in very rapid establishment of high population prevalence among users.

Despite the successes in reducing disease prevalence in some regions of the EU, available estimates clearly show that infections among people who inject drugs are not yet effectively prevented in all areas of the European neighbourhood. Although preventable, these infections continue to cause major disease burden in Europe and high levels of personal suffering.

Why is this important?

The main motivation for the prevention of infections among people who inject drugs is that prevention is feasible and effective, if properly implemented. Addiction to illicit drugs is a medical condition which, on public health and ethical grounds, demands the implementation of effective measures to prevent disease and minimise the harms caused by drug addiction. Effective measures to prevent infections exist, but are either not offered or not accessible to a high proportion of those in need of them.

From a public health perspective, subpopulations with a high burden of infections have both a direct and indirect burdening effect on society, and the prevention of infections can minimise these costs. Firstly, direct morbidity due to severe forms of chronic infections results in high costs of treatment and care among those infected. Secondly, the loss of human productivity among the severely affected increases the societal costs. Thirdly, a high prevalence of disease among drug users may enhance the risk of increasing prevalence in the wider population, especially if high prevalence is maintained for long periods of time.

Finally, failure to counteract an avoidable consequence of a particular form of severe addiction could be interpreted as indifference to the EU's pledge to promote social justice and protection, as committed to in international conventions, including the Charter of Fundamental Rights of the European Union and the Lisbon Treaty (22-23).

While the elimination of illicit drug use or of drug injecting would, in principle, be a good intervention for infectious disease prevention, global experience has shown that this cannot be achieved through public health measures alone. Strict drug control measures have not been successful in completely eliminating the risks and illicit drug-related harm. On the contrary: while clarifying that public health concerns were the driving concern behind drug control, an evaluation of a century of international drug control efforts by the UNODC found that the drug control system and its applications have had several unintended consequences, including a lack of investment in tackling the public health harms of drug use. Drug use is mainly dependent on other societal factors (a review of which is beyond the scope of this guidance), and drug use practices are highly dependent on drug user subcultures and economic realities, which may be difficult to influence. However, experience and evidence have shown that adopting a pragmatic approach which addresses and limits the direct infection risks associated with the injection procedure and which introduces measures that help stop or reduce injecting can have a strong effect on reducing the spread of blood-borne infections among people who inject drugs.

Aims, objectives and methodology

This evidence-based guidance is designed to inform the development, monitoring and evaluation of national strategies and programmes in countries in the EU and the European neighbourhood to prevent and treat infections among people who inject drugs. The guidance is in coherence with existing EU-policies in the field of drugs and infectious diseases (24-27).

The guidance relies on a foundation of core values described in a separate section below.

Seven key interventions are identified to reduce and prevent infections among people who inject drugs in Europe. These are based on the most robust scientific evidence available, combined with expert opinion and long-standing and well-documented experience of service providers and preferences of users of services.

Two ECDC/EMCDDA Technical Reports provide an overview of the evidence base behind the interventions recommended here: 'Evidence for the effectiveness of interventions to prevent infections among people who inject drugs. Part 1: Needle and syringe programmes and other interventions for preventing hepatitis C, HIV and injecting risk behaviour' and 'Part 2: Drug treatment for preventing hepatitis C, HIV and injecting risk behaviour'.

Evidence base

In the process of drawing up this guidance, evidence reviews covering a large number of primary studies on the key interventions in question were systematically assessed, using a highly standardised 'review of reviews' method¹. Outcomes of studies using the most robust scientific designs were collated and statements regarding their effectiveness were derived, synthesising results in terms of study design, number of cases included in the studies and number of studies sharing the same results – factors that determine the strength of the evidence. The resulting top-level evidence from this 'review of reviews' was combined with the most recent primary research results not yet captured by review papers. Primary studies were also used when no systematic reviews about the

¹ The 'review of reviews' methodology (Kelly et al., 2002) brings together evidence from published reviews rather than undertaking a systematic search of primary literature. The 'review of reviews' methodology involved a systematic search of the literature for published reviews; identification of relevant systematic, meta-analytic and narrative reviews; critical appraisal of the reviews; and synthesis of the findings.

effectiveness of an intervention were available. The methodology used for identifying and selecting the reviews and primary studies and results are described in detail in the two technical reports which accompany the guidance.

However, in the field of public health it is sometimes not possible to obtain the type of strong evidence levels that can be derived from experimental studies such as randomised controlled trials (RCTs). Some public health interventions can – for ethical reasons – not be tested in an experimental way (by providing them to one group and withholding them from another). Also, the control of confounding factors under real-world conditions would be very complex and require prohibitively expensive study designs. Another obstacle to the identification of statistically significant positive or negative outcomes of interventions in this field is the low incidence of relevant outcomes, so that research has to cover a very long period to accumulate a sufficient number of relevant events before drawing a conclusion (28).

The relationship between evidence and recommendations is not necessarily straightforward: high-quality evidence does not always lead to strong recommendations, and strong recommendations can arise from low-quality evidence. In those instances when review-level evidence on interventions was inconclusive or when there was a noted lack of evidence on interventions, this guidance draws instead on expert advice regarding the potential benefits and harms of certain interventions, looks at best practices in prevention services in the EU, and assesses studies on user preferences. While expert opinion is considered a weaker level of evidence, there are conditions under which an expert group may attribute high strength to recommendations in the absence of robust research evidence. Examples are hydration of hospital patients or blankets to prevent heat loss in trauma patients – interventions that are not based on a strong evidence base from scientific research studies, but are still highly recommended. Additional information on the reasoning behind each recommended intervention is available in Annex B.

Scope

This guidance builds on previous efforts in the area of infection prevention among people who inject drugs, particularly work conducted by the WHO, UNAIDS, and UNODC; in addition, multiple national guidelines and recommendations were consulted (see Annex C). The present guidance attempts to give a comprehensive overview of the best current knowledge in the field by expanding previous work to include combinations of key interventions. Its aim is to provide a thorough synthesis which is not only pertinent for the EU but also for the EU's neighbouring countries. The guidance contains references and links to further sources which provide additional in-depth information and descriptions of the technical implementation (Annex C).

This guidance mainly focuses on the interventions and preventive measures that address the infection risks directly. The main infections covered are HIV, hepatitis B, hepatitis C, and tuberculosis (TB). Some other infections for which people who inject drugs may be at higher risk, such as skin and soft tissue infections, hepatitis A, and sexually transmitted infections are discussed, but in less detail. The guidance addresses issues such as knowledge and understanding, risks of drug preparation and injection, equipment sharing, vaccinations, drug substitution and other forms of drug treatment in order to reduce injection frequency and increase treatment adherence. It also suggests ways of organising relevant services in an effective way.

People who inject drugs addressed in this guidance include opioid and stimulant injectors. While the focus of the guidance is on these 'traditional' injecting populations, the interventions proposed may also be relevant for new or emerging groups of injectors, such as those who inject performance-enhancing drugs like anabolic steroids. Observations from some countries suggest that the latter group of injectors may warrant further monitoring. Problem drug users who do not inject would likely benefit from many interventions discussed here, although they are not the key target for this guidance.

The guidance does not extensively discuss the use of antiviral treatment as prevention at the population level, but it makes clear that such treatment should be equally available and accessible to a person who injects drugs. Recently published work suggests that positive effects (reduced transmission) may be significant, providing an additional strong rationale for treating active drug users for HIV and hepatitis infections. There is evidence showing the beneficial effects of prophylactic TB treatment of those infected with latent TB in reducing population-level TB prevalence and incidence. As a consequence, the guidance includes treatment of infections as one of the key interventions.

The guidance document is designed to address the needs of adults who inject drugs. Minors and youths are beyond the scope of this guidance. It is nevertheless recognised that in some settings, minors and youths form a significant proportion of those who inject drugs. Addressing the needs of minors and youth would require customised, age-appropriate services (see text box, page 26).

From a prevention perspective, it is very important to protect the youngest sub-populations of those who inject drugs from chronic blood-borne diseases and TB. Therefore age limits to access services are not considered useful and may even be counterproductive as they tend to increase risks for persons who are under the age of legal adulthood.

This guidance on prevention of infections is mainly aimed at service providers in community settings. However, the guidance also has relevance for detention settings.

According to the principle of 'equivalence of service provision', prisoners are entitled to have access to the health services available in the country without discrimination, and prison health services are expected to provide treatment for problems related to drug use in conditions comparable to those offered outside prison (29-30).

Prisoners with a history of drug injecting often have multiple and complex health needs, requiring specialist medical care and a multi-disciplinary approach. Persons recently released from prisons form an important target group for prevention of infectious diseases and should be considered when planning national prevention strategies (31). Likewise, the needs of persons entering prisons should be considered (32).

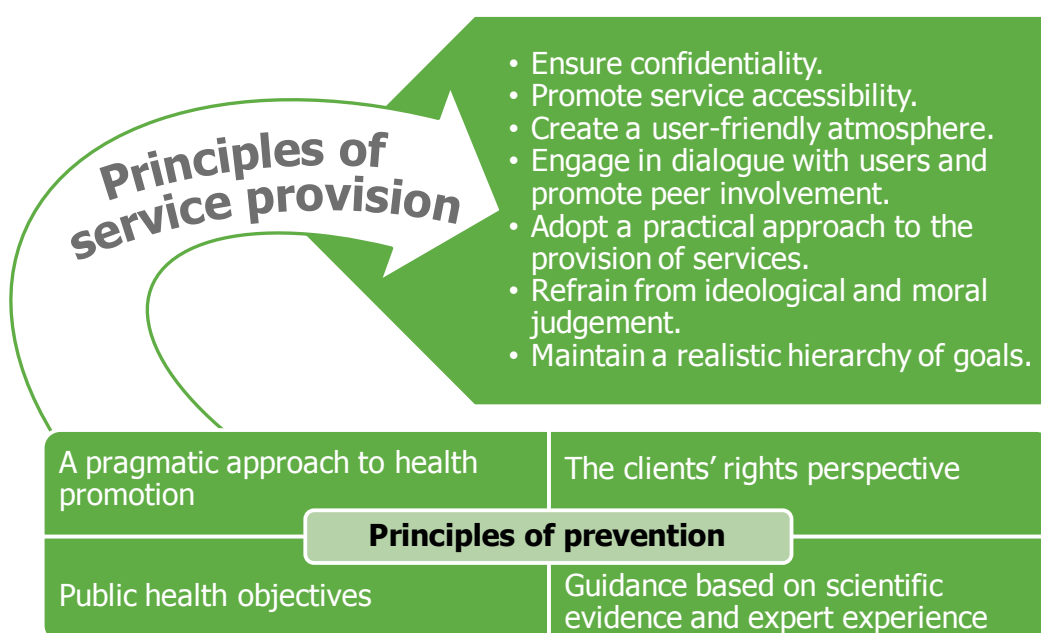
Target readership

This guidance aims to support decision makers in prevention programmes at national and regional levels, who work in the fields of infectious diseases, general public health, addiction and mental health, social services and drug control. It aims to help EU Member States and candidate (and potential candidate) countries in planning adequate and evidence-based, rationally designed public health responses to injecting drug use. The guidance identifies good EU practices for the prevention and control of infectious diseases among people who inject drugs. It is hoped that EU partnership countries may find the guidance useful and relevant. The guidance is not presented at a level of detail that prescribes the technical aspects of implementation, and it is up to implementing services to adapt the suggested intervention and prevention options to local and national circumstances. Despite this, the guidance may be of interest to managers of local services, as its aim is to comprehensively list and explain all components which should be part of a systematic approach to the prevention of key infectious diseases among people who inject drugs.

Core values of prevention of infections among people who inject drugs

The core values presented in this section are based on fundamental principles of public health, service provision, individual and public health ethics, combined with substantial experience in service implementation. They were developed by ECDC and the EMCDDA and are supported and endorsed by the ECDC/EMCDDA Technical Advisory Group. The core values were developed with a public health and human rights perspective and originate from work based in the United Kingdom and the Netherlands in the 1980s (the 'Mersey Harm Reduction Model', a population-based service model) (33-34). They focus on people who inject drugs and aim to reduce the negative consequences of drug use (35-36). The core values should be seen as the foundation of effective key interventions, as presented in this guidance. When developing services, planned interventions should conform to the core values. In this guidance, the core values are presented in two subsections, 'principles of prevention' and 'principles of service provision'.

Figure 3: Core values of prevention of infections among people who inject drugs



Principles of prevention

This guidance is based on four simple principles: a pragmatic approach to health promotion, a clients' rights perspective based on basic ethical principles, the resolve to achieve public health objectives, and scientific evidence combined with expert experience. The guidance does not work from the assumption that sobriety or abstinence is the ultimate goal of all drug-related public health policies (33,35,37-38). On the other hand, this guidance is neither incompatible with an abstinence framework nor does it explicitly exclude such a framework. It does not discuss drug control policies but restricts itself to address the immediate individual and societal harm caused by infections among people who inject drugs. The key interventions suggested in this guidance would be difficult to apply effectively if they were not built upon the following prevention principles:

'A pragmatic approach to health promotion' in this context means that rather than working from a hierarchy of goals within a full range of drug policies, this guidance – and the measures discussed in it – primarily address the spread of infections among injecting drug users and how the high risk of infection in this group could be curbed. Therefore, the approach makes no a priori assumptions on how prevention measures should be implemented, but argues for the independent public and individual health value of such measures. To be free of drugs should not be a condition for receiving help to prevent infections. Instead of a dogmatic approach in which the goal of preventing drug use overshadows other objectives, the pragmatic approach recognises that any health benefit has a value of its own and is worth pursuing, even when the underlying drug use may not be immediately

addressed (37). All users may not become drug-free, but risky injection practices and disease transmission can be prevented.

'The clients' rights perspective' in the context of this guidance means that the measures taken for prevention and intervention strictly adhere to the principle of using the client perspective. Prevention measures are developed first, based on the individual client's needs, and provider or societal needs are only addressed after the client's needs have been met. Also, all measures are provided to the client on a voluntary basis and no coercive or mandatory components should be used. Furthermore, access to prevention is seen as a personal right, not a benefit. Lastly, preventive measures should always benefit the individual and not only society (35,39).

'Public health objectives' in the context of this guidance means that although the benefits of the intervention methods should first address individual needs, the comprehensive approach should always strive to achieve societal as well as individual benefits. Intervention methods should include prevention of further transmission, reduction of total healthcare and social costs, improved productivity and reduced mortality and morbidity among the target group, including prevention of drug use, whenever compatible with the primary objectives (40).

'Guidance based on scientific evidence and expert experience' means that this guidance is based on scientific evidence in as far as robust studies for the discussed measures exist. For some of the recommended measures, robust studies demonstrating their efficacy have not been performed, either due to the complexity of the design requirements or due to ethical problems in conducting the studies (41-42). In some cases, the best available evidence comes from published ecological or descriptive studies, or has been captured by the experience and advice of the technical experts participating in the production of this guidance. Some measures in the guidance are recommended because their application is logical and considered to benefit the individual without incurring any undue risk, i.e. applying these measures makes sense from a pragmatic point of view.

Principles of service provision

In addition to the principles of prevention discussed above, the implementation of preventive measures in this guidance should adhere to the following core principles which all are derived from the need to adopt a client perspective in service provision (43). Without the application of these core principles, it is difficult to effectively apply the key interventions suggested in this guidance:

- Ensure confidentiality.
- Promote service accessibility.
- Create a user-friendly atmosphere.
- Engage in dialogue with users and promote peer involvement.
- Adopt a practical approach to the provision of services.
- Refrain from ideological and moral judgement.
- Maintain a realistic hierarchy of goals.

Obtaining the trust of the clients of the services is essential for the prevention of infectious diseases. As drug use and the possession of illicit drugs is criminalised in many countries, users are reluctant to reveal their identity even to health professionals for fear of becoming known to law enforcement or other authorities (44-45). This fear must be overcome so that clients can be attracted to health services. Being required to present full identification, often a standard practice for health service provision, will deter many users from obtaining services.

Ensure confidentiality. The first core principle means that it must be possible to access the preventive service anonymously or in a way that ensures full confidentiality, as seen from the client's perspective. Failure to do so will prevent or limit the client's use of the offered services and thus compromise any effects of 'herd immunity', which boost prevention at the population level (46-47). To ensure confidentiality, training in providing confidential services should be given to all staff. For the provision of certain services, such as testing, vaccinations and sometimes drug dependence treatment, a strictly confidential identification scheme may be necessary, which is usually acceptable to service users. Approaches to monitor service provision to acceptable levels of accuracy without compromising anonymity and confidentiality have been developed (48)².

Promote service accessibility. The second core principle ensures that services can be easily reached by people who inject drugs and that a low threshold of access is achieved. This means that services must be located where the users are, or where they can easily get to. Services need to be available at varying times of the day (46,49-52). Services should meet demand and be scalable, so that all in need can be offered appropriate, relevant and sufficient services (20,53).

² In service settings, a variety of approaches have been developed, including the use of nicknames, anonymous identification cards, or codes to track service use while maximising confidentiality.

Create a user-friendly atmosphere. A third core principle of service provision is the need to maintain a user-friendly atmosphere. This principle may seem intuitively self-evident, but its implementation is a key element in ensuring client uptake of services. A user-friendly atmosphere means that clients are addressed with dignity and a true willingness to help, whatever their appearance or social status. It also means that client wishes are respected, and services are not forced on them (50,52). It does not mean that clients can behave as they please, particularly if their behaviour creates disturbance or danger to others. On the contrary, service providers should develop and communicate clear rules of conduct for the service premises. Most services do not allow illicit drug dealing, financial transactions or injecting at the premises, and breaking of these rules can lead to a temporary ban from services (43). Many users suffer not only from drug addiction but also from mental health disorders (54). Such users are frequently the most marginalised and at a particularly high risk of infections. These users should not be labelled as 'too difficult' or 'too challenging' but services need to develop ways of working with them in a humane and respectful way.

Engage in dialogue with users and promote peer involvement. Conducting a dialogue and engaging clients actively in the work should be an integral part of the offered services. Actively listening to the clients and responding to changing needs in cooperation with the users helps to maintain the relevance of the services (55). Injecting rituals and habits are often passed on from more experienced users to novices (56). Secondary exchange of syringes, where syringes are distributed from one user to his or her peer network, is common (48,57-58). Prevention professionals need to be up-to-date on current drug use patterns, and users need to understand the health risks attached to these. Service providers can also arrange risk management and health promotion training for active users and encourage the participants to disseminate this information. This not only improves the usefulness of the services, but also empowers the users (59-60). Experience shows that involving active users in prevention work creates positive peer pressure, as clients learn safer drug delivery methods from each other (61-63). The main challenge among service providers is to acknowledge and embrace the cooperation with users.

Adopt a practical approach to the provision of services. The fifth core principle also takes the client perspective: services are built from the ground up, based on current needs and with the aim of closing gaps in prevention services that create infection risks and accurately addressing the health needs of the users (64). It also means recognising that even if all drug-related harm cannot be immediately addressed, there is value in every intervention as long as it responds to a true need (43). This is different from an ideological or top-down approach where the aims may be set so high that they may remain unreachable to the individual user, the service providers and the policy-setters.

Refrain from ideological or moral judgment. The sixth core principle recognises that services are provided to active drug users, and it is not helpful to judge or criticise the use itself from a moral or ideological point of view (65-66). Instead, the choices users make should be respected even if they are not agreed with and service personnel should be actively coached to demonstrate this respect (67). This does not mean that referral to addiction treatment services should not be offered. On the contrary, the threshold for this should be low, and information on avenues of access should be available at all premises that service drug users frequent (43,53,68).

Maintain a realistic hierarchy of goals. The final core principle advocates that short-term goals be set so that they can be realistically achieved. This approach can help to develop targets for service delivery (43). Setting prevention goals too high is frequently unrealistic and may lead to unnecessary disappointment and incorrect conclusions on the effects of interventions (69). The basic hierarchy of the goals of the services may vary according to local needs and situations, but should include goals such as reaching the majority of user groups, establishing trust with clients, responding to the practical needs of users, diminishing the immediate infectious disease risks, and increasing service volume over time.

The overarching goals of disease prevention such as protection from outbreaks and reduction of disease incidence and prevalence should be set at the programme level; they should also be adjusted to the current situation and realistic in their targets (53). Such goals are usually not useful as impact indicators for individual prevention services and should only be used for national-level benchmarking if there is a very good coverage of target populations and a comprehensive service package. It is important to recognise that especially if the prevalence of chronic infections has reached high levels, a long-term perspective to prevention has to be adopted, as disease indicators will improve slowly over time. Services need to be scaled up, and sufficient time needs to pass before effects become measurable (see section on 'Setting targets for intervention coverage', page 33).

Recommended interventions for the prevention of infections among people who inject drugs

The components listed in this chapter are recommended to be included in national comprehensive programmes which have the objective of effectively preventing and reducing infections among people who inject drugs.

Key intervention components

Based on the most robust evidence available, expert opinion, and best practice used within the EU/EEA, the following key intervention components should be applied and, if possible, be combined to achieve the maximum prevention effect through synergy.

- **Injection equipment:** Provision of, and legal access to, clean drug injection equipment³, including sufficient supply of sterile needles and syringes, free of charge, as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes.
- **Vaccination:** Hepatitis A and B, tetanus, influenza vaccines, and, in particular for HIV-positive individuals, pneumococcal vaccine
- **Drug dependence treatment:** Opioid substitution treatment and other effective forms of drug dependence treatment
- **Testing:** Voluntary and confidential testing with informed consent for HIV, hepatitis C (hepatitis B for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment.
- **Infectious disease treatment:** Antiviral treatment based on clinical indications for those who are HIV, HBV or HCV infected. Anti-tuberculosis treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated.
- **Health promotion:** Health promotion focused on safer injecting behaviour; sexual health, including condom use; and disease prevention, testing and treatment.
- **Targeted delivery of services:** Services should be organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings, offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.

³ In addition to needles and syringes, drug injection equipment includes cookers/spoons or drug mixing containers, filters, acidifiers, sterile water, dry swabs and alcohol swabs. See text box on page 16 for more details on drug injection equipment.

Combine key interventions to achieve synergy

The combined effect of multiple interventions show a drastically reduced incidence of HCV and HIV infection; self-reported injecting risk behaviour was also significantly reduced (70) (71-72).

Combination interventions

Whenever possible, interventions should be combined to achieve synergistic effects. Evidence suggests that the biggest reduction of HIV, HCV and injection risk behaviour can be achieved by providing both high coverage of needle and syringe programmes and opioid substitution treatment. It is likely that additional services, such as disease treatment and vaccination, offered in combination with needle and syringe programmes and drug dependence treatment, would still further prevent disease transmission among people who inject drugs.

While there is sufficient evidence on the positive effects of combining opiate substitution therapy and the provision of needles and syringes, it stands to reason that other interventions which have been shown to be beneficial would also lead to synergistic prevention effects when provided in combination with other interventions. The adherence to treatment for infectious disease, such as HIV, is known to improve when combined with drug dependence treatment (1-2). Some of the effects of the provision of combined services may be direct while some may be indirect through attracting and attaching clients to services, which improves service reach and coverage.

Strong collaboration between sectors is crucial as a prerequisite for service provision and in order to ensure the delivery of these key interventions. This aspect is discussed more thoroughly in the sections below.

Developing and providing programmes for infectious disease prevention and control among people who inject drugs

Effective delivery of key interventions can only be achieved through national and local cooperation and coordination between sectors.

Cooperation and coordination

National consensus building and mutually respected objectives that have been agreed on across all sectors by actors that engage with people who inject drugs are needed to effectively prevent spread of disease. Actors in infectious disease control, addiction medicine, mental health, social services, law enforcement, judiciary sectors, and narcotics control agencies as well as prison services are of national relevance and should be engaged and active in this process. In addition, local governments, citizen groups, associations for people who use drugs, as well as a multitude of other non-governmental or civil society organisations are relevant to include in coordination.

Drug use remains a crime or offence in a majority of European countries. Therefore, not only issues of health should be considered when prevention programmes are designed, but issues of law enforcement also have to be taken into account.

Similarly, people who inject drugs are frequently affected by social problems and mental illness, which increases the challenge of coordination of responses. As some services will have to be provided through referrals, links to health and social services need to be established and maintained.

A 'buy-in' from each of these actors is required if effective prevention results are to be achieved. For example, it is important to ensure the collaboration of law enforcement services to clarify that the provision of drug injection equipment is a public health measure, and that law enforcement should not interfere with the operation of needle and syringe programmes or outreach workers. Raids by law enforcement in the vicinity of service sites effectively undermine any chance of achieving the objectives of prevention services by scaring off potential clients. Law-enforcement policies are usually centrally determined and the strict, top-down leadership style that is common in most countries prevents deviations from local policy. This must be taken into account, and top-level cooperation agreements can help facilitate local-level collaboration in most settings.

It is therefore necessary to gain support for prevention activities not only from local actors and from the health branch of administration, but across all relevant central administrative branches, including law enforcement. This frequently requires top-level agreements or at least respect for the goals of the services, which is also clearly communicated down to the actor or service provision level.

Cooperation with local governments is also important. Service site establishment often is opposed by 'not in my backyard'-reactions among local residents fearing detrimental effects to the local environment. Strong leadership and community engagement is therefore required by local actors combined with a clear justification of documented local benefits such as the reduced littering of drug injection equipment (73).

Seven recommended key interventions

Injection equipment

Recommended intervention

Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes free of charge, as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes.

The main risk factor for acquiring blood-borne infections is the sharing of needles, syringes, and other drug preparation and injection equipment. Even among those people who report never sharing needles and syringes, it is common to share drug preparation equipment such as drug mixing containers, water for dissolving drugs, or drug filters, which could result in the transmission of hepatitis C or bacterial infections (74-75) (see text box on the spread of infection through drug preparation equipment, page 16). There is also evidence that people who inject drugs suffer from a large burden of skin, vein and blood infections due to non-sterile injection practices (17). There are reports of increased injection of prescription drugs crushed up from pill into powder form, which increases the risk for pulmonary emboli and endocarditis (76-78). Some homemade acidifiers, used to make certain drugs soluble, have been shown to harbour fungus which, when injected, can cause the heart infection endocarditis or an infection of the eyes which can lead to blindness called candidal endophthalmitis (79).

Considered judgement: Based on existing evidence, expert opinion and safe injection practice (80), the best way to minimise the spread of HIV and HCV among people who continue to inject drugs is to provide sterile needles and syringes and other clean injecting equipment (spoons/cookers, filters, water for injection, acidifiers, and dry and alcohol swabs) for each injection and in sufficient quantities. Provision should ideally be free of charge and organised through a mode of distribution that is acceptable and easily accessible to users.

Practice considerations: While some settings require the return of used needles and syringes in order to be given new ones, this policy can be counterproductive and act as a barrier to accessing and using sterile injection equipment. In order to achieve the goal of infectious disease prevention, easy access to needles and syringes should be promoted and the return of needles and syringes should be encouraged, but not absolutely required, in order to receive new supplies. The risk of needle stick injuries en route to the disposal site and for staff at the NSP has to be considered carefully. To encourage safe transportation and disposal of injection equipment, it is recommended to provide puncture-proof containers to collect and return injection equipment. Other strategies such as community-based safe disposal sites or home collection have also been successfully used in some settings. Coordination between needle and syringe exchange services and the police is essential to assure that carrying injection equipment will not be used as a reason for arresting drug users in the vicinity of NSPs.

Clients usually express a preferences for syringe types and needle sizes; this varies vary by setting and user sub-group. These preferences should be carefully considered in order to maximise service uptake. In some settings, for example, retractable needle-syringe combinations have been provided, where the needle retracts into the syringe after use, preventing re-use. However, clients in some settings found these unacceptable, which led to limited service uptake and retention. User-friendliness, acceptability and promotion of service uptake should be the main criteria for decisions on the type and variety of syringes and needles offered. Clients' views and preferences should also be taken into account regarding drug preparation equipment and the type and size of puncture-proof containers for storage of used needles and syringes, as these preferences will also vary by user sub-group.

There is evidence from systematic reviews that the provision of needles and syringes leads to significant reductions in self-reported injection risk behaviour (81). There is also evidence that needle and syringe programmes may reduce the prevalence of HIV (81) (82). Due to methodological limitations, it has been more difficult to conclusively study the link between the provision of drug preparation equipment, such as drug mixing containers, sterile water, and cotton filters, and reductions in HCV or HIV (83). However, HCV could be isolated from 67% of swabs, 40% of filters, 33% of water samples, and 25% of spoons that were used by HCV-positive individuals to prepare drugs for injection (84).

There is epidemiological evidence from primary studies that sharing drug preparation equipment, particularly drug cookers, is associated with HCV transmission among injectors who do not share needles or syringes (85) (75).

Spread of infection through drug preparation equipment

Water: Water is used to dissolve drugs prior to injecting and to rinse and flush the needle and syringe after injecting. Users may share a common source of water for this purpose, which potentially puts them at risk of contracting blood-borne viruses which may contaminate the water.

Spoons: Spoons or so-called 'cookers' (e.g. Stéricups®) are used to heat and dissolve drugs such as heroin prior to injecting or to mix crushed tablets with water. Users may share spoons for drug preparation and contact with re-used or contaminated water, or filters may spread bacterial or blood-borne viruses.

Acidifiers: Acidifiers are used to make insoluble drugs such as brown heroin or crack soluble. Some acidifiers may lead to bacterial and fungal infections. Infections can be avoided if single-use sachets of acidifiers, such as ascorbic acid, are provided to people who inject insoluble drugs.

Filters: Dissolved drugs are drawn into the syringe through a filter to prevent large particles from entering the bloodstream. Using a filter when injecting into the vein is important as it can prevent blood clots or emboli. However, sharing filters may lead to the transmission of blood-borne viruses. Filters tend to be re-used because they are thought to contain residual drugs, but some newer commercial filters are designed to minimise drug absorption and to dissolve after use.

Alcohol swabs and dry swabs: Alcohol pads should be used to clean the injection site before injecting. Clean dry swabs can be used after the injection to stop the bleeding, as alcohol pads will prolong the bleeding time.

It is recommended to provide water, spoons, acidifiers and filters, alcohol pads and dry swabs to reduce sharing or re-use and to minimise the potential risk for the transmission of blood-borne viruses and bacteria.

There is a lack of strong research evidence on the effectiveness of distributing injection preparation equipment such as sterile water, spoons/cookers, filters or alcohol swabs in reducing the incidence of HIV and HCV. One primary study suggests a relationship between sharing drug preparation or injection equipment and self-reported positive HCV status (86). There is also a risk of bacterial skin infections due to the reuse of injection equipment or unhygienic injection practices (17). However, there is evidence that the distribution of such equipment reduces injecting risk behaviour (87) (88) and acts as an incentive to attract and retain clients to services (89). Supply of citric acid sachets to people who inject drugs in one UK setting was found to be very well-received by clients, and helped to attract clients to needle and syringe services (90).

Sterile needles and syringes, as well as clean injection equipment should be provided along with health promotion messages about drug treatment services and information on the warning signs of soft tissue or skin infections (for additional information on health promotion messages for people who inject drugs see the box on health promotion, page 24). Attention should be paid to giving information about safe injection practices, which stress that each needle and syringe, as well as the equipment for the preparation of drugs for injection (cookers or mixing containers, cotton filters, water) should all be single-use and never shared among injecting partners. It may also be worth considering the provision of equally attractive non-injecting equipment, such as foil for heroin users or gelatine capsules for amphetamine users, which promote non-injecting routes of drug use (91-92).

Health promotion information should stress the washing of hands with soap and clean water and the cleansing of the injection site with an alcohol swab (or soap and clean water) prior to injecting. Dry cotton swabs, rather than the used alcohol swab, should be recommended to cover the injection site immediately after injection. Information should be given about early signs of skin infections or abscesses and phlebitis, and users experiencing such symptoms should be encouraged to seek early medical care.

Despite strong advice that needles and syringes, as well as drug preparation equipment, should not be shared or re-used, there is evidence in most settings that re-use does occur, often unintentionally. The first response to re-use should be to increase the availability and accessibility of needles, syringes, and drug preparation equipment so that a new set can be used for each injection. If this is not possible, there are two ways in which to assist people who inject drugs to minimise the harms which could result from the re-use of needles and syringes. First, syringes that come with numbers, colour codes, stickers, or some other system of anonymous identification can help to create a marker system to minimise inadvertent sharing of syringes. Second, while the use of chlorine bleach for the disinfection of injecting equipment is controversial, it might be considered in cases where known re-use is occurring. Although the efficacy of bleach in inactivating HIV in a laboratory setting has been demonstrated (93), there is insufficient evidence of its effectiveness in injection practice because disinfection protocols are not necessarily strictly adhered to. Providing bleach may be a 'second-line' alternative to providing sterile injection equipment, but providing sterile injection equipment is by far the preferred option.

Vaccination

Recommended intervention

Vaccination with hepatitis B and A, tetanus, and influenza vaccines, and, in particular for HIV-infected individuals, the pneumococcal vaccine.

Considered judgement: Based on existing evidence, vaccination is among the most effective prevention interventions available. In most settings, people who inject drugs are at increased risk of acquiring hepatitis B, hepatitis A and the bacterial infection tetanus. Persons infected with hepatitis C (for which no vaccine currently exists) and who are co-infected with hepatitis A or B suffer from accelerated progression of hepatitis C disease and much higher morbidity. Due to lifestyle, age, or HIV infection, some people who inject drugs might be at greater risk for influenza or pneumonia. However, effective vaccines are available which can prevent each of these infections by providing good clinical protection (94).

Practice considerations: Hepatitis B vaccination is now included in routine childhood vaccination programmes in most Member States, however since this policy was started in the 1990s, some adults who inject drugs were not vaccinated in childhood. Although 18 of 29 EU/EEA countries have hepatitis B vaccination programmes for adults who inject drugs, this vaccination is not always provided for free (8) (95).

Because some populations that inject drugs are 'hard to reach' for vaccination through traditional means, there is a unique opportunity to provide routine or 'one-off' vaccination services through fixed sites or mobile services which serve people who inject drugs. There is evidence that uptake of vaccination improves when integrated into other services (96). Vaccination of people who inject drugs has been found to be cost-saving when conducted at needle and syringe programmes, and there have been encouraging results from research on contingency management, which has been found to double hepatitis B vaccination completion rates (97-98). Additionally, outreach programmes might be an effective way to increase the uptake of repeat doses, while vaccination programmes offered in prison settings or residential drug rehabilitation centres can be effective in reaching those who are imprisoned or in drug treatment, including people who inject drugs.

The hepatitis B vaccine is typically administered as three separate injections, given over the course of a six month period, although an accelerated dosing schedule is possible. While it might be difficult to ensure that the client returns for doses two and three of the vaccine, it is still worthwhile to vaccinate a client who seeks a first dose, as even one dose of the hepatitis B vaccine may provide partial immunity (99). It is of note that the self-reported vaccination status of people who inject drugs is often inaccurate when compared with their actual serological status (100). Testing for hepatitis B serum markers at the first service contact can detect people who incorrectly reported hepatitis B vaccinations. Also, the rate of low- or non-responders among people who inject drugs is higher than in the general population (101).

Because of the possibility of a higher risk of hepatitis A outbreaks among people who inject drugs, the provision of a combined hepatitis A and B vaccination is suggested as the best way to prevent both infections in people who inject drugs (102-103). This is particularly crucial for those who are hepatitis C positive.

In all European countries tetanus vaccination are given as a part of childhood immunisation programmes, but a booster is typically given each five to ten years in adulthood. Tetanus vaccination status should be checked among people who inject drugs, and a booster vaccine should be offered if vaccination status is uncertain, particularly for those users who have injection site infections. Often the combined tetanus-diphtheria vaccination is given, and this is advisable because diphtheria, while rare in Europe, has a high case-fatality rate.

Finally, it is recommended to provide seasonal influenza vaccination and pneumococcal vaccination (particularly if the client is HIV positive and/or more than 50 years of age) in order to minimise the risk of influenza or pneumococcal infection (for more information see (16)).

It is important to note that vaccination against TB using the Bacillus Calmette-Guérin (BCG) vaccine is usually only recommended for infants living in areas where TB is highly endemic and for infants or children at particular risk of TB exposure in otherwise low-incidence areas. There is limited evidence for the use of BCG in adult patients, and it is contraindicated in individuals with impaired immunity such as symptomatic HIV infection (104).

Drug dependence treatment

Recommended intervention

Opioid substitution treatment and other forms of effective drug dependence treatment.

Drug dependence treatment represents an important component in a comprehensive response to prevent health-related harm associated with drug dependence (27,105-106). In many European countries, drug dependence treatment forms the centrepiece among a range of interventions to prevent the transmission of drug-related infections (54). It also plays a role in increased adherence to infectious disease treatment among people who use drugs (1-2,107-108). Drug treatment encompasses a range of medical (including pharmacological), psychological, social and behavioural strategies to stop or reduce drug use and injecting, and can be delivered in outpatient or in residential settings. Psychosocial therapeutic approaches can vary from individual counselling and motivational interviewing techniques to more structured psychological treatment interventions, matched to the individual's need and situation. Important current therapeutic approaches are cognitive and behavioural therapies, which aim to influence cognitions and unlearn conditioned drug use behaviour and their various combinations. Psychosocial interventions can be used alone or in combination with pharmacotherapy.

Pharmacological maintenance treatment for opioid dependence consists of the prolonged use of a prescribed opioid medication which prevents withdrawal symptoms and reduces craving, thereby allowing the user to lead a more stable life; reduce illicit heroin use, risk behaviour, and criminal activity; and improve health, well-being, and quality of life (68). Opioid substitution treatment (OST) is often provided in combination with psychosocial treatment and further support services (109-112).

Opioid agonists can also be used for detoxification treatment. However, inpatient detoxification should be integrated with other treatment options rather than being provided as a stand-alone service in order to avoid high relapse rates (111).

Effectiveness of opioid substitution treatment

Data from treatment outcome studies and controlled trials demonstrate the effectiveness of methadone and other drug substitution treatments in treating dependence on heroin and other opioids. A large body of evidence from reviews exists regarding the impact of OST on the incidence of infections as well as of injecting risk behaviour (81, 108-111,113-118).

With regard to risk behaviour, multiple studies with robust study designs that provide evidence for the effectiveness of OST in reducing risk behaviour were identified in three major reviews (108,115,118). All three reviews concluded that OST was associated with reductions in self-reported prevalence and frequency of injecting, in sharing of injecting equipment and injecting risk behaviour scores.

Assessing the evidence on the effectiveness of OST in reducing HIV transmission, the same reviews consistently found sufficient evidence to conclude that OST in community settings is effective in reducing HIV seroconversion, especially among those in continuous treatment and when dosages are adequate.

The evidence for the effect of OST on reducing HCV incidence has been harder to determine. This may largely be due to the fact that HCV is more easily transmitted through injecting and, probably, shared injecting equipment⁴, and to the much higher baseline prevalence levels among populations of people who inject drugs across Europe, constituting a reservoir of infection risk. However, recent data including community-based cohort studies of hepatitis C incidence among clients in OST, together with a meta-analysis of UK-based studies (70-71,119-121) suggest a strong positive impact of OST on preventing HCV infections. These studies point to higher benefits among those in continuous OST compared to those with interrupted OST; to a protective effect of methadone maintenance treatment against both primary⁵ and secondary⁶ HIV and HCV infection; and to 'dose-response' effects of OST, with those in treatment longer having lower HCV incidence rates.

A number of randomised controlled trials over the past 15 years have provided evidence of the efficacy of supervised injectable heroin-assisted treatment (HAT) for long-term refractory heroin dependent individuals, who

⁴ Hepatitis C infection is characterised by comparatively high concentrations of infectious virus in the blood circulation, not only during the primary infection phase but also in those individuals that become chronically infected (compared to HIV infection). This may lead to high HCV transmission rates upon exposure, as the minimum infectious dose is likely to often be exceeded in sharing situations among infected and non-infected people who inject drugs. This hypothesis is supported by the fact that hepatitis C prevalence often exceeds HIV prevalence in user communities, and hepatitis C epidemics usually precede HIV epidemics in the user communities. It may also explain why it is more difficult to curb the risk of HCV by single interventions alone and why higher coverage rates may be needed to reach an effect at population level.

⁵ Infection in non-infected individuals.

⁶ Infection with HIV or HCV in mono-infected individuals.

do not respond to standard treatments. The results show that when compared to classical or optimised OST, treatment-refractory clients in HAT show similar or greater treatment retention, major disengagement from criminal activities (such as acquisitive crime to fund continued use of street heroin and other street drugs) and achieve major reductions in the extent of injecting of street heroin which are sustained over time (122).

Considered judgment: Based on consistent evidence from multiple robust studies and reviews as well as expert opinion, drug dependence treatment should be available and easily accessible, in particular OST for opioid users. Psychosocial treatment enhances the effectiveness of OST when used in combination, is a main treatment option for stimulant users, and is recommended based on expert opinion.

Combination approaches enhance the impact of OST on infections

Studies on compliance, completion of treatment and abstinence outcomes at follow-up confirm that the effectiveness of OST can be improved when psychosocial interventions are also provided (123). In a randomised controlled study of the effect of behavioural interventions on HCV incidence among people who inject drugs in the UK (124), enhanced preventive counselling combined with OST was compared with OST alone. The results showed lower rates of HCV sero-conversion among the group receiving both interventions.

Recent research points to the importance of combining opioid substitution treatment with further harm reduction measures in order to reduce the incidence of infections, including HCV transmission. The Amsterdam cohort study (71) found that full participation in both methadone maintenance treatment and needle and syringe programmes over a six-month period was associated with a lower risk of HCV infection, albeit the effect could not be shown for methadone maintenance or needle and syringe programmes alone. A UK-based cohort study (119) also noted a greater impact of OST on reducing HCV incidence when combined with syringe provision. Most recently, a meta-analysis of six UK-based studies that collected individual-level data on intervention coverage as well as newly acquired HCV infection amongst people who inject drugs in the community documented that providing OST and needle and syringe programmes independently reduced HCV incidence rates among this group (70). In addition, the two interventions acted synergistically, reducing the odds of new HCV infection by nearly 80% when a high coverage of needle and syringe programmes was provided for those who continued to inject while on opioid substitution treatment.

The effectiveness of combination approaches on HIV transmission was further assessed in a study carried out in New York City (125), comparing the effectiveness of a 'combined prevention program' (methadone maintenance, education and outreach, risk reduction, HIV testing and needle and syringe programme) with an 'initial prevention program' excluding needle exchange (methadone maintenance, education and outreach, risk reduction, HIV testing). Over time, the observed HIV prevalence increased to a greater extent among those on the limited programme compared to those on the combined programme, which suggests that the combination of OST with syringe exchange may have played a role in limiting HIV transmission.

Effectiveness of other treatment approaches

There are a number of other drug treatment options available, including psychosocial treatment, cognitive behavioural interventions, contingency management, and peer-based support groups.

While no psychosocial treatment intervention alone has been shown to be clearly effective in treating opioid dependence (108), findings from observational studies (large cohort studies such as DATOS in the US and NTORS in the UK) show that residential, community, and methadone maintenance treatment programmes all reduced both injecting drug use and needle sharing. While in treatment, injecting and risk behaviours are reduced and consequently the risk of infections is lower (109). Psychosocial treatment can play a major role in addressing co-morbid psychological disorders of drug users, like anxiety, depression or low self-esteem, and in improving drug use-related coping skills.

Treatment for non-opioid dependent people who inject drugs

Although some pharmacological agents for the treatment of stimulant users have been found promising or are currently being tested, no pharmacological treatments have yet been found to be consistently efficacious in reducing drug use and increasing treatment retention for this group (108). Several randomised trials are underway to test new drugs for the treatment of cocaine dependence; at present, Disulfiram, a substance that interferes with the metabolism of alcohol, and Vigabatrin, an anti-epileptic drug are two substances that show some promise. Attempts to develop a cocaine vaccine are continuing (54).

In the absence of pharmacological treatments, psychosocial treatment is especially important for stimulant users. However, the only systematic review of the evidence regarding psychosocial treatment for psychostimulant abuse or dependence did not draw firm conclusions regarding the effectiveness of a single treatment approach in relation to psychostimulant dependence, owing to the heterogeneity of studies (126).

One major review found that contingency management (CM), which includes providing monetary incentives for remaining drug-free or in treatment, was associated with higher rates of abstinence and retention in treatment for stimulant users (108). If combined with methadone maintenance, CM showed positive outcomes for clients

dependent on both opioids and stimulants. However there is still a relative lack of evidence to consolidate these findings.

The same review highlighted that there is modest evidence of efficacy of other behavioural approaches, including cognitive behavioural therapy, community reinforcement with CM, and individual counselling to address stimulant abuse. There is weak evidence regarding the impact of motivational interviewing and for the effectiveness of therapeutic communities with regard to the treatment of stimulant users.

Providing opioid substitution treatment

Methadone maintenance treatment was developed in the USA in the 1960s, but its introduction in clinical practice in Europe increased only from the mid-1980s onwards. Today, methadone and buprenorphine, dihydrocodein, slow-release morphine, and diacetylmorphine (heroin) are in use in European countries⁷ (112). Following the adoption of comprehensive drug policies by EU countries, the provision of opioid substitution treatments accelerated since the mid-1990s and reaches now more than half of the estimated target population (54,127-128). The share of buprenorphine in opioid substitution treatments in Europe is smaller than that of methadone, but has been increasing, partly due to its better safety profile. Buprenorphine is a partial agonist, has weaker opioid effects and produces a lower level of physical dependence, but is less likely to result in overdose. It is often used in long-term substitution treatment provided by office-based physicians. The fact that a broad range of substances, including heroin, is nowadays available for the treatment of opioid users, allows clinicians to engage a wider number of drug users in optimised pharmacological treatments. Detailed guidance for the psychosocially assisted pharmacological treatment of opioid dependence was published by the World Health Organization in 2009 (111).

Quality and supervision: Treatment services must be well-organised, and of high-quality, including the level of training of staff, to achieve the best results. In particular, available international guidance on treatment regimens, dosage and supervision should be followed (111,129). Evidence indicates that flexible dosing structures should be encouraged, including a low starting dose and high maintenance dose, without restriction on dosage and duration of treatment (110,130). To optimise effectiveness of opioid substitution treatment, evidence further suggests that continuous treatment is more effective compared to short-term use of OST (108). Some forms of OST, such as methadone, will be less effective (i.e. have lower serum levels) if treatment for tuberculosis or HIV is taken at the same time; this should be monitored and the dose adjusted so that treatment is effective (131).

Accessibility: The provision of OST via low-threshold services is an additional consideration. Low-threshold programmes are oriented towards harm reduction rather than abstinence, and are more flexible in terms of eligibility requirements and service provision, compared to high-threshold programmes. The combined use of other harm reduction services, which can enhance the effect of the treatment, is encouraged in these settings. During drug treatment, many infection-related services, such as provider- and client-initiated testing and counselling, vaccinations, infectious diseases treatment, or preventive equipment should be offered to people with a history of current or past injecting drug use. Mental healthcare (and additional general healthcare by general medical practitioners and, if available, internal specialists) should be combined with drug dependence treatment. The accessibility of such care is especially important for people who inject drugs who are in contact with low-threshold facilities.

Dispensing: Opioid substitution medications can be dispensed in clinics, in specialised centres in the community or in pharmacies. In all settings, the direct supervision of the patient taking the medications can prevent diversion of drugs to the illicit market. However, take-home doses allow patients to follow family- or work-related obligations and lead a more 'normal' life. For all undergoing such treatment, regular medical examinations are an essential requirement (16,111).

Flexibility regarding the start of treatment: Primary research results show positive effects of interim methadone maintenance treatment on risk behaviour (132). Readily available treatment in the form of interim methadone provision allows people who inject drugs to benefit from the protective effect of opioid substitution treatment on risk behaviour.

Reaching difficult target groups: Long-term dependent heroin users who do not respond to standard treatments have been shown to benefit in programmes that provide supervised injectable heroin-assisted treatment (122). The delivery of HAT requires structurally adapted services to respect strict safety conditions and prevent any diversion to the illicit market. Clinics have to be open several sessions per day, every day of the year, in order to allow clients to inject their treatment under supervision as indicated in treatment guidelines (122). Although costs of this 'second line' treatment are higher than oral methadone treatment, this is compensated for by the significant savings to society – in particular the reduction in the cost of criminal procedures and imprisonment due to associated criminal behaviour (133).

⁷ Pharmacological treatment with the opioid antagonist naltrexone, which blocks the effects of heroin and other opioids, plays only a minor role in Europe, as the treatment has been associated with high attrition rates.

Prison setting: Reviews of experimental and observational studies on OST in prison show that benefits of prison-based maintenance treatment are similar to those in community settings (32,134-136). Making such treatment available in prisons presents an opportunity to reduce illicit opioid use and risk behaviours in prison. A good link between prison and community-based programmes is important to facilitate continuity of treatment (upon incarceration/after release), so that longer-term benefits can be achieved and high risks of harms, including death, in the period immediately after release, are prevented.

Testing

Recommended intervention

Voluntary and confidential testing with informed consent for HIV, HCV (HBV for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment.

Considered judgement: Expert opinion is in favour of voluntary and confidential infectious disease testing for its potential risk reduction, and because a test-based diagnosis is a prerequisite for treatment provision. Due to the risk of infection associated with injecting drug use, it is likely to be cost-effective in all European settings to test people who inject drugs for HIV, hepatitis B, hepatitis C. TB testing is likely to be cost-effective in most countries. Tests for other infections should be considered in a standard offer for a medical examination (such as hepatitis A, D, syphilis and other liver and general blood tests). The frequency of medical examination and testing as well as the consideration of which tests to perform should be adapted to the individual clinical signs and symptoms and the local epidemiological situation. In the case of people who inject drugs, this risk is often very high and testing should, in that case, be offered up to once or twice yearly (16).

A voluntary and confidential approach of routinely offered testing services is recommended. 'Voluntary' means that although testing is a standard of medical care, the individual is informed about the tests and their potential consequences and gives explicit consent to being tested. 'Routinely offered' means that care providers should recommend testing for infectious diseases as a standard component of medical care to people who inject drugs.

However, estimates reported by countries in the EU/EEA suggest that only between 10% and 60% of people who inject drugs were tested for HIV during the prior twelve months (137), and this is likely to be much lower for other infections. Timely detection of blood-borne viruses and other diseases allow clients to seek healthcare to treat the infection, prevent complications, and reduce the risk of further transmitting the disease (138). Testing offers an important opportunity to counsel and educate people who inject drugs about preventing infection (if tested negative) and onwards transmission (if tested positive). Risk-reduction counselling conducted in relation to the testing situation can result in reductions in risk behaviours (139).

Blood-borne infections

Operational guidelines for healthcare providers to initiate testing of their patients who inject drugs for HIV, viral hepatitis and other infections, including bacterial skin infections, sexually transmitted infections, and respiratory infections were issued by the EMCDDA in 2010 and can be useful in guiding programmes when implementing testing for people who inject drugs (16). General guidance on HIV testing has been issued by ECDC (138). In sum, people who inject drugs should be offered testing that follows the quality standards of national guidelines. However, greater care may need to be taken to reach and counsel this more vulnerable and hard-to-reach population so that good access to testing can be achieved, the reason for testing is understood, and consent for testing is clearly voluntary. Providing point-of-care testing in outreach settings can increase the uptake of HIV, HBV and HCV tests (see text box below on the Finnish experience with point-of-care testing). Even if confirmatory testing of positive point-of-care tests takes as long as with regular tests, negative test results are immediately available, and preliminary positive test results combined with risk-reduction counselling may reduce risk behaviours. Testing should be linked to treatment of those infected, with referral through local treatment care pathways to specialist services for assessment and follow-up for those who are confirmed positive for HIV, chronic HCV and HBV or other infections that require treatment.

Tuberculosis

Screening for TB presents additional and important challenges which are crucial to address in the population of people who inject drugs. The control of TB relies heavily on detecting infectious cases and treating these for at least six months with a combination of antibiotics according to international recommendations (140-141).

Patient delay in seeking care is common among people who inject drugs, which increases the risk for TB transmission and increases disease severity (142-143). Intensified case finding is important to reduce transmission and improve the treatment outcome and prognosis for the patient. TB screening can be performed to identify active or latent infection. From a public health perspective, identifying active TB is of key importance as it cuts immediate transmission. However, since people who inject drugs, and particularly those who are HIV seropositive, have an increased risk for progression to active disease, diagnosis of latent TB followed by preventive therapy is also important. Ideally, all people who inject drugs should be screened for active TB disease or latent TB infection.

Using point-of-care tests at low-threshold health service sites in Finland

Since 1999, a point-of-care (PoC) rapid HIV testing programme has been implemented in low-threshold health service centres (LTHSC) serving people who inject drugs in Finland. In 2011, 10 out of 34 LTHSCs offered rapid HIV tests, evaluated and recommended by the National Institute for Health and Welfare (THL).

THL supports the PoC testing programme by offering laboratory and counselling training, a quality assessment and monitoring programme and provides advice on the practical arrangements required for testing. Before introducing PoC rapid testing at a new LTHSC, all personnel required to work with rapid tests have to be trained at THL. The Institute organises HIV antibody quality assessment rounds in concert with external quality assessment services three times per year and performs confirmation testing for positive results. THL also gives day-to-day advice and monitors the testing programmes, collecting coverage and results data for programme surveillance and impact assessment.

Clients are offered free, anonymous, and rapid HIV tests in all LTHSCs, without the need for an appointment. The test is performed in a separate testing area that ensures privacy. Pre-test counselling includes a discussion of risk behaviour, safe sex practices, and the window period for HIV antibodies. The test is performed from blood collected by a finger prick, and the result is available within 15 minutes. Negative test results are given immediately after the test, positive results are further confirmed from separately drawn venous blood. The confirmatory result is ready after one week. Positive cases are referred to hospital care.

Between 1999 and 2010, more than 8000 samples from people using drugs were tested in LTHSCs, resulting in a total of 47 confirmed HIV-positive cases. The overall acceptance of the rapid test format among healthcare personnel and LTHSC clients has been positive. Most of the clients prefer PoC rapid testing to conventional testing.

TB screening is part of a comprehensive healthcare delivery process that requires access to microbiology services, treatment facilities, drugs and support for all diagnosed patients. TB screening/diagnosis includes medical history, chest x-ray, tuberculin skin testing (TST), and, if available, blood tests (interferon-gamma release assays, IGRA). The method used depends on national guidelines or, in their absence, on international guidelines for TB screening (131) (16) (144).

In addition, the presence of signs and symptoms of TB in people who inject drugs should be identified through a clinical examination and, ideally, clients should complete a questionnaire on possible symptoms prior to testing. Any TB screening, especially in people who inject drugs with symptoms or signs of TB, should be followed by at least sputum smear microscopy, with full access to laboratory facilities with the capacity, technical experience and proficiency for culture of all suspected cases of TB. Upon suspicion of active TB, definite TB diagnosis should be based on microbiological culture confirmation, including susceptibility drug testing.

It has been shown that people who inject drugs can be one of the groups with the lowest number needed to screen and treat prophylactically in order to prevent cases (145).

Other infections affecting people who inject drugs

Testing and treatment for sexually transmitted infections like chlamydia, gonorrhoea, and syphilis should be encouraged and be part of regular screening, especially among those with high-risk sexual behaviour and multiple sexual partners such as sex workers. Referrals, condoms and lubricants can be provided in all settings, even in settings where testing and treatment may not be possible to provide, such as outreach.

Additionally, people who inject drugs are at high risk of developing acute bacterial skin infections (including MRSA), soft tissue infections, abscesses, and collapsing veins, with potentially life-threatening complications. Causes of infection are the injection itself (providing a route for skin bacteria into the body), poor hygiene, poor injecting techniques, and contaminated drugs (e.g. the 2010 anthrax outbreak in Scotland). It is important that minor injuries and bacterial infections are recognised (diagnosed) and treated in a timely manner. In cases of abscesses or other skin lesions, a bacteriological test from pus, tissue, or other material should be taken and sent to a laboratory for examination (15).

Infectious disease treatment

Recommended intervention

Antiviral treatment based on clinical indications for those who are HIV, HBV or HCV infected. Anti-tuberculosis treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated.

Considered judgment: Recent studies have demonstrated clear benefits of antiviral treatment against HIV, HBV and HCV among people using drugs. Recent international guidelines do not restrict antiviral treatment to people who are drug-free, as long as there are no other clinical contraindications. There is strong evidence for the individual and population-level benefits of TB treatment.

Practical considerations: Testing should be closely linked to treatment, with clear referral patterns in place to provide care continuity to cases tested positive and medical monitoring of disease progression if treatment is not yet indicated. The high prevalence of co-infections among people who inject drugs needs to be considered. Referral and ensuring continuity of care for disease treatment is especially crucial when planning for release from prison. Drug interactions need to be carefully considered, especially in co-infected individuals.

Blood-borne infections

Provision of antiretroviral treatment (ART) is an essential part of care for people who inject drugs that are tested positive for HIV. For those tested positive for hepatitis B or hepatitis C infection, the provision of antiviral treatment is often clinically indicated and should be provided in accordance with national guidelines (1,53,146-148). All individuals with HIV or chronic hepatitis B or C require regular medical review even if they are not receiving antiviral treatment.

There is evidence that active drug injectors can successfully undergo treatment for HIV and benefit from it. There is equally strong evidence that there is no higher drug resistance in user populations than in other HIV-positive individuals who receive antiretroviral treatment (149). Research has also shown that people who inject drugs can achieve hepatitis C treatment outcomes comparable to those found in the non-injecting general population, if the treatment was accompanied with appropriate support (150). There is evidence that treatment for hepatitis C can be delivered in the framework of opioid substitution treatment programmes, and that both clients and staff support this 'one-stop shop' model of service provision (151-153).

Multiple studies have confirmed that those who are HIV positive or HIV and HCV co-infected and who receive OST are more likely to adhere to the treatment regimen of their infection(s), but there is no evidence on how this impacts viral load. (Further details regarding the impact of OST on adherence to ART can be found in the WHO Clinical Protocol for the European Region (1)).

There is also evidence from modelling studies that anti(retro)viral treatment for HIV and hepatitis C may influence the prevention of transmission of infectious disease: when adhering to treatment, the viral load can be reduced, thereby reducing the risk of onwards transmission, in addition to preventing complications of the infection for the individual HIV- or hepatitis C-positive person who inject drugs (154).

Post-exposure prophylaxis of HIV infection and Hepatitis B can be considered in accordance with international and national recommendations.

Tuberculosis

All patients diagnosed with active TB should be provided with the adequate treatment. Treatment should follow national guidelines or, in their absence, the international guidelines (140-141), which also provide specific guidance for special clinical situations such as co-morbidities like HIV infection. Response to treatment needs to be monitored clinically and bacteriologically. When a patient is found positive for active TB, contact tracing of index TB cases needs to be ensured.

In individuals with known HIV infection living in settings with a clear risk of recurrent TB exposure and in whom active TB is excluded, prophylactic treatment should be considered after an individual risk assessment. Also, where antiretroviral treatment is available, the achievement and maintenance of adequate CD4 counts in HIV-infected individuals will keep these individuals at a lower risk to develop TB after exposure. This should be taken into consideration in the individual risk assessment.

The use of prophylactic treatment in HIV-infected individuals should follow the 'WHO interim policy on collaborative TB/HIV activities' (155) and the 'Policy guidelines for collaborative TB and HIV services for injecting and other drug users. An integrated approach' (156).

According to the international standards for TB care, the strategy for patient adherence should include measures to both assess and promote adherence, and provisions should be made to address poor adherence. Therefore, directly observed treatment (DOT) is recommended to ensure multidisciplinary approaches in order to support the

patients and enhance treatment adherence. Incentive programmes to promote adherence to follow the DOT may be useful (157).

Other infections affecting people who inject drugs

If identified, sexually transmitted infections should be promptly treated according to national guidelines. Long-term injection often leads to chronic, non-healing wounds among people who inject drugs. Wound management procedures can be very effective if the client-staff relationship is stable and based on trust and adherence to the treatment. Wound care services should be offered along with needle and syringe services, as well as drug treatment, if possible.

Health promotion

Recommended intervention

Health promotion focused on safer injecting behaviour; sexual health including condom use; and disease prevention, testing and treatment.

Considered judgment: Health promotion is supported by expert opinion as a fundamental companion component for the delivery of all six interventions. It provides support for the implementation and social marketing of other direct interventions. Contents should be guided by user needs.

Health promotion is the 'process of enabling people to increase control over their health and its determinants and thereby improve their health' (WHO 1986). Health promotion includes not only information giving and support, but also risk-reduction counselling. Health promotion alone is not effective in reducing the risk of HIV among people who inject drugs, but combined with other prevention measures such as needle and syringe provision and drug treatment, health promotion can be effective (53,158). Health promotion messages should be gender and culturally sensitive, provided in different languages, and adapted to use terminology that is familiar to users and that they will easily understand.

Health promotion for safer injecting behaviour

- Use a new sterile needle and syringe and clean equipment for each injection: 'one needle – one syringe – one time'. Never share or borrow needles, syringes or other equipment.
- Be aware of, and prepared for, situations where it may be difficult to prevent infections. For example, if there is social pressure to share utensils or if the situation is somewhat chaotic when preparing an injection. Enact strategies to reduce the likelihood of unintentional sharing of injecting equipment (such as using colour-coded or labelled syringes).
- Encourage peers who do not inject not to start injecting. Encourage peers who do inject to use safe injection practices.
- Wash hands before and after injecting; clean the skin before injecting with alcohol or another disinfectant; use a filter; avoid the use of dangerous injection sites such as the neck and groin; avoid injecting under the skin or directly into a muscle; and clean all materials, including the table surface, with a disinfectant following injection.
- Rather than injecting, use non-injecting routes such as smoking or orally ingesting the drug. Foil or gelatine capsules can be used for these purposes.
- Prevent overdose by using smaller amounts of drugs (especially after periods of abstinence or less intense drug use), by not using drugs while alone, and by recognising signs of overdose in injecting partners and calling for help immediately upon their recognition. Take care when using drugs from new or unknown sources, and avoid mixing drugs such as alcohol, benzodiazapines and opioids. Utilise supervised health facilities for hygienic injecting, if such services are available.

Apart from written materials, there should be visual and interactive educational tools. Persons delivering health promotion activities should be specifically trained on how to provide health education. It is important to keep in mind that health promotion may need to be tailored to special personal conditions such as mental illness. This might influence the success of health promotion efforts.

The purpose of providing health promotion messages to people who inject drugs is to increase understanding about infectious diseases, infection transmission, and infection prevention, with the aim of reducing the risk of contracting and transmitting infectious diseases through the injection of drugs by promoting safer injecting behaviour, transition to non-injecting drug use, or cessation of drug use. Health promotion messages should be tailored to the needs of the user and provided at every possible opportunity: whether on a street corner when providing outreach services or in a drug treatment centre or a needle and syringe programme. Every contact with a person who is currently injecting drugs is a chance for a service provider to assess health promotion needs and to provide counselling and health promotion messages. Clients are often the best judge of their own needs for health

promotion information and, if trust is built up with the service provider, some clients will seek health information based on the needs that they themselves have identified.

Safer injecting behaviour

Key health promotion messages to promote safer injecting behaviour are listed in the box above. These should be adapted to the local context and the needs of specific users and individual lifestyles.

While the main focus of this guidance is on the prevention of infections among people who inject drugs, the main cause of mortality in opioid-using populations in many settings is still drug overdose (159), and health promotion related to overdose prevention is a key activity that those who work or come into contact with people who inject drugs should be engaged in. It is particularly important to reach people who are currently participating in formal drug treatment, undergoing drug detoxification, and those who inject drugs and are to be released from prison, and let them know that if drug use is resumed or intensified, they are at high risk for drug overdose due to reduced drug tolerance. Key overdose prevention messages directed at people who inject drugs can also promote the use of smaller amounts of drugs or encourage the recipients not to use drugs while alone (31). Training activities can be provided to instruct drug users how to recognise the signs of overdose in injecting partners and what to do in an emergency, e.g. putting victims in the recovery position and calling for an ambulance. Peer-delivered naloxone is used in some countries and positive results were reported (160). Additional possibilities to reduce the likelihood of harm associated with drug overdose are to encourage people who inject drugs to utilise supervised injecting facilities, if such services are available. Due to direct supervision by staff, immediate help is available in case of overdose. A recent study has documented an association between the existence of such facilities and the reduction in overdose deaths at population level (161). Finally, the vast majority of those who begin injecting do so in the company of peers with established injecting drug use. Key messages for health promotion, for example how to avoid being initiated into injecting drug use or how to use safe injection practices are most effectively delivered by peers.

Sexually transmitted infections and condom use

Data from EU/EEA countries on condom use among people who inject drugs range from less than 5% to nearly 60%, far lower than is necessary to prevent the spread of sexually transmitted infections, including viral hepatitis and HIV (137). Thus, it is particularly important that health promotion activities target the sexual transmission of infections among people who inject drugs. Condoms and lubricants should be provided along with information on their consistent use. Additional information should be given on screening and treatment for sexually transmitted infections, since there is evidence for the sexual transmission of infections, including HIV and hepatitis B, from people who inject drugs to and from their sexual partners (162-163). Drug use can also be associated with the exchange of sex for money or drugs, which puts users at a much higher risk of contracting or transmitting sexually transmitted infections if condoms are not used consistently and correctly.

Disease prevention, testing and treatment

Health promotion should include information which clarifies routes of transmission for diseases that are common among people who inject drugs. Information on infections like HIV, HCV and HBV should be provided, so that people understand that they can transmit the virus even if they show no symptoms. In the case of TB, there is often confusion regarding infection and disease, and which stages are infectious (142) (143) (164). Studies have suggested that HIV prevention information can be confused with TB prevention, such as the incorrect notion that TB can be prevented by condom use or bleaching needles, which may explain the longer patient delay in some settings (142).

Comprehensive, easily accessible information material as well as an active dialogue about TB and blood-borne viruses is essential. Equally important are efforts to correct misconceptions about disease while at the same time counteracting the stigmatisation of disease. Key health promotion messages should also focus on supporting the adherence to treatment so that the patient can be cured (TB, HBV and, if successful, HCV), thus reducing the risk of developing resistance towards the drugs and transmitting the infection to others.

A final important issue for many people who inject drugs is social support and social care. There is evidence that, for example, supervised housing is associated with a decreased risk of infection for people living with HIV (165). It is likely that many structural factors related to housing and economic well-being have a major impact on the quality of life and infection risk for many people who inject drugs. The provision of supportive services that address the extended needs of people who inject drugs such as housing, food, and low-threshold employment opportunities are likely to have a positive impact on health-related outcomes.

Targeted delivery of services

Recommended intervention

Services should be combined and organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings, offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.

Considered judgment: Evidence and expert opinion supports a targeted delivery of services according to user needs and local conditions.

Modes of service delivery: considerations for attracting users to services

As defined by the core principles of service delivery, it is essential to carefully consider how services for people who use drugs are organised and delivered in order to maximise their acceptability to clients and, thereby, service access and uptake. The effectiveness of service programmes depends on their ability to attract, motivate, and retain clients. Therefore, the planning of the services should aim at creating as low a threshold as possible for people who inject drugs, so they can easily attend and use the services provided.

Services must be delivered in locations that potential service users can recognise, access and feel comfortable entering. Additionally, services should be provided in a discrete environment and manner, where confidentiality can be ensured, and where clients do not feel threatened by judgmental attitudes of staff, by harassment, or have to fear arrest by law enforcement authorities. Sometimes offering the most basic social services, such as food, showers, and clothing, is a way to attract the most socially excluded and at-risk people who inject drugs to services.

Service access must be carefully planned based on the local context. Easy and timely access to services is particularly crucial in the provision of needles, syringes, and injecting equipment. Reducing the spread of HIV, hepatitis B, and hepatitis C is impossible without a constant supply of clean injection equipment.

Services for people who inject drugs will vary by country, region, available resources, and sub-population. This is mostly because characteristics of people who inject drugs will differ between and within countries, depending on the type of drugs used, age, gender, ethnic background, and income level. It is, thus, very important to involve the target population when designing and choosing delivery modes for service programmes in order to best address the local needs and context. If programmes are tailored to address the clients' needs and service preferences, there is a better chance of increased uptake of services.

Minors' access to needle and syringe programmes in Hungary

When the country's first comprehensive national guidelines for NSPs were developed in Hungary in 2010*, the need for a national consensus on the access of minors (legal age in Hungary: 18) to such services arose. The project's principles of anonymity, confidentiality and easy and unrestricted access to services, which are considered among the main advantages of low-threshold services for drug users, made it impossible to restrict NSP service access. At the same time, local regulations stipulated to report 'at-risk' children to child protection authorities.

The contradictory legal frameworks were the starting point for a national discussion process, bringing together experts from child welfare, representatives of all Hungarian NSPs and other stakeholders in a national meeting. Following presentations of international as well as local practice, and discussions about topics such as the need of minors for multiple services, such as in-depth pre-counselling and individual case assessment, the way for a consensus was paved. It was agreed that besides the upcoming general guidelines for the national level, each NSP should reconsider its own internal regulation, while at the same time child protection services should build partnerships with the with relevant drugs services, so that they could refer minors to drug counselling and treatment services. Regarding the contradiction between child protection legislation and low-threshold services, the ombudsman was asked for a resolution, which is reflected in the guidelines.

The final national guidelines for NSPs, published in July 2011 by the National Institute for Family and Social Policy, state that minors should not be excluded from NSPs, as anonymity is of high priority in such programmes. But the guidelines also made clear that minors should be encouraged to inform their parents. Where appropriate, it is recommended that the local child welfare service provider as one of the main local partners of NSPs is contacted. Based on the assessment of each individual case, co-operation and exchange of information between both organisations is considered beneficial for under-age clients of NSPs.

* The guidelines were formulated in the framework of an EU-funded priority project: 'Modernization of social services, reinforcement of central and local strategic planning capacities, supporting social policy decisions' of the Social Renewal Operational Programme.

Types of service delivery

There are a variety of modes of service delivery, each of which can function in combination with other services or in isolation. Many countries have found that integrating services into a 'one-stop shop' model of services with a low threshold for attendance is a more cost-effective and efficient way of delivering services, and that service integration is appreciated by clients (120,166-167). An example of a highly integrated, fixed-site service setting would be a site that provides needles, syringes and injection equipment, testing and possibly medical care (e.g. treatment for HIV, hepatitis B and C), general health information about hygiene and overdose prevention, referrals to drug treatment, and general health and social services. (See text box with examples of service integration on page 29.)

If it is not possible to integrate services due to health system organisation, funding, or client preferences, there is still great value in delivering individual services to address client needs. Many programmes begin with one mode of service delivery, and then add additional services as time goes on. Service delivery modes should be adapted to maximise effectiveness with regard to local needs. These service delivery modes have a variety of names, depending on the setting, but the general characteristics usually fall into the following categories:

Fixed sites: Services can be, and often are delivered through facilities at a fixed site which specifically target people who use drugs and aim at maintaining a low threshold for attendance (i.e. very few restrictions of use and a client perspective to service provision), to make access as easy as possible for users. Fixed-site services can be needle and syringe programme sites or opioid substitution or other drug treatment sites, which might also provide additional services for people who inject drugs, such as testing for HIV, hepatitis or TB, health education, or referral for treatment. Fixed site services may serve as a 'drop-in' centre or a place to be for people who inject drugs. The service site, which provides health and prevention services, can also be a place to rest, eat, read newspapers, use the internet and talk to staff and peers in a relaxed and accepting atmosphere. Fixed-site services provide an important place for peer education and often serve as a base from where professionals and peer workers conduct outreach activities. Needle and syringe programme sites often serve as a gateway to attract clients. Initially, many clients visit service sites for the social connections, syringes or drug preparation equipment provided there, but then come into contact with a range of other services and health education messages.

In more than 50 European cities⁸, spaces where drugs can be consumed under the direct supervision of health staff have been integrated into specialised fixed-site facilities. Such supervised injecting facilities are professionally run healthcare facilities where hygienic and safer use is promoted to reduce the morbidity and mortality associated with drug injecting (5). The facilities provide opportunities for health education and disease prevention and for immediate intervention by professionals in cases of overdose. A main objective is to reach out and stay in contact with people who are not able or willing to quit injecting drug use, to reduce health risks, and to provide access to other services, in particular medical care and drug treatment. Research has shown that supervised injecting facilities reach specific hard-to-reach target groups, and that service users report substantial reductions in risk behaviour as well as improved health.

Regardless of their type, fixed-site services should be located in an area in which sizeable clusters of people who use drugs live or spend time, or, alternatively, where large numbers of potential clients can easily obtain access to the service site. Fixed-site services are typically run by specialised staff; these should be well-trained to provide services and education in a client-centred and non-judgmental way. Advantages of fixed sites are that multiple services can be delivered in one location, and the services delivered can be tailored to the needs of the local population. For example, clients can select the types of needles, syringes and injection equipment they prefer, thereby minimising waste due to pre-packed kits that often include items that clients do not want or need. Disadvantages of fixed sites include that they can be expensive to run, which may limit opening hours and, in turn, access to services. Fixed sites can also be difficult to access for users outside of the immediate geographical area of the site. Therefore, attention must be paid to mapping the needs for services and matching those needs to sites that are easily accessible and offer convenient opening hours to as many people who inject drugs as possible. People who inject drugs and live in hard-to-reach areas may require mobile outreach services (see below).

Sometimes, fixed sites face negative reactions in the neighbourhood if they are viewed as attracting a problematic population, thus intensive communication within the community is needed to overcome these concerns. Fixed sites can also be viewed by clients as affiliated with undesired service providers, for example, government programmes, which in some settings can limit uptake. Services providing outpatient drug dependence treatment typically combine further health and social service offers relevant for the target group of injectors, including infectious disease prevention measures like counselling and testing, vaccinations, and referral to specialist care.

Pharmacy sites: In the majority of EU/EEA countries syringes are sold legally. In some countries, pharmacies are the main supplier of needles and syringes. Pharmacies can act as sales or distribution points for needles, syringes and injecting equipment, and can be service points for the collection of used needles and syringes. Testing or vaccination services could also be supplied by pharmacies to people who inject drugs. One example, from Scotland,

⁸ These cities are located in Germany, Luxembourg, the Netherlands, Norway, Spain and Switzerland.

uses an electronic system to track individual clients through the use of an anonymous card. With the card, clients can obtain free sterile needles and syringes from pharmacies. The system can also track those in need of referral to testing or vaccination services and provides information on the number of needles and syringes dispensed per client for health service planning. Furthermore, the community pharmacy can be an active partner in opiate substitution treatment, dispensing medication to registered patients, maintaining regular contact, reminding clients of medical appointments, or managing additional medication. Referral and follow-up to vaccination services can also be managed through this system. The main benefit of pharmacy services is that they can be more accessible to more people who inject drugs, both in big cities and in small towns, thanks to an existing infrastructure, which also reduces costs. However, most pharmacies focus on serving the general public and many are privately run, sometimes decreasing the feasibility and acceptability of providing services to people who inject drugs, who can be viewed as undesirable or non-paying clients. Client confidentiality and the possibility for more extensive health promotion can be an issue if the pharmacy has no private consultation area or lacks personnel. Finally, needles and syringes provided through pharmacies are often given in pre-packaged bundles, effectively limiting individual choice. While pharmacy-based distribution of services to people who inject drugs is a very effective method of service provision, pharmacies cannot cover all user needs.

Outreach services: Because many sub-groups of people who inject drugs are difficult to access through general health services, outreach services often provide an effective way of delivering services, for example the provision of needle, syringe and injecting equipment. Outreach services can also deliver condoms, opiate substitution treatment, and health promotion messages (158). 'Outreach' is a generic term used to cover several types of service delivery and can include mobile units or vans, street outreach by community health workers, and regular satellite services based at other agencies. Often outreach services are able to reach people who are not in contact with other health services and thus play an important role in identifying their needs for referral to fixed-site or general health services, such as HIV, hepatitis or TB testing or treatment, or drug treatment. (For more information on outreach see (158,168).) Outreach can include home visits, and outreach workers can accompany clients to other services. One benefit of outreach services is that, due to their mobility, they are often highly accessible to different populations of people who inject drugs because they can easily move into new areas with high concentrations of people who inject drugs. Mobile units can provide services, including the dispensing of opiate substitution medications in settings where fewer people who inject drugs are concentrated or where fixed sites are not possible due to community or law enforcement opposition. Sometimes cost considerations limit the extent to which mobile outreach is possible, and the hours of operation have to be curtailed. One review found that outreach services were seen by people who inject drugs as not providing a full range of services (169).

Peer-delivered services are a type of outreach service (although services can also be delivered from fixed sites) delivered by current or former drug injectors in order to refer other people who inject drugs to service centres. If no formal services are wanted, peer-delivered services distribute needles, syringes and equipment (this is sometimes referred to as 'secondary needle distribution'). Peer-delivered services can provide much easier access to the most at-risk populations, including new or young injectors. Peers handle equipment distribution, referrals to drug treatment (or other treatment and testing services), and health promotion messages in the language of the local drug use scene. Messages delivered by peers can thus have a greater impact (and lead to better intervention uptake) than those delivered by health workers – a big advantage, especially when taking into consideration that persons obtaining needles and syringes through secondary distribution services often show extreme high-risk behaviour. If peer-delivered services are used, training, supervision and support are particularly important, as well as thorough consideration of the ethical implications of employing former or current injectors to conduct outreach services to people who inject drugs. For more resources on this see (158) and (168,170).

Vending machines: Vending machines are used in some settings as a complementary method of distribution of needles, syringes and equipment, usually in the form of pre-filled packets. They are coin-operated and provide written drug treatment referral, safe injection information, and other health promotion messages along with the products dispensed. This mode of service delivery is always available to potential users and is highly anonymous, often attracting new or younger injectors. However, this type of service requires money or tokens to operate the machine, and a plan must be in place to ensure regular refilling and maintenance of the machines. Community concerns about the placement of vending machines are not uncommon, as are fears that minors can access them. It should also be obvious that syringe vending machines cannot provide a direct link to the service provider, which makes referrals to testing and treatment and face-to-face health promotion impossible. However, they can be a first step, offering the possibility of contact, generating name recognition as well as a certain level of confidence in the organisation running the syringe vending machine (171).

General health services: Hospital or primary care settings are another important source of service delivery and referrals to specialised services for people who inject drugs. Confidential testing, diagnosis and treatment for HIV, viral hepatitis, TB, bacterial skin infections and other diseases common among people who inject drugs are typically conducted in general health service facilities, and maintaining strong referral links between these services and fixed sites or mobile settings which serve people who inject drugs is important. General health services can also provide needles, syringes and other injection equipment, supervise hygienic injecting, assist during drug detoxification, provide condoms, and promote health in general. TB and HIV clinics are often organised by general

health services. Given the high proportion of people who inject drugs among clients, it is crucial that staff at general health service facilities are properly trained on pertinent health promotion messages and can either refer people to drug treatment and needle and syringe services, or know where referrals can be made. Ideally, all people who inject drugs would seek and receive high-quality mainstream health services. However, there is evidence from some settings that people who inject drugs only rarely visit general health service facilities, and alternative ways of reaching them are necessary. In the Netherlands, specialised services for people who inject drugs and other risk groups are offered alongside general health services. There are also examples of integrating drug and medical services (a 'one-stop shop' model) into one programme, which facilitates treatment adherence and completion (153,172-174). Examples are directly observed TB treatment and HCV antiviral treatment, both combined with methadone maintenance treatment. General health services are easily accessible to clients, particularly their emergency departments, which are always open. Care must be taken to sensitise both health and non-health staff in these more general health settings to the issues of people who inject drugs and to delivering non-judgmental and confidential care to them. In some countries, some general health services provide anonymous testing.

Prison settings: Finally, it is important to mention that many countries provide services to IDU populations in prison systems, and that prison settings are key to achieving a high and effective coverage of services for the prevention of infection among people who inject drugs. Correctional facilities are an important setting for injection-related infection prevention and control. The main reasons are: (a) the high prevalence of HIV, HCV and TB in prisons; (b) the fact that many people who inject drugs eventually get sentenced to a prison term; and (c) evidence that drugs continue to be used and also injected in prison – despite the strict prohibition of drugs (5). In some countries, the prison systems offer drug treatment, disease testing and treatment, vaccinations, health education, and even needle and syringe programmes. Following the principle of 'equivalence of service provision' between community and prison, there is a movement in many countries to provide the same services for people who inject drugs in prison settings as for people who inject drugs in the community.

The described modes of service delivery can be effective in targeting people who inject drugs. Emerging new methods for the delivery of health promotion information, such as mobile phone- and internet-based messaging show promise in improving treatment adherence. While services will at times only employ one mode of delivery, it is more likely that effective programmes will provide several services in one location or several modes of service delivery to reach the diverse needs of users. In order to better link programme services, it is essential that multiple services be co-located at the same place so that users can access them conveniently (see text box below on service integration). Additionally, outreach workers, case managers, and healthcare providers should receive further training in the treatment and/or case management of co-morbid conditions; areas of training should include drug treatment, the treatment of TB, viral hepatitis, and HIV. Specialist providers should also be involved in the care of such patients. In addition to these co-morbidities, there are often mental health diagnoses which necessitate good case management. Increased awareness and training can lead to enhanced monitoring of drug-drug interactions and adverse side effects, as well as maximise treatment outcomes and improve a client's quality of life.

Service integration

There are many successful examples of linking services for people who inject drugs in order to increase access to services, harmonise treatment, and optimise the distribution of prevention messages, thereby increasing the likelihood of treatment adherence and success. Co-location of service delivery sites for TB, viral hepatitis, HIV and opioid substitution treatment and/or needle and syringe programmes is an option that is in practice or under development in some countries. Not only is the physical proximity of services an advantage, but communication and sharing of expertise across different healthcare programmes also benefit from this (Sylla et al., 2007; Elk et al., 1993; Batki et al., 2002; Perlman et al., 1995; Deiss et al., 2009; Reilly et al., 2002).

A recent pilot programme in Estonia has shown that the uptake of TB screening services can be increased by offering TB screening at opiate substitution treatment facilities and more active referrals to TB services (reminders, incentives, transportation) (Rüütel et al., 2011). When planning service facilities, provisions for the co-delivery of services should be made. For example, HIV-seropositive persons who are not infected with TB should be kept apart from patients with active TB, due to the increased risk of TB infection for HIV-positive people.

Services could build off of existing drug rehabilitation programmes, syringe distribution programmes, or service providers for TB directly observed therapy (DOT), depending on what is considered best for particular setting. Mobile outreach healthcare programmes may be useful to reach certain populations of people who inject drugs, in particular through mobile radiographic screening units. Such units have been shown to have a positive effect on the reduction of TB among people who inject drugs in Rotterdam, Netherlands (de Vries et al., 2007).

Table 1: Modes of service delivery targeting people who inject drugs and their strengths and limitations

Model type	Types of services that could be provided to people who inject drugs	Strengths	Limitations
Fixed site dedicated low-threshold services	<ul style="list-style-type: none"> • Injection equipment provision/disposal • Counselling • Drug dependence treatment including opioid substitution treatment • Testing for HIV, hepatitis B, C and TB • Vaccination • Place to be • Food, shower, clothing • Peer education • Health promotion • Safer use education, incl. overdose prevention and management • Supervised facilities for hygienic injecting • Safer sex health promotion and condom distribution • Supervised antiviral treatment (or directly observed therapy for TB) 	<ul style="list-style-type: none"> + Potential for creating sense of belonging for clients + Potential to provide multiple services in one location + Can achieve favourable cost/client coverage ratio + Can offer service provision tailored to clients' needs + Usually run by specialist staff + No opposition by other clients + If well organised, access is easy + Provides a base for other services like outreach services 	<ul style="list-style-type: none"> - Fixed site might limit access of those who do not live in the vicinity - Can be expensive to run - Can have limited opening hours - Potential for harassment by police or other law-enforcement agents, particularly if cooperation contacts are not established/managed - Personnel security risk may be increased if not well managed - Potentially less access to short-term or young injectors - Fixed site might be more difficult to establish due to opposition in the neighbourhood
Pharmacy services	<ul style="list-style-type: none"> • Injection equipment provision/disposal • Dressings • Health promotion • Confidential testing • Information and referrals (infectious disease testing and treatment, vaccination and drugs services) • Provision of (rapid) tests for HIV/hepatitis C 	<ul style="list-style-type: none"> + Accessible/good geographical availability + Wide opening hours + Can be cost-effective + May be considered more anonymous + Access to medical advice/medically trained staff + Uses existing infrastructure 	<ul style="list-style-type: none"> - Payment may be required - Limited opportunity for health promotion and referral in busy pharmacies - Provision of pre-packed bundles reduces options for user preference - Reluctance of pharmacists to sell syringes to people who use drugs - Opposition of other clients
Outreach services (including peer-delivered services)	<ul style="list-style-type: none"> • Injection equipment provision/disposal • Health promotion • Information about appropriate specialists, clinics and medical services • Referrals to infectious disease testing and treatment, vaccination, and drugs services • Home visits, prison visits • Accompanied referrals to other services • Provision of rapid tests for HIV/hepatitis C • Counselling 	<ul style="list-style-type: none"> + Responsive and easy to adapt to user needs + Flexible regarding changing locations where people who inject drugs can be reached + 'Early warning' potential: Professionals learn what is happening among users + Accessible, especially to hard-to-reach and high risk users (young/new users, migrant users) + Peer-delivered services can increase service efficacy 	<ul style="list-style-type: none"> - Not all services can be provided - Cost and maintenance (mobile units) - Limited hours - More expensive staff time (due to time spent driving, etc.) - Some mobile units could make users feel too observed/uncomfortable - Peer-delivered services must be well supervised and require training
Vending machines	<ul style="list-style-type: none"> • Injection equipment provision/disposal • Referrals to infectious disease testing and treatment, vaccination, and drugs services • Health promotion (in written form) 	<ul style="list-style-type: none"> + Always accessible (especially to young/new users) + Cost-effective + Anonymous 	<ul style="list-style-type: none"> - Not all services can be provided - No personal contact possible - Potential for community concern about machine placement - Payment or tokens required - Maintenance and re-stocking must be ensured

Model type	Types of services that could be provided to people who inject drugs	Strengths	Limitations
General health services	<ul style="list-style-type: none"> • Confidential testing for HIV, hepatitis B, C and TB • Treatment of HIV, hepatitis B, C and TB • Care of skin infections/dressings • Vaccination • Health promotion • Injection equipment provision/disposal • Assistance with drug detoxification • Opioid substitution treatment 	<ul style="list-style-type: none"> + Accessible + Access to trained staff + Access to more/advanced testing and treatment services + Access to mainstream health services (services used by the rest of the community) 	<ul style="list-style-type: none"> - Might not be tailored to user needs - Some health staff may be reluctant to provide care to people who use drugs - Opposition of other clients - Clients might be reluctant to use site if e.g. perceived as too closely affiliated with government services - Clients may not trust confidentiality - Anonymity may be difficult to ensure for all services - Limited/no access to individuals without health insurance - Stigma
Services in prison settings	<ul style="list-style-type: none"> • All services available to drug users in the community <p>Examples include:</p> <ul style="list-style-type: none"> • Confidential testing for HIV, hepatitis B, C and TB • Treatment of HIV, hepatitis B, C and TB • Vaccination • Health promotion • Injection equipment provision/disposal • Assistance with drug detoxification • Counselling • Drug dependence treatment, incl. OST 	<ul style="list-style-type: none"> + High risk groups can be reached + Interventions are cost-effective + Risk of post-release mortality/morbidity can be reduced + Community-based agencies can deliver services + Easier possibilities to provide disease treatment + Time for health promotion 	<ul style="list-style-type: none"> - Prison health budget may be insufficient - Investment in training of prison health staff and officers needed - Confidential service provision may be difficult to ensure

Knowing and understanding the national situation

The epidemiology of both drug use and infections among users is subject to rapid changes due to different illicit drugs, changing drug cultures and population movement. The dynamics of these changes are complex, multi-factorial and dependent on social and economic situations, prevention activities, and other societal factors (175).

In order to ensure that national or sub-national strategies best serve the population of people who inject drugs, as well as prevent and control infectious disease, there must be sufficient surveillance of drug use and infections among people who inject drugs. Similarly, measures taken should be continuously monitored and evaluated in terms of response, impact, relevance, and scale of coverage. Such monitoring is necessary not only to ensure that prevention remains relevant, but also to maintain effectiveness both in terms of health impact and cost.

To ensure that prevention resources are well spent, infectious disease prevention efforts should be targeted to populations of people who inject drugs and where the risk of transmissions of infections is greatest. Investment in adequate surveillance systems for both drug use and infectious disease is necessary and likely cost-effective. Failure to implement such systems may not only hide a growing problem, leading to high health and social costs, but also result in ineffective use of resources.

Monitoring problem drug use and responses

Surveillance of problem drug use is a necessary component of any national effort to prevent harm caused by drugs. A review of this activity is beyond the scope of this guidance, but the EMCDDA has issued a set of key indicator protocols and toolkits for monitoring drug use and problem drug use (including injecting drug use) and their consequences (4).

Estimating the size of the populations of people who inject drugs is a key component of surveillance; these estimates not only quantify the magnitude of infection risks, but also to determine potential service needs and help to estimate the coverage of service provision. Together with its network of national partners (the Reitox network of National Focal Points) (176) and expert groups, the EMCDDA provides and implements a standardised methodology for estimating the size of problem drug user populations (including people who inject drugs) (4) which describes different methodological approaches to produce national and local estimates.

Through a set of standardised monitoring tools (data tables and structured questionnaires), the EMCDDA also collects harmonised information about health and social responses to drug use and injecting drug use in the EU Member States, candidate countries, and Norway (112). Routinely collected data include information on drug prevention and harm reduction policies; on provision of health and social key interventions, including drug treatment (e.g. the number of clients receiving opioid substitution treatment); and on types, number and geographical distribution of needle and syringe programmes as well as the number of syringes provided.

Surveillance of infections

The epidemiological picture of infections among drug users may change rapidly, especially if prevention is weak. A good infectious disease surveillance system, built on the principle of 'surveillance for action', i.e. with an active link between prevention and surveillance structures, is a necessity if infection risks among people who inject drugs are to be controlled.

ECDC coordinates case-based surveillance of all newly reported cases of blood-borne infections at the European level, including those infections that can be transmitted through the sharing of injection equipment. Case-based surveillance is useful for monitoring disease trends and may also be useful in the early detection of disease outbreaks, particularly if the national coverage of the system is good and reporting delays are minimal. The success of outbreak-response interventions are highly dependent on the ability to rapidly detect new outbreaks and having the means to respond appropriately. If national reporting is performed with some delay, this may be compensated by much faster local or regional reporting. EU-wide case definitions exist for HIV, hepatitis B, hepatitis C and hepatitis A infections, but the transmission category (i.e. risk factor) is systematically collected only for HIV infection (hepatitis B and C surveillance case definitions are currently under review and are anticipated to contain transmission category information). Many national systems, however, collect more detailed information, which is important for local prevention measure implementation. Disease notification rates may reflect disease incidence, but are usually an underestimation thereof. Additionally, only generic population denominator data can usually be applied to this type of surveillance. Changes in testing patterns and frequency can easily skew the

results. Case-based reporting also requires the maintenance of a basic level of infrastructure and processing time over substantial periods of time and requires significant support from healthcare providers to produce adequate risk factor information.

The EMCDDA monitors the prevalence of infectious diseases in injecting drug users by developing data collection standards and guidance on bio-behavioural surveys and other data collection methods in injecting drug users (2). This work is done in close collaboration with ECDC, who coordinates general infectious diseases surveillance in Europe, and national and international partners (177-178). Data collection is focused around HIV and hepatitis B and C in injecting drug users. An early warning system and expert network are being maintained for infectious disease outbreaks in injecting drug users that can include other diseases, such as anthrax and botulism

Other types of surveillance systems, such as various types of surveys and bio-behavioural studies, have their own distinct advantages in terms of providing strategically important information. Surveys can provide estimates of prevalence among the target population, which is usually not achievable through case-based surveillance. Bio-behavioural surveys in injecting drug users, such as promoted by the EMCDDA and ECDC, can provide information on both drug use patterns and infectious diseases. However, these studies have to be repeated over time if trends are to be followed, which can be costly. An additional limitation is a lack of consensus on the best way to achieve representative sampling over time although this consensus is being built by the work of the two agencies.

Countries should make decisions on the parameters of their own data collection systems for surveillance based on their own needs, but such a system should produce sufficient information to inform the development of a prevention strategy based on a health needs assessment of the local problem, while being efficient in terms of resources and costs.

Monitoring and evaluation of programmes

Monitoring systems should serve the needs of a country or a region for continuous process evaluation and adaptability to changes in user habits and profiles; such evaluation assists programme managers and policy makers in understanding which components of a prevention programme are successful and which require improvement. Monitoring can also indicate to programme planners and policy makers whether the mix of service delivery modes, the combination of services provided, and the coverage of interventions appears to be effective in reducing or preventing increases in the incidence of disease in the target group of people who inject drugs. If no monitoring is carried out, it will be impossible to measure programme impact or to attribute changes in behaviour or disease incidence to interventions. Both process and outcome indicators can be used and be useful, but it is worth to consider setting realistic goals for the latter category. Many hard outcome indicators such as prevalence of infections or changes in risk behaviour may take years or even decades to change significantly.

Indicators

This guidance does not cover the indicators for programme monitoring and evaluation in detail, as considerable work has already been conducted in this area (see (4,53,137)). It should be emphasised that all nationally monitored indicators should be used for national planning and evaluation purposes. Monitoring should be helpful, rather than a hindrance to achieving national or regional programme goals. Monitoring and evaluation data should feed into the process of continuous assessment and adaptation of service programmes in order to meet changing epidemiological and user characteristics. Obviously, not all national indicators are useful for international reporting, and not all international reporting indicators are necessarily useful for national monitoring. A frequent misunderstanding is to assume that all international indicators have to be rigorously followed, even if they are nationally irrelevant.

Setting targets for intervention coverage

At the population level, coverage is commonly defined as the proportion of the population in need of an intervention that actually received that intervention (179). In order to optimise prevention, it is crucial to know which proportion of the target population of people who inject drugs is reached by the specific preventive interventions. In the field of vaccines, the level of coverage determines the effects achieved by an intervention: at a certain level of coverage herd immunity effects introduce protection, even for unvaccinated populations. These findings are also supported by modelling studies.

Common measures in the field of infectious disease prevention among people who inject drugs are the number of syringes distributed per injecting drug users per year, or the percentage of problem opioid users receiving opioid substitution treatment. The proportion of people who inject drugs receiving treatment for HIV, hepatitis B, and/or hepatitis C is another important indicator of the coverage of infection treatment services (180). Indicative targets for preventative services have been set, but it is indispensable to consider those in the context of the specific national (or local) situation, based on a well-performed needs assessment (53,179). There is growing evidence that higher levels of coverage of needle and syringe programmes and opioid substitution treatment are more effective

than lower levels of coverage per drug injector (71,181) and that large differences in coverage may exist between countries (180,182). According to data from the EMCDDA, the current EU average of syringes distributed in the year 2009 by specialist NSP facilities is 90 per drug injector. At national level, the highest reported number was over 300 syringes per injector (183). In addition, pharmacy sales constitute another major source of clean injecting equipment in most countries. In the same year, on average one in two problem opioid users received opioid substitution treatment, with the highest national percentage in Malta 68% (central estimate between 65% and 71% (128). Ideally, there should always be sufficient supplies of needles and syringes to keep services running. Unmet demand for needle and syringe exchange services or waiting times for drug treatment indicate an unmet demand for services and are a sign that service coverage needs to be increased.

Scaling-up coverage of syringe programmes: experience from Estonia

Estonia is one of the countries in the EU that has faced a heavy burden of injecting drug use, with a high rate of injecting drug use in the general population as well as a very high HIV prevalence among people who inject drugs. Injecting drug use is mostly concentrated in the capital city Tallinn and northeastern Estonia. It is estimated that Tallinn has about 10 000 injecting drug users who use mostly fentanyl analogues and amphetamines. Needle and syringe exchange services were initiated in Tallinn in 1997, and opioid substitution treatment with methadone followed in 2001, although the scale of services was limited. In 2005, HIV prevalence among people who inject drugs was 54% and a high proportion of new injectors (those injecting for ≤ 3 years) was reported (21%). It was decided at the national level that it was necessary to rapidly scale-up the coverage of prevention programmes in order to meet these increasing public health concerns, and this was planned into the National HIV/AIDS Prevention Strategy. Between 2003 and 2009, the number of fixed site and outreach service locations in Tallinn increased from 1 to 10, service visits increased 27-fold, the number of syringes distributed increased 43-fold (from 1.8 to 77 syringes/drug injector/year), and the number of positions for methadone treatment increased more than 4-fold. Approximately 80% of IDUs report ever being in contact with syringe exchange services, and for approximately 60% of users, syringe exchange services are the main source of clean needles and syringes. The percentage of people who inject drugs reporting sharing syringes during the last four weeks has decreased from 32% (2005) to 22% (2009). During that period, HIV incidence among new injectors decreased from 21% in 2005 to 9% in 2009, with the percentage of new injectors among all injecting users decreasing from 21% to 12%. It is likely that some of the decreased HIV incidence observed during the study period can be attributed to the scale-up of needle and syringe services, as access to drug treatment and antiretroviral treatment were provided at fairly low levels during that period. Continued provision of needles and syringes at even higher levels, combined with scale-up to high levels of drug and HIV treatment to those in need, is likely to further decrease HIV incidence in Estonia over time.

Source: Uuskula et al., 2011

Annex A. Epidemiology of injecting drug use and major infections among people who inject drugs in the EU/EEA

Injecting drug use

People who inject drugs are one of the groups at highest risk of acquiring negative health consequences as a result of their drug use due to the risk of blood-borne infections like HIV and hepatitis B and C. They are also susceptible to drug overdose and infections such as tuberculosis, hepatitis A virus, bacterial skin infections, systemic infections, and sexually transmitted infections.

In many European countries, injecting drug use is synonymous with opioid use, but there are some countries in which amphetamines are the predominant drug injected (5). The EMCDDA collects estimates of the prevalence of injecting drug use from European Member States and, in 2010, 12 countries provided recent estimates which suggested large differences in the prevalence of injecting drug use by country. The weighted average estimate of injecting drug users is 2.5 per 1000 adults aged 15 to 64 years for those countries providing estimates. If this average were extrapolated to the European population, it would correspond to an estimate of between 750 000 and 1 million active injecting drug users in the EU/EEA. In addition to this, there is likely to be a significant population of former injecting drug users (5). While the injecting drug user population, as a whole, is aging in most of the western part of Europe, younger people who inject drugs have been highly prevalent in other parts of the EU.

HIV

HIV prevalence rates among people who inject drugs, as reported by EU countries range from less than 1% to more than 60% (based on specific studies or sentinel surveillance) (137). Of all newly diagnosed HIV cases reported in 28 countries in the EU/EEA Europe in 2009 (25 917 cases), 1 298 were identified as people with a current or past history of injecting drug use (a rate of 5.7 per 100 000 population). Despite the 2009 European average of 5% of reported HIV cases being due to injecting drug use, national figures varied widely, and the proportion of people who inject drugs among newly reported HIV cases ranged from 65% in Lithuania and 43% in Bulgaria to less than 1% in the Netherlands and Romania. Since 2004, the number of new HIV diagnoses reported among people who inject drugs has declined by 40% in the 26 EU/EEA countries with consistent HIV reporting systems (6). National trends have been similar, with most countries reporting declining numbers of cases of HIV among people who inject drugs during the last six years, except Bulgaria, Estonia, Latvia and Lithuania, with the three Baltic countries most affected by a rapid increase in rates of HIV diagnoses in 2001–02. Since then, these countries have reported declines, although a resurgence of HIV was reported in Latvia in 2007 and in Lithuania in 2009. In west European countries the HIV epidemic among people who inject drugs is much older and peaked in the mid-1980s(6).

Despite the decreasing trend of HIV cases among injecting drug users in the EU/EEA, there are still countries with populations of injecting drug users where significant HIV transmission is occurring (184). It is also likely that sexual transmission of HIV takes place between people who inject drugs and their sexual partners. Despite the relatively low absolute number of cases diagnosed among people who inject drugs, they are disproportionately affected by the HIV epidemic as compared to people who do not inject drugs.

Hepatitis B and C

Hepatitis B (HBV) and hepatitis C (HCV) viral infections are important public health issues for the European Union as both infections have substantial morbidity and mortality. Both infections may result in chronic disease which may lead to cirrhosis of the liver and possibly liver cancer and death. HBV and HCV can easily be transmitted through injecting drug use due to unsafe injection practices which include the sharing of needles and syringes and other injection materials.

In Europe, injecting drug use is a major transmission route for HCV infections, and people who inject drugs account for the majority of newly reported cases of HCV infection. Estimates suggest that there are around one million current or former injecting drug users who may have chronic HCV infection in Europe (5). HCV infection rates are often very high amongst people who inject drugs, ranging from between 12% to 85% (54) and between 50 and 90% of people who are infected with hepatitis C virus are unable to spontaneously eradicate the infection. The prevalence of HCV among people who inject drugs has been observed to be declining in nine countries in

Europe but increasing in three others, and data from four other countries shows no obvious trends (8). In six countries where risk factors are known, trends in notified cases of HCV have shown a drop in the proportion of people who inject drugs among notified cases, but an increase in three other countries (54). The data is difficult to interpret as data quality is often poor but there are indications that overall levels of HCV infection among people who inject drugs may be starting to decline. The risk of becoming infected with HCV is known to increase with injecting duration (10), but recent studies also indicate that many injectors contract the virus early in their injecting careers (54). The high levels of HCV infection among people who inject drugs is made worse by the fact that many of those who have contracted HCV through injecting drug use are unaware of their infection status. These factors indicate that early initiation of prevention measures is important.

In addition to high levels of hepatitis C infection, people who inject drugs are often infected with other viruses, including hepatitis B or HIV. Having concurrent hepatitis infections greatly increases the risk of death due to sudden liver failure. Levels of hepatitis B antibodies are often very high among injectors but prevalence varies considerably between countries. This may be partly due to differences in vaccination levels among people who inject drugs (54). Recent data from nine European countries indicated that anti-HBc prevalence levels among people who inject drugs were over 40%. Among notified acute cases of hepatitis B with documented transmission routes, one in five cases has been infected by injecting drugs. Trend data indicate that the proportion of people who inject drugs among notified cases of HBV has declined in eight out of 17 countries between 2003 and 2008 (54).

Tuberculosis

Injection drug use is associated with a multitude of environmental risk factors and risk behaviours. The combination of social risk factors such as poor living conditions, homelessness, incarceration, poverty, tobacco use and alcohol abuse, together with physiological effects of drug use, can place people who inject drugs at higher risk for developing TB, being infectious from TB, and at an increased risk of mortality (142,185). Further, HIV-induced immunosuppression is, as mentioned above, one of the most significant risk factors for the development of TB and a major reason for the high prevalence of TB among people who inject drugs. A recent systematic review of TB-HIV co-infection in the EU/EEA found that the rate of HIV co-infection in TB patients ranged from 0 to 15%, and that injecting drug use was one of the risk factors for co-infection (186).

The EU has some of the lowest TB notification rates in the world, but there is large heterogeneity between EU countries. In 2009, notification rates ranged between 2.8 and 108.2 cases per 100 000 population (187). The most vulnerable and excluded groups are the ones that carry the most significant burden of disease and which have the poorest access to services.

There is no EU-wide collection of data recording of social risk factors for notified TB cases, therefore estimates on TB incidence in people who inject drugs rely on regional or, in some cases, country-specific studies. There is however ample evidence that drug use is associated with a higher prevalence of latent TB infection, and people who inject drugs are at increased risk of active TB disease. Depending on setting and country, about 10 to 60% of people who inject drugs test tuberculin skin test (TST) positive (142). Studies have shown that drug users, whether or not they inject drugs, face a similar risk of being TST positive (142).

A large majority of *M. tuberculosis*-infected individuals never become ill, but bacteria persist in a subclinical status with minimal replication. Latent TB infection (LTBI) is therefore defined as the condition of an individual being infected, but without clinical manifestation of disease and from whom *M. tuberculosis* bacilli cannot be identified by culture. Active TB disease is diagnosed by evaluating the medical history, symptoms, radiography and microbiological or molecular identification of *M. tuberculosis*. The risk of progression to active TB disease is influenced by the individual's immunologic status. People without HIV co-infection have a 5 to 10% lifetime risk of progressing to TB disease, while people with HIV have been reported to have a 5 to 10% annual risk of progressing to TB disease (185).

Hepatitis A virus

Hepatitis A is a viral illness with acute onset that is usually transmitted by fecal-oral contact, with outbreaks often traced to contaminated food and water supplies or to specific risk groups including men who have sex with men or people who inject drugs. Because it is not routinely monitored by risk group membership, the true burden of hepatitis A among people who inject drugs is unknown. There have, however, been reports of outbreaks of hepatitis A within the European Union concentrated in groups of people who inject drugs, such as in Latvia in 2008, where the population notification rate increased from 0.66 to 123 per 100 000 due to a community outbreak (13). Additional outbreaks have been linked to groups of people who inject drugs in the Czech Republic (12), Finland (15) and Norway (14). It is unclear whether these outbreaks were related to injection preparation practices or to other behaviours associated with poor hygiene.

Bacterial skin and systemic infections

It is difficult to estimate the true extent of bacterial and systemic infections due to injecting drug use as most of these are not monitored at the European level. Based on a 2010 survey conducted in England, Wales and Northern Ireland, 40% of those currently injecting reported a sore, abscess or open wound, common symptoms of an injection site infection, during the previous year (17). These infections are typically the result of the use of non-sterile injecting equipment or unclean drug preparation equipment. The most common pathogen that causes skin and soft tissue infections among people who inject drugs is *Staphylococcus aureus*, and a high proportion of this infection is methicillin-resistant *Staphylococcus aureus* (MRSA) (188). While most infections are minor, they can also become serious and systemic, resulting in osteomyelitis, bacteremia, septic deep-vein thrombosis, and endocarditis (189-190). Other bacterial skin, soft tissue and systemic infections are caused by group A streptococci (GAS), while still others are due to clostridial infections resulting in wound botulism or tetanus (191-192). Outbreaks of wound botulism (193), tetanus (18), and other clostridial infections (194) have been detected in people who inject drugs throughout Europe. While these systemic infections appear to be fairly rare, they can result in severe illness and death. Anthrax is one such acute disease caused by the bacteria *Bacillus anthracis*. It is rare in Europe, but in late 2009 and 2010, 42 cases were reported among injecting drug users in Scotland, 13 of which resulted in death. Further fatalities which were linked to the Scottish cases via the same anthrax strain were reported from England and Germany, and the source was thought to be a contaminated batch of heroin (54).

Sexually transmitted infections

The use of drugs, including injecting drugs, is associated with high-risk sexual practices and high prevalence of STIs, although the epidemiology of STIs among people who inject drugs is not well-documented in Europe. It is thought that people who inject drugs are at a higher risk of STIs because of the higher likelihood of exchanging sex for money or drugs or because of the impaired judgment in negotiating safer sex behaviour while under the influence of drugs (162). It has also been suggested that drug use may make it more difficult for some people who inject drugs to attend health services or STI screenings and that standard STI clinic services do not reach many people who inject drugs. Still, there is some evidence that sexual transmission of, for example, hepatitis B and HIV does occur between people who inject drugs and their sexual partners and, therefore, it is important to target this population for screening and prevention of sexually transmitted and other blood-borne viruses.

Human T-lymphotropic virus type II (HTLV-II)

HTLV-II is transmitted through shared injecting equipment, sexually, as well as through infected blood products. Since its discovery in 1982, human T-lymphotropic virus type II (HTLV-II) has held a controversial role as a pathogen, and literature on disease outcomes is limited. There is accumulating evidence of neurological disease and increased incidence of pneumonia, bronchitis and possible autoimmune disease among patients infected with HTLV-II (11). HTLV-II has been found among people who inject drugs in the United States and Europe, with an estimated prevalence of between 1.6 to 8% in Italy (195-196) and 0.4 to 11.5% in Spain (197). In these studies and others, HTLV-II co-infection with HIV is common. In northern Europe, HTLV-II is found at a comparatively lower frequency among people who inject drugs, but has been reported in Sweden (198) and France (199). One study in Ireland found a high seroprevalence (15%) of HTLV-II among people who inject drugs (200).

Annex B. Key interventions to prevent infections among people who inject drugs

As described in the section on 'Aims, objectives and methodology', several factors were taken into account when generating the key intervention components indicated in this guidance. For each key intervention, evidence which was based on published peer-reviewed research was taken into account by carrying out a systematic review of reviews published since the year 2000 ('review of reviews' exercise) (201). Reviews are considered high-level evidence because they summarise and collate findings from the primary literature using systematic criteria to select the studies and assess their results. Reviewing reviews is an efficient method of bringing high-level evidence together, but has specific limitations (see technical reports on background evidence base). To compensate for those limitations, this guidance takes recently conducted primary research as well as expert opinions into consideration to complement the evidence statements based on the 'review of reviews'. Outcomes of primary research were considered for interventions for which no systematic reviews were as yet available. The ECDC/EMCDDA Technical Advisory Group provided advice on all key intervention components.

Additionally, we confirmed whether an intervention was considered best practice in the EU and thus featured in national and international guidance and policy documents. Finally, we also consulted studies of user and service provider preferences, in relation to how users/providers described their criteria for the most efficient delivery of prevention services. For each of the recommended key interventions, the considered judgement on how we weighed the evidence for the inclusion of the intervention in the guidance is provided.

Table B1: Summary of the effectiveness of interventions to reduce injecting risk behaviour and the transmission of HIV and HCV, as a basis for the recommendation and considered judgement regarding seven key interventions

Key intervention/subcomponents	Expert opinion/implementation practices	Evidence from review of published reviews (for symbols, see Table B2 below)	Findings from primary studies
Injection equipment	Recommendation and considered judgement: Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes, free of charge, as part of a combined multi-component prevention approach, implemented through harm-reduction, counselling and treatment programmes is recommended, based on consistent review-level evidence, primary studies and expert opinion.		
Needle and syringe provision	Expert opinion in favour.	Injecting risk behaviour: ++ HIV transmission: + HCV transmission: ?	<ul style="list-style-type: none"> Ecological studies of NSPs demonstrate stable or declining HCV transmission rates. A recently published meta-analysis indicates that the combination of OST with NSP is effective in reducing HCV transmission.
Other injecting paraphernalia	Expert opinion in favour.	Injecting risk behaviour: + HIV transmission: ? HCV transmission: +/-	In vitro studies demonstrate strong potential for transmission of HCV.
Foil to stimulate route-transmission	Expert opinion in favour.	Injecting risk behaviour: ? HIV transmission: ? HCV transmission: ?	Lack of studies.
Vaccination	Recommendation and considered judgement: Vaccination of people who inject drugs with hepatitis B and A, tetanus and influenza vaccines, and – in particular for HIV-infected individuals – the pneumococcal vaccine. This is recommended based on expert opinion, implementation practice and primary studies.		
HBV, HAV, tetanus, influenza vaccines (pneumococcal vaccine for HIV-infected individuals)	<ul style="list-style-type: none"> Expert opinion in favour as a targeted service for people who inject drugs. Vaccine efficacy is well-established. Widely implemented public health practice. 	(Not included in review)	Strong evidence for individual and population-level reduction of HBV, HAV and tetanus following vaccination, even if only part of the full course is given.
Drug dependence treatment	Recommendation and considered judgment: Opioid substitution treatment (OST) and other forms of effective drug dependence treatment should be available and easily accessible, based on expert opinion and – in the case of OST – consistent evidence from multiple robust studies and reviews. While evidence of effectiveness of psychosocial treatments is lacking, it is recommended based on expert opinion.		

Key intervention/ subcomponents	Expert opinion/ implementation practices	Evidence from review of published reviews (for symbols, see Table B2 below)	Findings from primary studies
Agonist (opioid) pharmacological treatment (OST)	Expert opinion in favour.	Injecting risk behaviour: ++ HIV transmission: ++ HCV transmission: +	<ul style="list-style-type: none"> Combination of OST with NSP further enhances effectiveness in preventing HCV transmission. Increased adherence to ART and increased virological success of ART in HIV-positive persons on OST. Use of OST in combination with psychosocial treatment is beneficial for compliance, completion of treatment and abstinence at follow-up.
Antagonist pharmacological treatment	<ul style="list-style-type: none"> Option for those who do not commence agonist pharmacological treatment. Further research needed. 	Injecting risk behaviour: +/- HIV transmission: +/- HCV transmission: +/-	Potential benefits if combined with psychosocial treatment to reduce drug use.
Psychosocial treatment	<p>Main option for stimulant users, in absence of pharmacological treatments;</p> <ul style="list-style-type: none"> enhances effectiveness of OST if combined an option for opioid users not interested in pharmacological treatment 	Injecting risk behaviour: +/- HIV transmission: +/- HCV transmission: +/-	<ul style="list-style-type: none"> Potential benefits due to reductions in drug use Contingency management may provide benefit for stimulant users Combination with OST is beneficial for compliance, completion of treatment and abstinence at follow-up
Testing	Recommendation and considered judgement: Voluntary and confidential testing with informed consent for HIV, HCV (HBV for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment.		
Infectious disease testing	<ul style="list-style-type: none"> Expert opinion in favour. Included in national and international guidelines. Widely implemented public health practice. Necessary basis for any decisions on prevention and treatment. 	Injecting risk behaviour: +/- HIV transmission: ? HCV transmission: ?	Studies and modelling suggest that efficient linkage to treatment access reduces forward transmission.
Infectious disease treatment	Recommendation and considered judgement: Based on evidence and expert opinion, antiviral treatment should be provided based on clinical indications to all those who are HIV, HBV or HCV infected. Anti-tuberculosis treatment should be provided for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated. For all treatment, universal access is recommended, including access for active injectors ⁹ .		
	<ul style="list-style-type: none"> Expert opinion in favour Included in international and national guidelines, which increasingly state that active drug use should not be considered an exclusion criteria for receiving antiviral treatment. Failure to treat could result in harm in the form of morbidity and potentially death. 	(Not included in review.)	<ul style="list-style-type: none"> Strong evidence for TB treatment of active and latent cases. Modelling evidence suggests possible population-level prevention effects for HCV treatment Evidence for HIV and HCV treatment success in cohorts of active drug users
Health promotion (IEC and outreach)	Recommendation and considered judgement: Health promotion focused on safer injecting behaviour; sexual health including condom use; and disease prevention, testing and treatment is recommended, based on evidence from reviews, primary studies and expert opinion.		
Information, education and counselling	<ul style="list-style-type: none"> Expert opinion in favour Considered a fundamental companion component for the delivery of all of the other six interventions 	Injecting risk behaviour: + HIV transmission: +/- HCV transmission: ?	<ul style="list-style-type: none"> Multi-component package based on client populations' specific needs Supports prevention objectives

⁹ Drug interactions and stable contact with a medical provider need to be considered.

Key intervention/ subcomponents	Expert opinion/ implementation practices	Evidence from review of published reviews (for symbols, see Table B2 below)	Findings from primary studies
Targeted delivery of services	Recommendation and considered judgement: Services should be combined and organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings, offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.		
Fixed low-threshold sites offering NSP and other prevention services	Expert opinion in favour, allows for client needs-oriented service mix and gaining contact with users.	The scientific literature was reviewed for NSP programmes Injecting risk behaviour: ++ HIV transmission: + HCV transmission: +/-	<ul style="list-style-type: none"> In individual studies, low prices, geographical proximity, encouraging staff attitudes and the option to receive additional services from a needle and syringe programme were facilitating factors for people who inject drugs to visit the service site. Geographical distance, a fear of being caught by the police whilst attending an NSP, opening hours and a lack of privacy were found to act as barriers.
Referrals to general primary healthcare services and to specialist medical, drug prevention, other harm reduction, counselling and treatment services	Expert opinion in favour; included as a necessary and basic component of user care following accepted standards of health and social care delivery.	The scientific literature was not formally reviewed in relation to the effect of referrals to services.	The scientific literature was not formally reviewed in relation to the effect of referrals to services.
Pharmacy syringe access	Expert opinion in favour, broadens accessibility of sterile syringes.	Injecting risk behaviour: + HIV transmission: +/- HCV transmission: ?	Ecological and cross-sectional studies document decreased user syringe sharing following the introduction of syringe sales in pharmacies.
Secondary distribution of syringes	Expert opinion in favour, allows broadening the reach of syringe programmes.	Injecting risk behaviour: +/- HIV transmission: +/- HCV transmission: ?	Lack of studies.
Outreach syringe provision	Expert opinion in favour, allows to reach hard-to-reach, marginalised populations.	Injecting risk behaviour: ? HIV transmission: +/- HCV transmission: ?	Lack of studies.
Syringe vending machines	Expert opinion in favour, allows syringe access independent of service opening hours.	Injecting risk behaviour: +/- HIV transmission: +/- HCV transmission: ?	Lack of studies.
Multi mode injection equipment service delivery	Expert opinion in favour, use of multiple distribution channels is recommended.	The scientific literature was not formally reviewed in relation to the effect of multi mode service delivery.	Evidence from primary studies that combination of channels of service delivery is more effective.
Supervised injecting facilities	Expert opinion in favour, allow 'tailor-made', individual safer use education.	Injecting risk behaviour: + HIV transmission: ? HCV transmission: ?	Lack of studies. Impact on overdose deaths in the community.

Table B2: Types of evidence statements and the level of evidence that was required to support each statement (modified from Ellis et al., 2003)

Evidence statement	Level of evidence
'++' or '--' Sufficient review-level evidence to either support or discount the effectiveness of an intervention	<ul style="list-style-type: none"> • Clear and consistent statement from one or more core reviews based on multiple robust studies, <i>or</i> • consistent evidence across multiple robust studies within one or more core reviews, in the absence of a clear and consistent statement in the review(s).
'+' or '-' Tentative review-level evidence to either support or discount the effectiveness of an intervention	<ul style="list-style-type: none"> • A tentative statement from one or more core reviews based on consistent evidence from a small number of robust studies or multiple weaker studies, <i>or</i> • consistent evidence from a small number of robust studies or multiple weaker studies within one or more core reviews, in the absence of a clear and consistent statement in the review(s), <i>or</i> • conflicting evidence from one or more core reviews, with the stronger evidence weighted towards one side (either supporting or discounting effectiveness) and a plausible reason for the conflict, <i>or</i> • consistent evidence from multiple robust studies within one or more supplementary reviews, in the absence of a core review.
'+/-' Insufficient review-level evidence to either support or discount the effectiveness of an intervention	<ul style="list-style-type: none"> • A statement of insufficient evidence from a core review, <i>or</i> • insufficient evidence to either support or discount the effectiveness of an intervention (either because there is too little evidence or the evidence is too weak), in the absence of a clear and consistent statement of evidence from (a) core review(s), <i>or</i> • anything less than consistent evidence from multiple robust studies within one or more supplementary reviews.
'?' No reviews	No core or supplementary reviews of the topic identified, possibly due to a lack of primary studies.

Annex C. Additional guidance and technical guidelines

Title	Organisation (year)	Link
Best practice portal: evidence base, standards and guidelines, and evaluated practice Key epidemiological indicators	EMCDDA	http://www.emcdda.europa.eu/best-practice http://www.emcdda.europa.eu/themes/key-indicators
Use of interferon-gamma release assays in support of TB diagnosis	ECDC (2011)	http://ecdc.europa.eu/en/publications/Publications/1103_GUI_IGRA.pdf
Guide to infection prevention in outpatient settings: minimum expectations for safe care	CDC (2011)	http://www.cdc.gov/HAI/pdfs/guidelines/Ambulatory-Care-04-2011.pdf
EASL clinical practice guidelines: management of hepatitis C virus infection	EASL (2011)	http://www.easl.eu/assets/application/files/4a7bd873f9ccbf_file.pdf
HIV testing: increasing uptake and effectiveness in the European Union	ECDC (2010)	http://ecdc.europa.eu/en/publications/Publications/101129_GUI_HIV_testing.pdf
Guidelines for testing HIV, viral hepatitis and other infections in injecting drug users	EMCDDA (2010)	http://www.emcdda.europa.eu/publications/manuals/testing-guidelines
Treatment of tuberculosis: guidelines, fourth edition.	WHO (2010)	http://whqlibdoc.who.int/publications/2010/9789241547833_eng.pdf
Guidelines for services providing injecting equipment: best practice recommendations for commissioners and injecting equipment provision (IEP) services in Scotland	Scottish Government (2010)	http://www.scotland.gov.uk/Publications/2010/03/29165055/0
Harm reduction at work: a guide for organizations employing people who use drugs	Open Society Institute (2010)	http://www.soros.org/initiatives/health/focus/ihrd/articles_publications/publications/harmreduction-work-20110314/work-harmreduction-20110314.pdf
Good practice guide: HIV and drug use – community responses to injecting drug use and HIV	International HIV/AIDS Alliance (2010)	http://www.aidsalliance.org/publicationsdetails.aspx?id=454
Needle and syringe programmes: providing people who inject drugs with injecting equipment	National Institute for Health and Clinical Excellence (NICE) (2009)	http://www.nice.org.uk/nicemedia/live/12130/43301/43301.pdf
International standards for tuberculosis care, second edition	Tuberculosis Coalition for Technical Assistance (2009)	http://www.tbcta.org/Uploaded_files/Zelf/ISTCReport2ndEdition1258118339.pdf
Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users	WHO, UNODC, UNAIDS (2009)	http://www.unaids.org/en/media/unaids/contentassets/dataimport/pub/manual/2010/idu_target_setting_guide_en.pdf
Guidance on testing and counselling for HIV in settings attended by people who inject drugs	WHO, UNAIDS (2009)	http://www.who.int/hiv/topics/idu/care/GuidanceTC_IDUsettings.pdf

Title	Organisation (year)	Link
Policy guidelines for collaborative TB and HIV services for injecting and other drug users	WHO (2008)	http://www.who.int/rpc/guidelines/9789241596930/en/index.html
EASL clinical practice guidelines: management of chronic hepatitis B	EASL (2009)	http://www.easl.eu/assets/application/files/b73c0da3c52fa1d_file.pdf
Safety, risks and outcomes from the use of injecting paraphernalia	Scott (2008)	http://www.scotland.gov.uk/Resource/Doc/127313/0057758.pdf
Guide to starting and managing needle and syringe programmes	WHO, UNAIDS, UNODC (2007)	http://www.who.int/hiv/idu/Guide_to_Starting_and_Managing_NSIP.pdf
HIV/AIDS treatment and care: clinical protocols for the WHO European Region	WHO (2007)	http://www.euro.who.int/_data/assets/pdf_file/0004/78106/E90840.pdf
Correlation – Guidelines on providing integrated outreach services	Correlation Network (2007)	http://www.correlation-net.org/doccenter/pdf_document_centre/book_outreach_fin.pdf
Ontario needle exchange programs: best practice recommendations	Strike (2006)	http://www.health.gov.on.ca/English/providers/pub/aids/reports/ontario_needle_exchange_programs_best_practices_report.pdf
Policy and programming guide for HIV/AIDS prevention and care among injecting drug users	WHO (2005)	http://www.who.int/hiv/pub/prev_care/en/policyprogrammingguide.pdf
Advocacy guide: HIV/ AIDS prevention among injecting drug users	WHO, UNAIDS, UNODC (2004)	http://www.who.int/hiv/pub/advocacy/en/advocacyguideen.pdf
Evidence for action: effectiveness of community-based outreach in preventing HIV/AIDS among people who inject drugs	WHO (2004)	http://www.who.int/hiv/pub/prev_care/evidenceforactionreprint2004.pdf
Interim policy on collaborative TB/HIV activities. 1st ed.	WHO (2004)	http://whqlibdoc.who.int/hq/2004/WHO_HTM_TB_2004.330_eng.pdf
BCG vaccine: WHO position paper	WHO (2004)	http://www.who.int/wer/2004/en/wer7904.pdf
Background paper for the technical consultation on effective coverage of health systems	WHO (2001)	http://www.who.int/health-systems-performance/technical_consultations/effcov_background.pdf

References

1. WHO Regional Office for Europe. HIV/AIDS treatment and care: clinical protocols for the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2007.
2. Malta M, Magnanini MM, Strathdee SA, Bastos FI. Adherence to antiretroviral therapy among HIV-infected drug users: a meta-analysis. *AIDS Behav.* 2010 Aug;14(4):731-47.
3. MacGregor S, Whiting M. The development of European drug policy and the place of harm reduction. In: Rhodes T, Hedrich D, editors. *Harm reduction: evidence, impacts, and challenges.* Lisbon: EMCDDA; 2010.
4. European Monitoring Centre for Drugs and Drug Addiction. Key indicators. Lisbon: EMCDDA; 2011 [cited 5 August 2011]. Available from: <http://www.emcdda.europa.eu/themes/key-indicators>.
5. European Monitoring Centre for Drugs and Drug Addiction. Trends in injecting drug use in Europe. Lisbon: EMCDDA; 2010.
6. European Centre for Disease Prevention and Control, WHO Regional Office for Europe. HIV/AIDS surveillance in Europe: 2009. Stockholm: ECDC; 2010.
7. European Centre for Disease Prevention and Control. Annual epidemiological report on communicable diseases in Europe 2010. Stockholm: ECDC; 2010.
8. European Centre for Disease Prevention and Control. Surveillance and prevention of hepatitis B and C in Europe. Stockholm: ECDC; 2010.
9. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet.* 2011 Jul 27.
10. Hickman M. HCV prevention – a challenge for evidence-based harm reduction. In: Rhodes T, Hedrich D, editors. *Harm reduction: evidence, impacts, and challenges.* Lisbon: EMCDDA; 2010.
11. Roucoux DF, Murphy EL. The epidemiology and disease outcomes of human T-lymphotropic virus type II. *AIDS Rev.* 2004 Jul-Sep;6(3):144-54.
12. Castkova J, Benes C. Increase in hepatitis A cases in the Czech Republic in 2008 – an update. *Euro Surveill.* 2009 Jan 22;14(3).
13. Perevoscikovs J, Lucenko I, Magone S, Brila A, Curikova J, Vennema H. Community-wide outbreak of hepatitis A in Latvia in 2008 – an update. *Euro Surveill.* 2009 Jan 22;14(3).
14. Blystad H, Hoel T, Høiby E, Nilsen O. Infections among injecting drug users in Norway, 1997-2000. *Euro Surveill.* 2001;5(1).
15. Kuusi M, Nuorti P, Rostila T, Jokinen C. Hepatitis A infections in intravenous drug users, Finland, 2002. *Euro Surveill.* 2003 30 January 2003;7(5).
16. European Monitoring Centre for Drugs and Drug Addiction. Guidelines for testing HIV, viral hepatitis, and other infections in injecting drug users: a manual for provider-initiated medical examination, testing and counseling. EMCDDA manuals. Lisbon: EMCDDA; 2010.
17. Health Protection Agency CfI, Health Protection Scotland, National Public Health Service for Wales, Communicable Disease Surveillance Centre Northern Ireland, Centre for Research on Drugs and Health Behavior LSoHaTM. Shooting up: infections among injecting drug users in the United Kingdom 2007. An update: October 2008. 2008.
18. Hahne SJ, White JM, Crowcroft NS, Brett MM, George RC, Beeching NJ, et al. Tetanus in injecting drug users, United Kingdom. *Emerg Infect Dis.* 2006 Apr;12(4):709-10.
19. Beeching NJ, Crowcroft NS. Tetanus in injecting drug users. *BMJ.* 2005 Jan 29;330(7485):208-9.
20. Wiessing L, van de Laar MJ, Donoghoe MC, Guarita B, Klemptova D, Griffiths P. HIV among injecting drug users in Europe: increasing trends in the East. *Euro Surveill.* 2008;13(50).
21. Tefanova V, Tallo T, Kutsar K, Priimgi L. Urgent action needed to stop spread of hepatitis B and C in Estonian drug users. *Euro Surveill.* 2006;11(1):E060126 3.
22. Commission of the European Communities. Charter of fundamental rights of the European Union. 2000/C 364/01. Brussels: Commission of the European Communities; 2000.
23. Commission of the European Communities. Treaty of Lisbon. 2007/C 306/01. Brussels: Commission of the European Communities; 2007.
24. Commission of the European Communities. Combating HIV/AIDS in the European Union and neighbouring countries, 2009–2013. Brussels: Commission of the European Communities; 2009.
25. Dublin declaration on partnership to fight HIV/AIDS in Europe and Central Asia. Dublin; 2004.
26. EU Drugs Action Plan for 2009–2012. Official Journal of the European Union. 2008 Dec 20:C 326/7-25.
27. Council of the European Union. EU Drugs Strategy (2005–2012). Brussels; 2004.
28. European Centre for Disease Prevention and Control. Evidence-based methodologies for public health. Stockholm: ECDC; 2011.
29. European convention for the prevention of torture and inhuman or degrading treatment or punishment. 2002.
30. UN General Assembly. Basic principles for the treatment of prisoners. UN General Assembly Resolution. Geneva; 1990.
31. WHO. Prevention of acute drug-related mortality in prison populations during the immediate post-release period. Copenhagen: WHO European Regional Office; 2010.

32. WHO. Health in prisons: A WHO guide to the essentials in prison health. Copenhagen: WHO Regional Office for Europe; 2007.
33. O'Hare P. Merseyside, the first harm reduction conferences, and the early history of harm reduction. *Int J Drug Policy*. 2007 Mar;18(2):141-4.
34. Buning EC, Coutinho RA, van Brussel GH, van Santen GW, van Zadelhoff AW. Preventing AIDS in drug addicts in Amsterdam. *Lancet*. 1986 Jun 21;1(8495):1435.
35. International Harm Reduction Association. What is harm reduction? A position statement from the International Harm Reduction Association. London: International Harm Reduction Association; 2010.
36. Advisory Council on the Misuse of Drugs. AIDS and drug misuse: Part I. London: Advisory Council on the Misuse of Drugs (ACMD); 1988.
37. Rhodes T, Hedrich D. Harm reduction and the mainstream. In: Rhodes T, Hedrich D, editors. *Harm reduction: evidence, impacts and challenges*. Lisbon: EMCDDA; 2010.
38. Hunt N. Public health or human rights: what comes first? *Int J Drug Policy*. 2004;15:231-7.
39. Jurgens R, Csete J, Amon JJ, Baral S, Beyrer C. People who use drugs, HIV, and human rights. *Lancet*. 2010 Aug 7;376(9739):475-85.
40. WHO. Ottawa Health Charter. First International Conference on Health Promotion; 1986; Ottawa, Canada: World Health Organization.
41. Davoli M, Simon R, Griffiths P. Current and future perspectives on harm reduction in the European Union. In: European Monitoring Centre for Drugs and Drug Addiction. *Harm reduction: evidence, impacts and challenges*. Lisbon: EMCDDA; 2010.
42. Wodak A, Cooney A. Effectiveness of sterile needle and syringe programming in reducing HIV/AIDS among injecting drug users. Geneva: World Health Organization; 2004.
43. Arponen A, Brummer-Korvenkontio H, Liitsola K, Salminen M. Trust and free will as the keys to success for the low threshold service centers (LTHSC): An interdisciplinary evaluation study of the effectiveness of health promotion services for infectious disease prevention and control among injecting drug users. Helsinki: Finnish National Public Health Institute and Department of Infectious Disease Epidemiology and Control; 2008.
44. Kerr T, Hayashi K, Fairbairn N, Kaplan K, Suwannawong P, Zhang R, et al. Expanding the reach of harm reduction in Thailand: Experiences with a drug user-run drop-in centre. *Int J Drug Policy*. 2010 May;21(3):255-8. Epub 2009 Sep 18.
45. Trubnikov MN, Khodakevich LN, Barkov DA, Blagovo DV. Sources of injecting equipment for drug users in Moscow, Russia. *Int J Drug Policy*. 2003 Dec;14(5):453-55.
46. Voytek C, Sherman SG, Junge B. A matter of convenience: Factors influencing secondary syringe exchange in Baltimore, Maryland, USA. *Int J Drug Policy*. 2003 Dec;14(5):465-67.
47. Curth NK, Hansson LN, Storm F, Lazarus JV. Select barriers to harm-reduction services for IDUs in eastern Europe. *Cent Eur J Public Health*. 2009 Dec;17(4):191-7.
48. Irwin K, Karchevsky E, Heimer R, Badrieva L. Secondary syringe exchange as a model for HIV prevention programs in the Russian Federation. *Subst Use Misuse*. 2006;41(6-7):979-99.
49. Williams CT, Metzger DS. Race and distance effects on regular syringe exchange program use and injection risks: a geobehavioral analysis. *Am J Public Health*. 2010 Jun;100(6):1068-74.
50. Sarang A, Rhodes T, Platt L. Access to syringes in three Russian cities: implications for syringe distribution and coverage. *Int J Drug Policy*. 2008 Apr;19 Suppl 1:S25-36.
51. Gindi RM, Rucker MG, Serio-Chapman CE, Sherman SG. Utilization patterns and correlates of retention among clients of the needle exchange program in Baltimore, Maryland. *Drug Alcohol Depend*. 2009 Aug 1;103(3):93-8.
52. Strike CJ, Challacombe L, Myers T, Millson M. Needle exchange programs. Delivery and access issues. *Can J Public Health*. 2002 Sep-Oct;93(5):339-43.
53. WHO, UNODC, UNAIDS. Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users. Geneva: WHO; 2009.
54. European Monitoring Centre for Drugs and Drug Addiction. Annual Report 2010: The state of the drugs problem in Europe. Lisbon: EMCDDA; 2010.
55. Scottish Government. Guidelines for services providing injecting equipment: Best practice recommendations for commissioners and injecting equipment provision (IEP) services in Scotland. Edinburgh; 2010.
56. Vlahov D, Fuller CM, Ompad DC, Galea S, Des Jarlais DC. Updating the infection risk reduction hierarchy: preventing transition into injection. *Journal of Urban Health*. 2004;81(1):14-9.
57. Tyndall MW, Bruneau J, Brogly S, Spittal P, O'Shaughnessy MV, Schechter MT. Satellite needle distribution among injection drug users: policy and practice in two Canadian cities. *J Acquir Immune Defic Syndr*. 2002 Sep 1;31(1):98-105.
58. Latkin CA, Hua W, Davey MA, Sherman SG. Direct and indirect acquisition of syringes from syringe exchange programmes in Baltimore, Maryland, USA. *Int J Drug Policy*. 2003 Dec;14(5):449-51.
59. Latka MH, Hagan H, Kapadia F, Golub ET, Bonner S, Campbell JV, et al. A randomized intervention trial to reduce the lending of used injection equipment among injection drug users infected with hepatitis C. *Am J Public Health*. 2008 May;98(5):853-61.
60. Latkin CA. Outreach in natural settings: the use of peer leaders for HIV prevention among injecting drug users' networks. *Public Health Rep*. 1998 Jun;113 Suppl 1:151-9.
61. Aitken CK, Kerger M, Crofts N. Peer-delivered hepatitis C testing and counselling: a means of improving the health of injecting drug users. *Drug Alcohol Rev*. 2002;21(1):33-7.
62. Broadhead RS, Volkanevsky VL, Rydanova T, Ryabkova M, Borch C, van Hulst Y, et al. Peer-driven HIV interventions for drug injectors in Russia: First year impact results of a field experiment. *Int J Drug Policy*. 2006 Sep;17(5):379-92.

63. Garfein RS, Golub ET, Greenberg AE, Hagan H, Hanson DL, Hudson SM, et al. A peer-education intervention to reduce injection risk behaviors for HIV and hepatitis C virus infection in young injection drug users. *Aids*. 2007 Sep;21(14):1923-32.
64. Hunt N, Trace M, Bewley-Taylor D. Reducing drug related harms to health: An overview of the global evidence, Report 4. London: The Beckley Foundation; 2005.
65. Southwell M. People who use drugs and their role in harm reduction. In: Rhodes T, Hedrich D, editors. *Harm reduction: evidence, impacts and challenges*. Lisbon: EMCDDA; 2010.
66. Keane H. Critiques of harm reduction, morality, and the promise of human rights. *Int J Drug Policy*. 2003;14(3):227-32.
67. National Treatment Agency for Substance Misuse. *Engaging and retaining clients in drug treatment*. London: National Treatment Agency for Substance Misuse; 2004.
68. WHO, UNODC, UNAIDS. *Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention*. Geneva: WHO; 2004.
69. Strike C, Leonard L, Millson M, Anstice S, Berkeley N, Medd E. *Ontario needle exchange programs: Best practice recommendations*. Toronto; 2006.
70. Turner K, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. *Addiction*. 2011 May 25.
71. Van Den Berg C, Smit C, Van Brussel G, Coutinho R, Prins M. Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and hepatitis C virus: evidence from the Amsterdam Cohort Studies among drug users. *Addiction*. 2007 Sep;102(9):1454-62.
72. Hagan H, Pouget ER, Des Jarlais DC. A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs. *J Infect Dis*. 2011 Jul;204(1):74-83.
73. Wood E. Summary of findings from the evaluation of a pilot medically supervised safer injecting facility. *Canadian Medical Association Journal*. 2006;175(11):1399-404.
74. Crofts N, Nigro L, Oman K, Stevenson E, Sherman J. Methadone maintenance and hepatitis C virus infection among injecting drug users. *Addiction*. 1997;92(8):999-1005.
75. Hagan H, Thiede H, Weiss NS, Hopkins SG, Duchin JS, Alexander ER. Sharing of drug preparation equipment as a risk factor for hepatitis C. *Am J Public Health*. 2001 Jan;91(1):42-6.
76. Hind CR. Pulmonary complications of intravenous drug misuse. 1. Epidemiology and non-infective complications. *Thorax*. 1990 Nov;45(11):891-8.
77. Del Giudice P. Cutaneous complications of intravenous drug abuse. *Br J Dermatol*. 2004 Jan;150(1):1-10.
78. Roux P, Carrieri MP, Keijzer L, Dasgupta N. Reducing harm from injecting pharmaceutical tablet or capsule material by injecting drug users. *Drug Alcohol Rev*. 2011 May;30(3):287-90.
79. Gallo J, Playfair J, Gregory-Roberts J, Grunstein H, Clifton-Bligh P, Billson F. Fungal endophthalmitis in narcotic abusers. Medical and surgical therapy in 10 patients. *Med J Aust*. 1985 Apr 1;142(7):386-8.
80. US Center for Disease Control and Prevention. *Guide to Infection Prevention in Outpatient Settings: Minimum Expectations for Safe Care*. CDC: Atlanta; 2011.
81. Kimber J, Palmateer N, Hutchinson S, Hickman M, Goldberg D, Rhodes T. Harm reduction among injecting drug users: evidence of effectiveness. In: Rhodes T, Hedrich D, editors. *Harm reduction: Evidence, impacts, challenges*. Lisbon: EMCDDA; 2010.
82. 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 May;105(5):844-59.
83. De P, Roy E, Boivin JF, Cox J, Morissette C. Risk of hepatitis C virus transmission through drug preparation equipment: a systematic and methodological review. *J Viral Hepat*. 2008 Apr;15(4):279-92.
84. Crofts N, Caruana S, Bowden S, Kerger M. Minimising harm from hepatitis C virus needs better strategies. *BMJ*. 2000 Oct 7;321(7265):899.
85. Thorpe LE, Ouellet LJ, Hershov R, Bailey SL, Williams IT, Williamson J, et al. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. *Am J Epidemiol*. 2002 Apr 1;155(7):645-53.
86. Morissette C, Cox J, De P, Tremblay C, Roy E, Allard R, et al. Minimal uptake of sterile drug preparation equipment in a predominantly cocaine injecting population: implications for HIV and hepatitis C prevention. *Int J Drug Policy*. 2007 May;18(3):204-12.
87. Ouellet L, Huo D, Bailey SL. HIV risk practices among needle exchange users and nonusers in Chicago. *J Acquir Immune Defic Syndr*. 2004 Sep 1;37(1):1187-96.
88. Longshore D, Bluthenthal RN, Stein MD. Needle exchange program attendance and injection risk in Providence, Rhode Island. *AIDS Educ Prev*. 2001 Feb;13(1):78-90.
89. Matheson C, Anthony GB, Bond C, Rossi MK. Assessing and prioritizing the preferences of injecting drug users in needle and syringe exchange service development. *J Public Health (Oxf)*. 2008 Jun;30(2):133-8.
90. Garden J, Roberts K, Taylor A, Robinson D. Evaluation of the provision of single use citric acid sachets to injecting drug users Glasgow. NHS Greater Glasgow, Scottish Centre for Infection and Environmental Health and NHS Lanarkshire; 2003.
91. Advisory Council on the Misuse of Drugs. *Consideration of the use of foil, as an intervention, to reduce the harms of injecting heroin*. London: Advisory Council on the Misuse of Drugs; 2010.
92. Mravcik V, Skarupova K, Orlikova B, Zabransky T, Karachaliou K, Schulte B. Use of gelatine capsules for application of methamphetamine: a new harm reduction approach. *Int J Drug Policy*. 2011 Mar;22(2):172-3.

93. Abdala N, Crowe M, Tolstov Y, Heimer R. Survival of human immunodeficiency virus type 1 after rinsing injection syringes with different cleaning solutions. *Substance Use & Misuse*. 2004;39(4):581-600.
94. Baral S, Sherman SG, Millson P, Beyrer C. Vaccine immunogenicity in injecting drug users: a systematic review. *Lancet Infect Dis*. 2007 Oct;7(10):667-74.
95. Mereckiene J, Cotter S, Lopalco P, D'Ancona F, Levy-Bruhl D, Giambi C, et al. Hepatitis B immunisation programmes in European Union, Norway and Iceland: where we were in 2009? *Vaccine*. 2010 Jun 17;28(28):4470-7. Epub 2010 May 6.
96. Stancliff S, Salomon N, Perlman DC, Russell PC. Provision of influenza and pneumococcal vaccines to injection drug users at a syringe exchange. *J Subst Abuse Treat*. 2000 Apr;18(3):263-5.
97. Hu Y, Grau LE, Scott G, Seal KH, Marshall PA, Singer M, et al. Economic evaluation of delivering hepatitis B vaccine to injection drug users. *Am J Prev Med*. 2008 Jul;35(1):25-32.
98. Stitzer ML, Polk T, Bowles S, Kosten T. Drug users' adherence to a 6-month vaccination protocol: effects of motivational incentives. *Drug Alcohol Depend*. 2010 Feb 1;107(1):76-9.
99. Szmunes W, Stevens CE, Harley EJ, Zang EA, Taylor PE, Alter HJ. The immune response of healthy adults to a reduced dose of hepatitis B vaccine. *J Med Virol*. 1981;8(2):123-9.
100. Topp L, Day C, Dore GJ, Maher L. Poor criterion validity of self-reported hepatitis B infection and vaccination status among injecting drug users: a review. *Drug Alcohol Rev*. 2009 Nov;28(6):669-75.
101. Quaglio G, Talamini G, Lugoboni F, Lechi A, Venturini L, Jarlais DC, et al. Compliance with hepatitis B vaccination in 1175 heroin users and risk factors associated with lack of vaccine response. *Addiction*. 2002 Aug;97(8):985-92.
102. Ambrosch F, Wiedermann G, Andre FE, Delem A, Gregor H, Hofmann H, et al. Clinical and immunological investigation of a new combined hepatitis A and hepatitis B vaccine. *J Med Virol*. 1994 Dec;44(4):452-6.
103. Perrett K, Granerod J, Crowcroft N, Carlisle R. Changing epidemiology of hepatitis A: should we be doing more to vaccinate injecting drug users? *Commun Dis Public Health*. 2003 Jun;6(2):97-100.
104. BCG vaccine. WHO position paper. *Wkly Epidemiol Rec*. 2004 Jan 23;79(4):27-38.
105. Council of Europe. Council recommendation on the prevention and reduction of health-related harm associated with drug dependence. *Official Journal of the European Union*. 2003;OJ L165(03/07/2003):31-3.
106. Commission of the European Communities. Report from the Commission to the European Parliament and the Council on the implementation of the Council Recommendation of 18 June 2003 on the prevention and reduction of health-related harm associated with drug dependence. Brussels; 2007.
107. Malta M, Strathdee SA, Magnanini MM, Bastos FI. Adherence to antiretroviral therapy for human immunodeficiency virus/acquired immune deficiency syndrome among drug users: a systematic review. *Addiction*. 2008 Aug;103(8):1242-57.
108. Tilson H, Aramrattana A, Bozzette SA, Celentano DD, Falco M, Hammett TM, et al. Preventing HIV infection among injecting drug users in high-risk countries: an assessment of the evidence. Washington: Institute of Medicine; 2007.
109. Farrell M, Gowing L, Marsden J, Ling W, Ali R. Effectiveness of drug dependence treatment in HIV prevention. *Int J Drug Policy*. 2005;16(Suppl. 1):S67-S75.
110. Mattick RP, Kimber J, Breen C, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*. 2008(2):CD002207.
111. WHO. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. WHO: Geneva; 2009.
112. European Monitoring Centre for Drugs and Drug Addiction. *Statistical Bulletin*. EMCDDA: Lisbon; 2011 [cited 5 August 2011]. Available from: <http://www.emcdda.europa.eu/stats11>.
113. Degenhardt L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed. *Lancet*. 2010 Jul 24;376(9737):285-301.
114. Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De AD, et al. Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. *BMJ*. 2010;341:c3172.
115. Sorensen JL, Copeland AL. Drug abuse treatment as an HIV prevention strategy: a review. *Drug Alcohol Depend*. 2000 Apr 1;59(1):17-31.
116. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treat*. 2005;28(4):321-9.
117. Wright NMJ, Tompkins CNE. A review of the evidence for the effectiveness of primary prevention interventions for Hepatitis C among injecting drug users. *Harm Reduct J*. 2006;3.
118. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database Syst Rev*. 2011(8):CD004145.
119. Craine N, Hickman M, Parry JV, Smith J, Walker AM, Russell D, et al. Incidence of hepatitis C in drug injectors: the role of homelessness, opiate substitution treatment, equipment sharing, and community size. *Epidemiol Infect*. 2009;137(9):1255-65.
120. Hallinan R, Byrne A, Dore GJ. Harm reduction, hepatitis C and opioid pharmacotherapy: An opportunity for integrated hepatitis C virus-specific harm reduction. *Drug Alcohol Rev*. 2007 Jul;26(4):437-43.
121. Miller CL, Wood E, Spittal PM, Li K, Frankish JC, Braitstein P, et al. The future face of coinfection: prevalence and incidence of HIV and hepatitis C virus coinfection among young injection drug users. *J Acquir Immune Defic Syndr*. 2004;36(2):743-9.
122. European Monitoring Centre for Drugs and Drug Addiction. Heroin-assisted treatment. Lisbon: EMCDDA; 2011 (in press).

123. Amato L, Minozzi S, Davoli M, Vecchi S, Ferri MM, Mayet S. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *Cochrane Database Syst Rev.* 2008(4):CD005031.
124. Abou-Saleh M, Davis P, Rice P, Checinski K, Drummond C, Maxwell D, et al. The effectiveness of behavioural interventions in the primary prevention of hepatitis C amongst injecting drug users: a randomised controlled trial and lessons learned. *Harm Reduct J.* 2008;5:25.
125. Des Jarlais DC, Arasteh K, McKnight C, Hagan H, Perlman DC, Torian LV, et al. HIV infection during limited versus combined HIV prevention programs for IDUs in New York City: The importance of transmission behaviors. *Drug Alcohol Depend.* 2010 Jun 1;109(1-3):154-60. Epub 2010 Feb 16.
126. Knapp WP, Soares BG, Farrel M, Lima MS. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. *Cochrane Database Syst Rev.* 2007(3):CD003023.
127. Hedrich D, Pirona A, Wiessing L. From margin to mainstream: The evolution of harm reduction responses to problem drug use in Europe. *Drugs Educ Prev Pol.* 2008;15(6):503-17.
128. European Monitoring Centre for Drugs and Drug Addiction. Figure HSR-1. Opioid substitution treatment clients as a percentage of the estimated number of problem opioid users, 2009 or most recent year available. Lisbon: EMCDDA; 2011.
129. European Monitoring Centre for Drugs and Drug Addiction. EMCDDA best practice portal. Lisbon: EMCDDA; 2011 [cited 4 August 2011]. Available from: <http://www.emcdda.europa.eu/best-practice>.
130. Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opioid dependence. *Cochrane Database Syst Rev.* 2003(3):CD002208.
131. International Union against Tuberculosis and Lung Disease. Management of tuberculosis: a guide to the essentials of good clinical practice. 6th edition. 2010.
132. Wilson ME, Schwartz RP, O'Grady KE, Jaffe JH. Impact of interim methadone maintenance on HIV risk behaviors. *Journal of Urban Health.* 2010;87(4):586-91.
133. Dijkgraaf MG, van der Zanden BP, de Borgie CA, Blanken P, van Ree JM, van den Brink W. Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *BMJ.* 2005 Jun 4;330(7503):1297.
134. Dolan K, Wodak A. An international review of methadone provision in prisons. *Addiction Research* 1996;4:85-97.
135. Stallwitz A, Stover H. The impact of substitution treatment in prisons – a literature review. *Int J Drug Policy.* 2007;18(6):464-74.
136. Jurgens R, Ball A, Verster A. Interventions to reduce HIV transmission related to injecting drug use in prison. *Lancet Infect Dis.* 2009 Jan;9(1):57-66.
137. European Centre for Disease Prevention and Control. Implementing the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2010 progress report. Stockholm: ECDC; 2010.
138. European Centre for Disease Prevention and Control. HIV testing: increasing uptake and effectiveness in the European Union. Stockholm: ECDC; 2010.
139. McCoy CB, De Gruttola V, Metsch L, Comerford M. A comparison of the efficacy of two interventions to reduce HIV risk behaviors among drug users. *AIDS Behav.* 2011 Jun 17.
140. WHO. Treatment of tuberculosis guidelines. Geneva: World Health Organization; 2010.
141. Blumberg HM, Burman WJ, Chaisson RE, Daley CL, Etkind SC, Friedman LN, et al. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: treatment of tuberculosis. *Am J Respir Crit Care Med.* 2003 Feb 15;167(4):603-62.
142. Deiss RG, Rodwell TC, Garfein RS. Tuberculosis and illicit drug use: review and update. *Clin Infect Dis.* 2009 Jan 1;48(1):72-82.
143. Perlman DC, Salomon N, Perkins MP, Yancovitz S, Paone D, Des Jarlais DC. Tuberculosis in drug users. *Clin Infect Dis.* 1995 Nov;21(5):1253-64.
144. European Centre for Disease Prevention and Control. Use of interferon-gamma release assays in support of TB diagnosis. Stockholm: ECDC; 2011.
145. Rose DN. Benefits of screening for latent Mycobacterium tuberculosis infection. *Arch Intern Med.* 2000 May 22;160(10):1513-21.
146. WHO, UNAIDS. Guidance on provider-initiated HIV testing and counselling in health facilities. WHO: Geneva; 2007.
147. European Association for the Study of the Liver (EASL). EASL clinical practice guidelines: management of chronic hepatitis B. *J Hepatol.* 2009 Feb;50(2):227-42.
148. European Association for the Study of the Liver (EASL). EASL clinical practice guidelines: management of hepatitis C virus infection. *J Hepatol.* 2011 Feb 28.
149. Werb D, Mills EJ, Montaner JS, Wood E. Risk of resistance to highly active antiretroviral therapy among HIV-positive injecting drug users: a meta-analysis. *Lancet Infect Dis.* 2010 Jul;10(7):464-9.
150. Lindenburg CE, Lambers FA, Urbanus AT, Schinkel J, Jansen PL, Krol A, et al. Hepatitis C testing and treatment among active drug users in Amsterdam: results from the DUTCH-C project. *Eur J Gastroenterol Hepatol.* 2011 Jan;23(1):23-31.
151. Novick DM, Kreek MJ. Critical issues in the treatment of hepatitis C virus infection in methadone maintenance patients. *Addiction.* 2008 Jun;103(6):905-18.
152. Litwin AH, Harris KA, Jr., Nahvi S, Zamor PJ, Soloway IJ, Tenore PL, et al. Successful treatment of chronic hepatitis C with pegylated interferon in combination with ribavirin in a methadone maintenance treatment program. *J Subst Abuse Treat.* 2009 Jul;37(1):32-40.
153. Treloar C, Rhodes T. The lived experience of hepatitis C and its treatment among injecting drug users: qualitative synthesis. *Qual Health Res.* 2009 Sep;19(9):1321-34.

154. Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility. *J Hepatol.* 2011 Jun;54(6):1137-44.
155. WHO. Interim policy on collaborative TB/HIV activities. Geneva: WHO; 2004.
156. WHO, UNODC, UNAIDS. Policy guidelines for collaborative TB and HIV services for injecting and other drug users, an integrated approach. Geneva: WHO; 2008.
157. Tuberculosis Coalition for Technical Assistance. International standards for tuberculosis care (ISTC). The Hague; 2009.
158. WHO. Effectiveness of community-based outreach in preventing HIV/AIDS among injecting drug users. WHO: Geneva; 2004.
159. Degenhardt L, Bucello C, Mathers B, Briegleb C, Ali H, Hickman M, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction.* 2011 Jan;106(1):32-51.
160. Strang J, Manning V, Mayet S, Best D, Titherington E, Santana L, et al. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction.* 2008 Oct;103(10):1648-57.
161. Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet.* 2011 Apr 23;377(9775):1429-37.
162. Jenness SM, Kobrak P, Wendel T, Neaigus A, Murrill CS, Hagan H. Patterns of exchange sex and HIV infection in high-risk heterosexual men and women. *J Urban Health.* 2011 Apr;88(2):329-41.
163. Ward H, Pallearos A, Green A, Day S. Health issues associated with increasing use of 'crack' cocaine among female sex workers in London. *Sex Transm Infect.* 2000 Aug;76(4):292-3.
164. Salomon N, Perlman DC, Friedmann P, Buchstein S, Kreiswirth BN, Mildvan D. Predictors and outcome of multidrug-resistant tuberculosis. *Clin Infect Dis.* 1995 Nov;21(5):1245-52.
165. Leaver CA, Bargh G, Dunn JR, Hwang SW. The effects of housing status on health-related outcomes in people living with HIV: a systematic review of the literature. *AIDS Behav.* 2007 Nov;11(6 Suppl):85-100.
166. Islam MM, Grummett S, White A, Reid SE, Day CA, Haber PS. A primary healthcare clinic in a needle syringe program may contribute to HIV prevention by early detection of incident HIV in an injecting drug user. *Aust N Z J Public Health.* 2011 Jun;35(3):294-5.
167. Day CA, Islam MM, White A, Reid SE, Hayes S, Haber PS. Development of a nurse-led primary healthcare service for injecting drug users in inner-city Sydney. *Aust J Prim Health.* 2011;17(1):10-5.
168. Correlation Network. Outreach work among marginalized populations in Europe: Guidelines on providing integrated outreach services. Amsterdam; 2007.
169. Cattani M, Bagnall A-M, Akhionbare K, Burrell K. Injecting equipment schemes for injecting drug users – qualitative evidence review. London: National Institute for Health and Clinical Excellence (NICE); 2008.
170. Balian R, White C. Harm reduction at work: A guide for organisations employing people who use drugs. New York: Open Society Foundations; 2010.
171. Islam MM, Conigrave KM. Assessing the role of syringe dispensing machines and mobile van outlets in reaching hard-to-reach and high-risk groups of injecting drug users (IDUs): a review. *Harm Reduct J.* 2007;4:14.
172. Ruutel K, Loit HM, Sepp T, Kliiman K, McNutt LA, Uuskula A. Enhanced tuberculosis case detection among substitution treatment patients: a randomized controlled trial. *BMC Res Notes.* 2011 Jun 15;4(1):192.
173. Strauss SM, Mino M. Addressing the HIV-related needs of substance misusers in New York State: the benefits and barriers to implementing a 'one-stop shopping' model. *Subst Use Misuse.* 2011;46(2-3):171-80.
174. Grebely J, Genoway K, Khara M, Duncan F, Viljoen M, Elliott D, et al. Treatment uptake and outcomes among current and former injection drug users receiving directly observed therapy within a multidisciplinary group model for the treatment of hepatitis C virus infection. *Int J Drug Policy.* 2007 Oct;18(5):437-43.
175. UNODC. Annual Report 2009. Geneva: United Nations Office on Drugs and Crime; 2009.
176. European Monitoring Centre for Drugs and Drug Addiction. Reitox Network Lisbon: EMCDDA; 2011 [cited 5 August 2011]. Available from: <http://www.emcdda.europa.eu/about/partners/reitox-network>.
177. Hope V, Jeannin A, Spencer B, Gervasoni JP, van de Laar M, Dubois-Arber F, et al. Mapping HIV-related behavioural surveillance among injecting drug users in Europe, 2008. *Euro Surveill.* 2011;16(36).
178. European Centre for Disease Prevention and Control. Mapping of HIV/STI behavioural surveillance in Europe. Stockholm: ECDC; 2009.
179. Wiessing L, Denis B, Guttormsson U, Haas S, Hamouda O, Hariga F, et al. Estimating coverage of harm reduction measures for injection drug users in the European Union. In: Proceedings of the third annual Global Research Network meeting on HIV prevention in drug-using populations, 5–7 July 2000. Durban: National Institute on Drug Abuse; National Institutes of Health; US Department of Health and Human Services; 2011.
180. Mathers BM, Degenhardt L, Ali H, Wiessing L, Hickman M, Mattick RP, et al. HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. *Lancet.* 2010 Mar 20;375(9719):1014-28.
181. Bluthenthal RN, Anderson R, Flynn NM, Kral AH. Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients. *Drug Alcohol Depend.* 2007 Jul 10;89(2-3):214-22.
182. Wiessing L, Likatavicius G, Klempova D, Hedrich D, Nardone A, Griffiths P. Associations between availability and coverage of HIV-prevention measures and subsequent incidence of diagnosed HIV infection among injection drug users. *American Journal of Public Health.* 2009;99(6):1049-52.

183. European Monitoring Centre for Drugs and Drug Addiction. Figure HSR-3. Syringes distributed through specialised programmes per estimated IDU in 2009 or more recent year. Lisbon: EMCDDA; 2011.
184. Paraskevis D, Nikolopoulos G, Tsiara C, Paraskeva D, Antoniadou A, Lazanas M, et al. HIV-1 outbreak among injecting drug users in Greece, 2011: a preliminary report. *Euro Surveill.* 2011;16(36).
185. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *N Engl J Med.* 1989 Mar 2;320(9):545-50.
186. Pimpin L, Drumright LN, Kruijshaar ME, Abubakar I, Rice B, Delpech V, et al. TB-HIV co-infection in EU and EEA countries. *Eur Respir J.* 2011 Jul 7.
187. European Centre for Disease Prevention and Control, WHO Regional Office for Europe. Tuberculosis surveillance in Europe 2009. Stockholm: ECDC; 2011.
188. Lloyd-Smith E, Hull MW, Tyndall MW, Zhang R, Wood E, Montaner JS, et al. Community-associated methicillin-resistant *Staphylococcus aureus* is prevalent in wounds of community-based injection drug users. *Epidemiol Infect.* 2010 May;138(5):713-20.
189. Cooke FJ, Gkrania-Klotsas E, Howard JC, Stone M, Kearns AM, Ganner M, et al. Clinical, molecular and epidemiological description of a cluster of community-associated methicillin-resistant *Staphylococcus aureus* isolates from injecting drug users with bacteraemia. *Clin Microbiol Infect.* 2010 Jul;16(7):921-6.
190. Fah F, Zimmerli W, Jordi M, Schoenenberger RA. Septic deep venous thrombosis in intravenous drug users. *Swiss Med Wkly.* 2002 Jul 13;132(27-28):386-92.
191. Lamagni TL, Neal S, Keshishian C, Hope V, George R, Duckworth G, et al. Epidemic of severe *Streptococcus pyogenes* infections in injecting drug users in the UK, 2003-2004. *Clin Microbiol Infect.* 2008 Nov;14(11):1002-9.
192. Efstratiou A, Emery M, Lamagni TL, Tanna A, Warner M, George RC. Increasing incidence of group A streptococcal infections amongst injecting drug users in England and Wales. *J Med Microbiol.* 2003 Jun;52(Pt 6):525-6.
193. Akbulut D, Dennis J, Gent M, Grant KA, Hope V, Ohai C, et al. Wound botulism in injectors of drugs: upsurge in cases in England during 2004. *Euro Surveill.* 2005 Sep;10(9):172-4.
194. Jones JA, Salmon JE, Djuretic T, Nichols G, George RC, Gill ON, et al. An outbreak of serious illness and death among injecting drug users in England during 2000. *J Med Microbiol.* 2002 Nov;51(11):978-84.
195. Giuliani M, Rezza G, Lepri AC, Di Carlo A, Maini A, Crescimbeni E, et al. Risk factors for HTLV-I and II in individuals attending a clinic for sexually transmitted diseases. *Sex Transm Dis.* 2000 Feb;27(2):87-92.
196. Giacomo M, Franco EG, Claudio C, Carlo C, Anna DA, Anna D, et al. Human T-cell leukemia virus type II infection among high risk groups and its influence on HIV-1 disease progression. *Eur J Epidemiol.* 1995 Oct;11(5):527-33.
197. Henrard DR, Soriano V, Robertson E, Gutierrez M, Stephens J, Dronda F, et al. Prevalence of human T-cell lymphotropic virus type 1 (HTLV-1) and HTLV-2 infection among Spanish drug users measured by HTLV-1 assay and HTLV-1 and -2 assay. HTLV-1 and HTLV-2 Spanish Study Group. *J Clin Microbiol.* 1995 Jul;33(7):1735-8.
198. Krook A, Albert J, Andersson S, Biberfeld G, Blomberg J, Eklund I, et al. Prevalence and risk factors for HTLV-II infection in 913 injecting drug users in Stockholm, 1994. *J Acquir Immune Defic Syndr Hum Retrovirol.* 1997 Aug 15;15(5):381-6.
199. Vignoli C, Zandotti C, De Lamballerie X, Tamalet C, Gastaut JA, De Micco P. Prevalence of HTLV-II in HIV-1-infected drug addicts in Marseille. *Eur J Epidemiol.* 1993 May;9(3):351-2.
200. Egan JF, O'Leary B, Lewis MJ, Mulcahy F, Sheehy N, Hasegawa H, et al. High rate of human T lymphotropic virus type IIa infection in HIV type 1-infected intravenous drug abusers in Ireland. *AIDS Res Hum Retroviruses.* 1999 May 20;15(8):699-705.
201. Kelly M, Swann C, Killoran A, Naidoo B, Barnett-Page E, Morgan A. Methodological problems in constructing the evidence base in public health. London: Health Development Agency; 2002.