

Report on the current state of play of the 2003 Council Recommendation on the prevention and reduction of health-related harm, associated with drug dependence, in the EU and candidate countries

Final Report – Annex 2: Systematic Literature Reviews – part of Deliverable 2

On behalf of the European Commission



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This report was produced under the Health Programme (2008–13) in the frame of a contract with the Executive Agency for Health and Consumers (EAHC) acting on behalf of the European Commission. The content of this report represents the views of Sogeti and Gesundheit Österreich Forschungs- und Planungs GmbH and is their sole responsibility; it can in no way be taken to reflect the views of the European Commission and/or EAHC or any other body of the European Union. The European Commission and/or EAHC do not guarantee the accuracy of the data included in this report, nor do they accept responsibility for any use made by third parties thereof.



Vienna, April 2013
On behalf of the European Commission

ZI. FP/4170

Environmentally friendly publication:

The present report has been printed on paper bleached without chlorine and without optical brighteners.

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Introduction

Concerning the prevention of drug related infectious diseases, good quality literature reviews are available (see general literature review). Due to this fact, the research questions for the systematic literature reviews at hand focus on the prevention of drug-induced deaths. Another issue, which is neither covered by the predecessor report nor by the systematic literature reviews on prevention of infectious diseases, is the topic of route of administration. It is relevant regarding the risk of infection as well as the risk for drug-induced death. A third focus of the systematic literature review is the prison setting.

For the systematic literature reviews the following questions were defined:

- » Are peer programmes with naloxone distribution for opioid users (in combination with first aid training) effective in reducing the numbers of drug-induced deaths?
- » How effective are prison release management programmes among opioid users in reducing the number of drug-induced deaths?
- » Is it possible to reduce human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) infections of opioid users by providing needle exchange programmes (NSPs) in prisons?
- » Which interventions focus on the route of administration (e. g. avoid shifting to injecting drug use (IDU) from other routes or promote shifting from IDU to other routes of administration)?
How successful are these programmes concerning the reduction of drug-induced deaths?

1 Definition of PICO–Questions

For the concrete definition of the questions, the PICO scheme was used for all four research questions.

Are peer programmes with naloxone distribution for opioid users (in combination with first aid training) effective in reducing the numbers of drug-induced deaths?

Table 1.1:
PICO–scheme for systematic literature review 1

PICO		
P	Population	opioid users
I	Intervention	peer programmes with naloxone distribution (in combination with first aid training)
C	Comparison	first aid training only
O	Outcome	reduction of drug-induced deaths (deaths due to overdoses)
S	Study type	studies with control group

Source: GÖG–own presentation

How effective are prison release management programmes among opioid users in reducing the number of drug-induced deaths?

Table 1.2:
PICO–scheme for systematic literature review 2

PICO		
P	Population	opioid users in prison / after prison
I	Intervention	prison release management programmes
C	Comparison	no control group required
O	Outcome	» reduction of drug-induced deaths (deaths due to overdoses) » non fatal overdoses
S	Study type	all studies

Source: GÖG–own presentation

Is it possible to reduce HIV, hepatitis B and hepatitis C infections of opioid users by providing needle exchange programmes in prisons?

Table 1.3:
PICO-scheme for systematic literature review 3

PICO		
P	Population	opioid users in prison
I	Intervention	needle exchange / needle distribution programmes in prison
C	Comparison	no needle exchange programmes in prison
O	Outcome	primary outcomes: <ul style="list-style-type: none"> » reduction of HIV infections » reduction of hepatitis B infections » reduction of hepatitis C infections secondary outcome: <ul style="list-style-type: none"> » reduction of reported needle sharing
S	Study type	studies with control group, studies based on statistical modelling

Source: GÖG-own presentation

Which interventions focus on the route of administration of opioids (e. g. avoid shifting to IDU from other routes or promoting shifting from IDU to other routes of administration)? How successful are these programmes concerning the reduction of drug-induced deaths (deaths due to overdoses)?

Table 1.4:
PICO-scheme for systematic literature review 4

PICO		
P	Population	opioid users
I	Intervention	interventions focusing on changing the route of administration (e. g. avoid shifting to injecting drug use (IDU) from other routes or promoting shifting from IDU to other routes of administration)
C	Comparison	no control group required
O	Outcome	<ul style="list-style-type: none"> » reduction of drug-induced deaths (deaths due to overdoses) » change of administration route from intravenous to sniffing/smoking » avoid change from sniffing/smoking to intravenous
S	Study type	all studies

Source: GÖG-own presentation

2 Review on naloxone distribution

Are peer programmes with naloxone distribution for opioid users (in combination with first aid training) effective in reducing the numbers of drug-induced deaths?

2.1 Background

Epidemiological background: The average number of drug-induced deaths („overdoses“) in the EU is about 20 deaths per million (population aged 15–64 years). Most of those are caused by the intake of opioids (e. g. heroin, methadone) (EMCDDA 2012a). Most overdoses occur in the presence of other persons and most injecting drug users (IDUs) have witnessed or experienced overdoses (Bennett et al. 2011; Darke/Hall 1997; Maxwell et al. 2006; Strang et al. 1999a). Naloxone was available in 2007 on a “take-home” basis in Italy, Germany, Spain, Lithuania and Norway (Kimber et al. 2010). Pilot studies in the UK, Scotland (McAuley et al. 2012) and Wales (Bennett/Holloway 2012) have started since then (Advisory Council on the Misuse of Drugs 2012). In Scotland, the provision of “take-home-naloxone” to all at-risk individuals leaving prison was introduced nationally in 2010. Furthermore, the government is supporting a national “take-home” naloxone programme for those deemed to be at risk of opioid overdose and those who may come into contact with these persons (EMCDDA 2012a). No evidence could be found concerning the programmes in Lithuania, Norway and Italy (Advisory Council on the Misuse of Drugs 2012). New initiatives are reported by Bulgaria, Denmark and Portugal (EMCDDA 2012a).

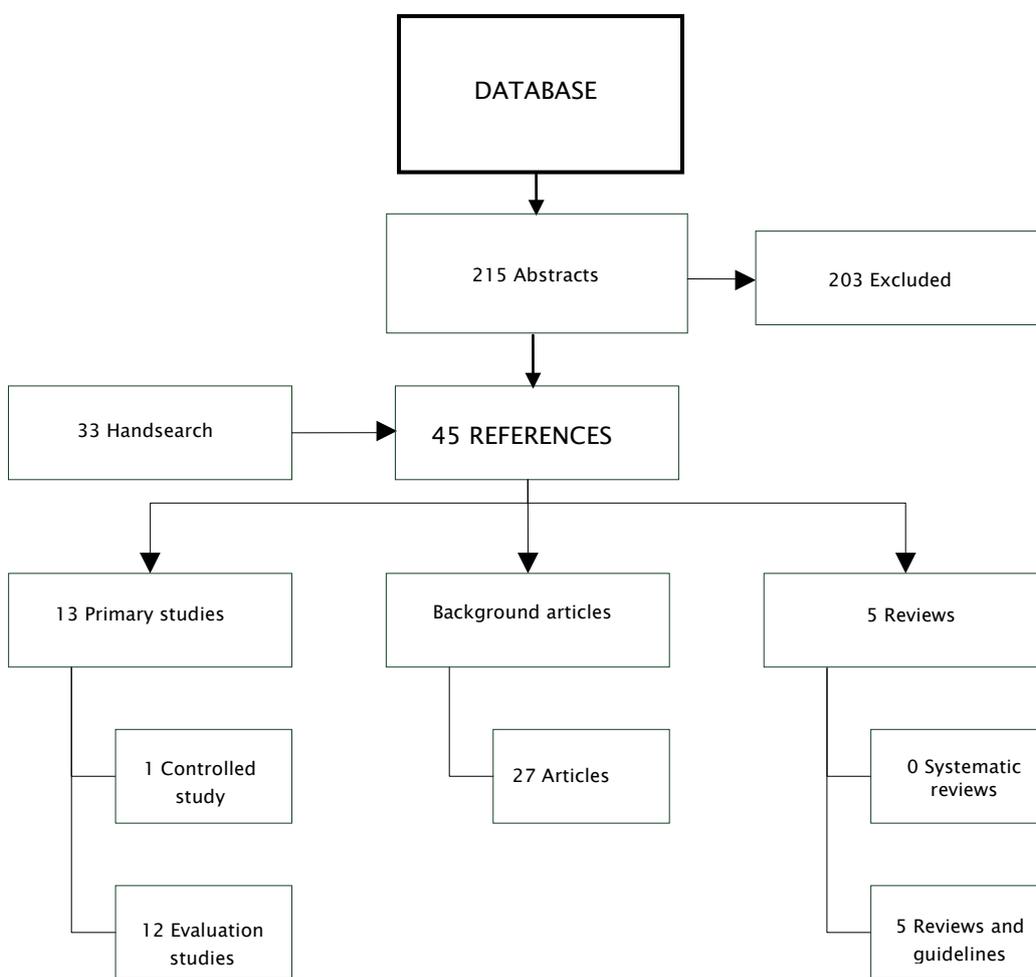
Medical background: Naloxone is a non-selective opioid-antagonist which can be administered intravenous, intramuscularly or subcutaneously (Baca/Grant 2005). The intranasal treatment of opioid overdoses in pre-hospital settings by paramedics is found to be effective (Kerr et al. 2009), but is not studied for peer administration and the evidence for its effectiveness is lacking (Advisory Council on the Misuse of Drugs 2012). Naloxone is readily transported across the blood-brain barrier and therefore quickly reverses the opioid effects (e. g. respiratory depression). The onset of the reverse effects depends on the opioid agonist. The reversal of morphine-induced symptoms can be reached within several minutes. The administration of naloxone to other opioid agonists such as buprenorphine differs and for naloxone other routes of administration (i. e. infusion) are recommended.

As naloxone rapidly (but temporarily) inhibits the effects of opioids, it can induce severe withdrawal syndromes when applied to opioid-dependants such as vomiting. It is important to note that naloxone has a short half-life from around 60 to 90 minutes

whereas most opioids have longer half-lives (Advisory Council on the Misuse of Drugs 2012; Darke/Hall 1997). Therefore it is vital to monitor the patient after administering naloxone as the symptoms of the overdose may return.

2.2 Methods

Figure 2.1:
Identification and selection of articles for peer-naloxone programmes



Source: GÖG-own presentation

A systematic literature search was performed in Medline, Eric, Psycinfo, Embase and the Cochrane Library with predefined keywords (for details see search strategy in

section 6). To identify relevant publications, two keyword-clusters were connected, one with terms related to peer programmes and self-administration, the other with terms related to naloxone. The selection of abstracts and full-text versions was performed according to predefined selection criteria (see below). To determine the quality of the studies, internal validity (risk for biases) and external validity (application of study-results for people beyond the study-populations) were evaluated, both with predefined criteria (see Table 2.2) (Fröschl et al. 2012). The contents of primary studies are displayed in table format.

For the 215 identified abstracts, the exclusion criteria were: studies not published in English or German, studies not carried out in a European or comparable (US, Canada, New Zealand, Australia) country, other research question, other study population (e. g. training for healthcare professionals), other study design (case studies). All types of studies were included (randomised control trials (RCT), cohort studies, systematic literature review, health technology assessments (HTAs) and meta-analysis).

2.3 Results

On the basis of the systematic literature research in the databases, 215 abstracts were identified. After the selection of abstracts according to the predefined selection criteria 13, full-text articles were retrieved. Most articles were excluded due to other research questions. 33 publications were added by hand search. After the selection of full-text articles, one primary study with a control group, twelve articles of non-controlled studies and 5 reviews were included in the analysis. In addition, 27 articles for background description (Chapter 2.1) were also included.

2.3.1 Primary studies and systematic reviews

One quasi experimental controlled cohort study was identified regarding the “take-home” naloxone programme in Wales. The outcomes were changes of knowledge in the treatment group and the self-reported management of overdose events compared to the control group. No objective outcome measure (e. g. mortality rates) is reported in the study and the article does therefore not provide information on the outcomes stated in the PICO (Table 1.1). The control group consisted of 50 clients entering drug treatment services who were asked about their last overdose events and the results were compared to the self-reported overdose events at the follow-up of the treatment group.

However, since this is the only controlled study available, the results and data quality are presented and discussed in table format (“data extraction”).

Table 2.1:
Data extraction controlled studies

Title	The impact of "take-home" naloxone distribution and training on opiate overdose knowledge and response
Research question	Evaluate the effectiveness of the "take-home" naloxone programme in Wales
Author	Bennett, T.; Holloway, K.
Country, Year	Wales, 2012
Study design	Controlled study with repeated-measures
Time to follow-up	Unclear, follow-up up to six months after training
Study population size	Treatment Group: 521 opiate users and 4 non-opiate users at 5 community sites and 3 prisons Control Group: 50 drug service users
Selection criteria of study population	Volunteer participation of injecting drug users, Control Group: comparison area of injecting drug users where no naloxone training was available
Setting	Treatment agencies
Intervention	Training in recognition of opiate overdose risk factors, signs of overdose and appropriate methods for dealing with an overdose
Measured outcomes	<ul style="list-style-type: none"> • Self-reported knowledge pre- and post treatment • Self-reported events of overdoses
Results	<p>Knowledge (intervention group only): High knowledge prior to training, significant increased knowledge, confidence and willingness to take action after the training</p> <p>Management of overdoses: Treatment Group: 28 overdose events (no own overdose event reported), naloxone administered in all cases (27 survived), recovery position used in 81 % of cases, ambulance called in 85 % of cases Control Group: 38 overdose events (1/3 own overdose), recovery position used in 40 % of cases, ambulance called in 60 % of cases</p>
Bias-Risk	Medium to high
Limitations	Selection of intervention group unclear (probably self-selection of volunteers)
Sponsoring	None
Conclusions	Increased self-efficacy among the intervention group, use of naloxone in all reported cases of intervention groups, higher rates of emergency calls in the intervention group than in the control group
Comments	Only study with control group design (major other impact factors are levelled out e. g. opioid supply) but many methodological problems remain (medium to high Bias Risk)

Source: (Bennett/Holloway 2012), GOG-own presentation

Table 2.2:
Bias Assessment controlled studies

Quality criteria	Yes	No	Unclear
Selection			
Selection of the study population at the same time from the same source?		x	
Comparability			
Do the intervention and control group share the same distribution regarding influencing factors?			x
Outcomes			
Were the outcomes measured in a standardised way?	x		
Were influencing factors analysed?		x	
Was the study period adequate?	x		
Was the drop-out rate below 20 %?			X (for the treatment group)
Was the differential drop-out-rate between study populations around 15 percentage points?			(no drop-outs for the control group)
Assessment of Bias Risk	Low	Medium	High
		x	
Comments	Pre- and post test only for the treatment group, quasi experimental design with a small control group. No control for pre-test differences between groups		

Source: (Bennett/Holloway 2012), GOG-own presentation

2.3.2 Reviews and Guidelines

A Medline search from 1990 to 2004 had been conducted by Baca and Grant (Baca/Grant 2005). Quality and selection criteria were unclear but the authors reviewed several studies. Thus they concluded that naloxone is the single most important resuscitative action for opioid overdoses and naloxone is a safe medication. However, a few problems remained and one focus should be put on the training of the peers with regards to cardiopulmonary resuscitation (CPR) (in particular rescue breathing) and the possibility of a second dose of naloxone. The authors also stress that more scientific research and evidence were needed.

The Centre for Disease Control and Prevention conducted a survey among the 50 naloxone distribution programme in the US and received 48 replies (Center for Disease Control and Prevention (CDC) 2012). According to the survey, 53.302 persons have

been trained in naloxone administration since the introduction of the first programme in 1996 and 10.171 overdose reversals were reported. For a recent 12-months period the participating programmes reported the distribution of 38.600 naloxone vials (including refills). The programmes were located in 15 states and compared to the annual crude rates of unintentional drug overdose deaths per 100.000 inhabitants in all states. Nineteen of the states with higher drug overdose rates than the median in 2008 and nine of the states in the highest quartiles of drug-induced deaths did not provide a community-based peer-naloxone distribution programme. The authors conclude that the distribution of naloxone and training among peers have prevented numerous death from overdoses in the 15 states.

The British Advisory Council on the Misuse of Drugs (ACMD) published a report on the consideration of naloxone in 2012 (Advisory Council on the Misuse of Drugs 2012). The report is based on evidence available from three studies in the UK, the USA and Australia. No evidence from controlled studies was found (for the prescriptions of primary studies see 2.3.3). The authors conclude that there were hardly any side-effects reported when naloxone was administered. One of the reasons could be that naloxone is only provided in small doses to peers. The authors developed the following three recommendations from the research:

Recommendation 1: Naloxone should be made more widely available, to tackle the high numbers of fatal opioid overdoses in the UK.

Recommendation 2: The government should ease the restriction on who can be supplied with naloxone.

Recommendation 3: The government should investigate on how people supplied with naloxone can be suitably trained to administer it in an emergency and respond to overdoses" (Advisory Council on the Misuse of Drugs 2012, 5).

The Open Society Foundation recommends the peer-based distribution of naloxone as it can reverse overdoses and increase empowerment and self-efficacy among drug users (Open Society Foundations 2011). The evidence on the effectiveness to reduce mortality is based on US studies and experiences from Russia and China.

The Drug Policy Alliance of the US recommends "to remove barriers to naloxone access" (Drug Policy Alliance, 6) along other measures to reduce drug-induced deaths such as enhanced overdose prevention education and the promotion of the "Good Samaritan immunity law".

2.3.3 Evaluation of "take-home"-programmes

Twelve studies were identified on "take-home" naloxone programmes for actively injecting opioid users and peers. None of these studies have control groups in place and

the main outcomes are (non-standardised) experiences from opioid-users with naloxone. All of the studies conclude that naloxone is a safe drug to use and that negative consequences (e. g. severe withdrawal symptoms) are rare. More information on the outcomes of the studies is presented in Table 2.3. All studies focus on peer training and peer distribution of naloxone. Most peer training programmes include didactic and interactive components (e. g. practicing with a resuscitation dummy), opioid symptom recognition and response training (administration of naloxone, rescue breathing, ...) and contacting emergency medical service¹. Most persons were recruited at needle exchange or treatment sites. The measured outcomes are usually self-reported use of naloxone at peer-overdose when re-filling naloxone or contacting the site. The duration of the training varies significantly: 10 to 30 minutes in New York (Piper et al. 2008), 25 minutes in Pittsburgh (Bennett et al. 2011) and 8 hours in New York (Seal et al. 2005).

Table 2.3:
Studies on peer-naloxone

Authors and dates	Design and Size of Study Population	Outcome measures and results	Findings
(Maxwell et al. 2006)	Evaluation study in Chicago 3.500 10ml vials of naloxone prescribed (2001 to 2006)	319 reported overdose reversal from peers (one case of unsuccessful revival, 5 instances of second injections of naloxone, one case of severe opiate abstinence syndrome inducing vomiting). The number of drug-induced deaths) decreased from 446 cases in 2000 to 324 in 2003.	positive
(Sherman et al. 2008)	Qualitative study 31 clients of the Chicago recovery alliance needle exchange programme	All of the interviewed clients reported that naloxone was administered successfully in 58 % of the last witnessed overdoses.	positive
(Green et al. 2008)	Evaluation study at six study sites in the US 62 current or former drug users selected by site staff (half trained in naloxone, half not trained)	Trained participants recognised more opioid overdose scenarios accurately and instances where naloxone administration was indicated than untrained participants. Trained respondents showed the same skills as medical experts in recognising opioid overdose situation and the indication of naloxone. The study also concludes that the knowledge and recognition of non-opioid overdose (e. g. cocaine overdose) are rather low among trained and untrained persons.	positive

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¹

Some curricula are available at www.anypositivechange.org and www.harmreduction.org

Table 2.3, continued

(Bennett et al. 2011)	Evaluation study of Overdose Prevention Program Pittsburgh 426 self-selected individuals received training and naloxone 141 of the 426 trained individuals returned for a naloxone refill and filled in a questionnaire	89 of the 141 individuals reported administering naloxone in 249 separate overdose-situations. In two cases (despite calling emergency service and administering naloxone) a fatal overdose was reported. These two cases showed high use of Benzodiazepine and cocaine. In the vast majority of the cases (96 %) the overdosed person is reported to be „okay“. 51 persons of the 141 returning for a refill did not use naloxone during an overdose. On average, naloxone prescriptions were refilled 9,6 months after initial training. Of the 426 individuals participating in the training one third claimed to have called emergency services on the overdoses they witnessed prior to the training. The 249 individuals returning for a naloxone-refill reported to have called emergency services in only 10 % of the overdose incidents. The authors stress that the rates of calling emergency services vary substantially between the states and different legal situations apply.	positive
(Seal et al. 2005)	Pilot study 24 IDUs (12 pairs of injection partners) self-selected from street-setting in San Francisco	In the 6 months follow-up, participants witnessed 20 heroin overdoses and performed cardiopulmonary resuscitation in 16 events and administered naloxone in 15 events and took one of these measures in 19 cases. All overdosed individuals survived. The knowledge of heroin overdose management increased among the participants and heroin use decreased.	positive
(Gaston et al. 2009; Strang et al. 2008)	Evaluation study 239 opiate users in treatment from 20 drug services in England	At a 3-months follow up, 186 clients showed significant improvements in knowledge of handling overdoses (risks, recovery position, etc.). 18 overdoses have been experienced or witnessed and 12 successfully reversed with naloxone (2 by ambulance). 6 overdoses, where no naloxone was used, were reported, one of which led to death. No formal adverse events reported. More than one quarter had subsequently trained another person (friend, partner) to administer naloxone in the event of an overdose. A 6 months follow-up among a sub-group (46 patients) showed high knowledge rates but most patients did not carry naloxone with them and it was therefore not available at overdose events. One reason is the fear of detrimental reactions from police or ambulance.	positive
(Piper et al. 2008)	Skills and Overdose Prevention (SKOOP) Evaluation study 122 IDUs patients in New York for follow-up	Of the 122 patients returning for a naloxone refill 71 patients had witnessed an overdose, naloxone was administered 82 times (some patients witnessed more overdoses and used naloxone more than once), 68 of the 82 overdosed persons lived; the outcome is unknown for 14 persons.	positive

Continued next Page

Table 2.3, continued

(McAuley et al. 2012)	Scottish pilot studies 200 trained clients	13 naloxone uses reported, 12 successfully reversed, one deceased (before administration of naloxone). Ambulance called in 7 cases. Increased knowledge and self-perceived capacities among trained clients.	positive
Ross 2010 unpublished quoted in (McAuley et al. 2012)	Scottish pilot study 170 clients (including 68 prisoners)	37 uses of naloxone reported within one year, 36 successful reversals, one fatality (late administration of naloxone). 70 % of the overdoses required cardiopulmonary resuscitation in addition to naloxone administration. Ambulance called on 17 occasions, of which 13 led to police attendances and warrants.	positive
(Galea et al. 2006)	Evaluation study of pilot overdose prevention programme in New York 25 volunteer clients at syringe exchange programme	22 returned for follow-up after 3 months, 11 clients reported witnessing an overdose (26 cases of overdose). At 17 most-recent overdose events naloxone was successfully administered 10 times (all persons survived).	positive
(Dettmer et al. 2001)	Evaluation of pilot naloxone schemes in Berlin and Jersey 124 opiate users in Berlin 1999 101 drug users in Jersey 1998	Berlin: of the 124 users 40 reported for follow-up. 22 patients of the 40 reported administering naloxone in emergency situations (in 29 cases, all persons survived). Withdrawal symptoms reported in 10 instances, ambulance called in 9 cases. 1 reported case of inappropriate use (cocaine overdose) No increase of risky consumption detected. Jersey: 5 instances of naloxone administration reported, all persons survived. No reports of adverse consequences besides withdrawal symptoms.	positive
(Enteen et al. 2010)	1.942 persons trained in drug overdose and prevention and education (DOPE) in San Francisco in six sites (syringe exchange, maintenance treatment, ...)	24 % returned for naloxone refill, 11 % report using naloxone in 399 overdose events. Of the 399 incidents 89 % were successfully reversed, in 9 % of the reported overdose incidences the outcome is unknown and fatality was reported in 6 cases. For less than 1 % of the cases, serious adverse side effects (e. g. seizures) are reported. Rescue breathing was conducted in 50 % of the cases and emergency services were called in 29 % of the cases.	positive

Source: GÖG-own presentation

2.4 Remarks from general guidelines

The Centre for Disease Control and Prevention of the US recommends the implementation of community-based opioid overdose prevention programmes, including training and providing naloxone to potential overdose witnesses as part of a comprehensive prevention programme. The Centre for Disease Control and Prevention also concludes

that more IDUs could be reached through the provision of opioid prevention training (including naloxone) in jails and prisons, substance abuse programmes, parent support groups and physicians' offices than can be reached by the common approach through syringe-exchange programmes.

The Global Fund to fight AIDS, Tuberculosis and Malaria recommends naloxone distribution as part of comprehensive services for drug users (The Global Fund to Fight AIDS 2011).

2.5 Discussion

Quality of the studies

Only one primary study with a control group was identified. This study shows reduced methodological quality: in particular, the recruitment periods differ and the outcomes are all self-reported. Because of the primary studies' lack of power it cannot be precluded, that investigations of higher methodological quality could reveal contradicting results.

The quality of the other primary studies without control groups was considered low to medium, whereas the size of the study groups was usually small. One of the main problems is the lack of control groups, especially since changes in drug-induced deaths or behaviour could also be influenced by other factors (e. g. heroin availability). In particular, most studies report a very low follow-up rate. This withholds a great bias risk since the outcomes of most members of the intervention group remain unclear.

Another important limitation is the self-selection bias for most recruiting settings. Volunteers participating in an emergency training could lead to an over assessment of the effectiveness. Another limitation of this review is a potential publication bias. As mainly small-scale studies are conducted, a low publication rate of ineffective or unsuccessful studies can be assumed.

The conduction of long-scale longitudinal studies among injecting drug users is a difficult task (Piper et al. 2007). One of the participant's main concerns is confidentiality and data protection. Furthermore, in order to be sufficiently powered to observe a significant difference among intervention and control, they should enrol a big cohort. In addition to that there would be an ethical concern in providing a save-life drug only to a group of drug-users and enrol a control group exposed to overdose risks. However, cohort studies are valid to study mortality, provided they respect some methodological accuracy and that the results are considered with some caution.

Theory-based validity and results

Due to the lack of high quality controlled studies, the evidence on the effectiveness of naloxone distribution through peer programmes remains unclear. Important insights are expected from the ongoing randomised controlled trial “N-ALIVE” among 5.600 drug users released from prisons in England.

Discussions and recommendations on the use of naloxone often take place at a theoretical level. Therefore, we’re trying to summarise in this review the most common reasons for and against naloxone distribution through peer-programmes. The theoretical analysis e. g. by Darke and Hall (Darke/Hall 1997) are summarised with available evidence from the primary studies conducted.

One often stated fear is that the availability of naloxone as a “safety net” could encourage more risky patterns of drug use. A study conducted in relation with this risk, expressed that injecting drug users would not use more heroin when naloxone is available. This is due to the unpleasant withdrawal symptoms caused by naloxone and the fact that heroin is too expensive to be “wasted” (once naloxone is administered the euphoric effect of heroin would vanish) (Darke/Hall 1997). A small scale study showed a decrease of heroin use after an intensive overdose prevention training including naloxone distribution (Seal et al. 2005). This training associated with naloxone prescription could increase self-efficacy and awareness and therefore reduce risky patterns (Advisory Council on the Misuse of Drugs 2012). The authors conclude that there was no evidence to prove that “take-home” naloxone will increase a riskier use of drugs; the same was shown by Dettmer (Dettmer et al. 2001).

Another main objective against “take-home” naloxone is that it would deter persons from seeking help. Only one study (Bennet et al. 2011) reported a decrease in the use of emergency services after the administration of naloxone. Other evaluation studies show that the call for emergency services is deterred in most overdose situation whether naloxone is available or not (Darke/Hall 1997; Maxwell et al. 2006). Substantial work is needed to increase the use of emergency services among drug users, regardless of naloxone, in order to reduce the number of drug-induced deaths. In particular, legal issues (e. g. police arrests) and compensation (for emergency services) need to be addressed.

The prescription of naloxone is associated with legal issues such as the medical liability of physicians. In most countries, naloxone can only be prescribed and administered by a medical practitioner or a licensed paramedic. Administration of naloxone by other persons is therefore a criminal offence (Darke/Hall 1997). It is important to address the legal issues in these countries before starting a naloxone distribution programme.

Another issue often discussed is the expenses associated with naloxone distribution. Although the generic formula of naloxone is inexpensive (Maxwell et al. 2006) However large numbers of ampoules need to be distributed to provide a coverage of naloxone that is large enough to avert fatal overdoses. In particular, the fatality rates at overdose events are rare and naloxone will be used more often than actually needed (Darke/Hall 1997). However, naloxone has the benefit of preventing hypoxic brain injury by reducing respiratory depressions even among overdoses that would not have been fatal. The number of naloxone distribution needed to prevent one death (e. g. 300 doses to prevent one death) leads to a cost-effective intervention (Baca/Grant 2005). The same conclusion was drawn for the “N-ALIVE” project (Advisory Council on the Misuse of Drugs 2012).

The two main medical objections are based on the pharmacological aspects of naloxone and the risks of severe withdrawal symptoms. As described in the section about the medical background (see 0) and in the Chicago field study (Maxwell et al. 2006) naloxone has a shorter half-life than opioids. Thus, in several cases the administration of a second dose of naloxone is vital when the symptoms of overdose recur. It is essential to address this fact during the training and information of peers (Maxwell et al. 2006). Naloxone can induce severe withdrawal symptoms, which could lead to death. Severe complications such as seizures were reported and were mainly associated with severe pre-conditions of health in a very limited number of cases only (Kim et al. 2009).

Among the main arguments for the distribution of naloxone among drug users is the fact that naloxone has no pharmacological effects in the absence of opioids. Therefore, it imposes no risks for non-opioid users such as children of heroin users (Baca/Grant 2005; Darke/Hall 1997). Besides, naloxone has no abuse potentials (Darke/Hall 1997) and it is not possible to overdose on naloxone (Darke/Hall 1997; Drug Policy Alliance). Therefore, from a medical perspective the “current opinion is that naloxone is a safe drug to use” (van Dorp et al. 2007, 90).

Researches on drug overdoses suggest that bystanders are present during most cases of overdoses (Advisory Council on the Misuse of Drugs 2012; Darke/Hall 1997; Strang et al. 1999b) and peers are willing to administer naloxone when necessary (Bennett/Holloway 2012; Strang 1999). Many overdoses occur at home, where naloxone can be stored (Darke/Hall 1997) and overdoses do not occur instantaneously, but over a course of one to three hours giving a lot of opportunity for interventions such a naloxone administration (Sherman et al. 2008).

None of the identified discussions and recommendations states that naloxone is unsafe. The general conclusion is that the potential benefits of naloxone programmes outweigh the potential risks (Bazazi et al. 2010; Kim et al. 2009).

2.6 Conclusions and Recommendations

No controlled study was identified on the selected primary outcomes of mortality among injecting drug users. Only self-reported experiences of overdoses were presented in the studies indicating positive effects of “take-home” naloxone programmes on preventing drug-induced deaths.

Based on the results from the evaluation studies, on the recommendations from experts and on the analysis of the objections against naloxone, the authors come to the conclusion that naloxone is a safe drug to use and that naloxone distribution programmes, in combination with emergency trainings, should be expanded in Europe. Additionally, the following recommendations can be derived from the literature analysis:

- » Naloxone peer-programmes should include identifying and responding to opioid-overdoses and essential first aid training.
- » Further research in particular large scaled studies is essential to monitor any negative side-effects and consequences of peer- naloxone-programmes.
- » The legal regulations when calling an ambulance to a potential overdose vary in Europe. Calling emergency services are an important aspect of harm reduction and possible barriers (and legal regulation) for contacting emergency services should be addressed in order to reduce drug-induced deaths.
- » The legal aspects of naloxone prescription need to be addressed at national level. Additionally, liability aspects (e. g. another person administering naloxone) should be solved before starting naloxone programmes (Strang et al. 2008). This could help overcoming the fear of patients carrying naloxone along (Gaston et al. 2009).

3 Review on prison release management

How effective are prison release management programmes among opioid users in reducing the number of direct drug-induced deaths?

3.1 Background

The first weeks following a prison release are associated with an increased risk of fatal overdoses among drug users. A meta-analysis of studies concerning drug-induced deaths closely following a prison release shows that six out of ten deaths in the first twelve weeks following a prison release are drug-induced. A three- to eightfold increased risk was found comparing week one and two to week three to twelve (Merrall et al. 2010). Similar results were shown by Lyons (Lyons et al. 2010) for Ireland. Beside the decreased tolerance after a period of relative abstinence, the concurrent use of multiple drugs, the lack of pre-release counselling, the lack of post-release follow-up and the failure to identify those at risk are reasons for overdoses following a release from prison (WHO 2010).

In literature various possible measures are described to possibly prevent fatalities due to overdoses like opioid maintenance treatment, naloxone peer programmes, pre-release counselling, first aid training and overdose management. The aim of this literature review is to find evidence of the effectiveness of a bundle of measures (or single measures) that could be addressed as “prison release management”.

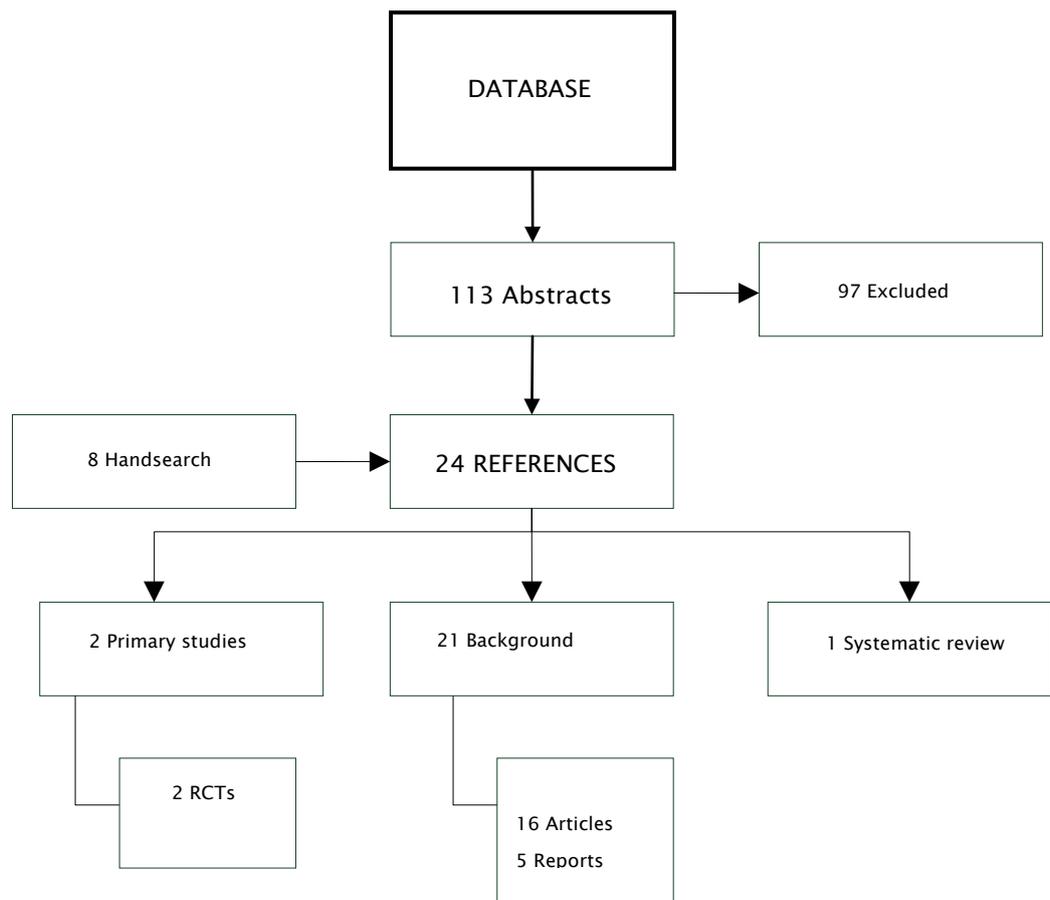
3.2 Methods

Since a first literature search for the term “prison release management” in major databases did not result in any matches, it was decided to broaden the scope. Subsequently, a systematic literature research was performed in Medline, Eric, Psycinfo, Embase and the Cochrane Library with predefined keywords. To identify relevant publications, three keywords-clusters were connected, one with the terms prison or jail, the second with the terms opiate or opioids and a third using terms related to release (for details see search strategy in section 6).

The selection of abstracts and full-text versions was performed according to predefined selection criteria. The exclusion criteria for the 113 identified abstracts were: studies not published in English or German, studies not carried out in a European or

comparable (US, Canada, New Zealand, Australia) country, studies on other outcome measures (not referring to overdoses), studies conducted before the year 2000 and studies that were already included in meta-analyses or systematic reviews that were already selected for this review.

Figure 3.1:
Identification and selection of articles for the description of measures to prevent drug-induced fatalities after prison release



Source: GÖG-own presentation

3.3 Results

On the basis of the systematic literature research in major databases, 113 abstracts were identified. After the selection of abstracts according to predefined selection criteria (see 3.2) 16 full-text articles were chosen. Eight publications were added by hand search. After the selection of the full-text articles one systematic review, two RCTs, one evaluations study and 21 articles and reports for the description of the background were included in the analysis.

3.3.1 Systematic review and primary studies

In the systematic literature only three articles (1 systematic review and 2 RCTs) that met the inclusion criteria for this review could be found – all concerning opioid substitution treatment (OST). The systematic review was done by Hedrich et al. (2011) and includes four European and 17–Non–European studies on the effectiveness of OST in prison settings. One of the RCTs was carried out by Kinlock et al. (2009) and is included here as well, although the study is already covered by the systematic review since the comparison of three groups (counselling only, counselling and transfer to methadone treatment upon prison release and counselling and methadone treatment) might provide indirect answers to the initial question concerning prison release management. The second RCT was done by McKenzie et al. (2012) and compares initiation of OST pre-release and continuous treatment (with payment of treatment costs) and referral post release to the same programme (with payment of treatment costs) and finally referral post release to the same programme (*without* payment of treatment costs). Design, population, outcome measures and results are presented in Table 3.1.

None of the studies was designed to evaluate the influence of OST on mortality hence overdoses or fatalities after prison release due to overdoses were not primary outcome measures. The two RCTs show some evidence that suggests that pre-release OST may be associated with reduced post-release mortality. OST seems to be more effective than counselling only, but results cannot be generalised as the process of transfer or referral is not described in detail in the studies.

Table 3.1:
Selected studies on effectiveness of OST in prison

Authors and Dates	Design and Size of Study Population	Outcome Measures / Methods and Results	Findings
Hedrich et al. (2011)	Systematic review of 21 experimental and observational studies of prisoners receiving OST. Population size between 32 and 2.994 individuals.	Outcome measures: treatment retention, opioid use, risk behaviours, HIV/HCV incidence, criminality, re-incarceration and mortality. Results (selection): All four studies comparing OST to no OST in terms of treatment entry and retention after release found that prison OST was strongly associated with significantly higher levels of post-release treatment entry and retention. Four of five studies reporting on opioid use after release from prison found significant reductions in heroin use among OST subjects compared to controls or no OST comparison groups. Only 3 studies provide data on mortality, but no study was designed to evaluate the influence of prison OST on mortality. The evidence of effectiveness concerning the reduction of post-release overdose fatalities is weak.	Among others: prison OST positive for post-release treatment entry and retention and relapse rate. Weak evidence for reduction of mortality
Kinlock et al. (2009)	3-arm RCT with 12-months follow up 211 male heroin-dependent pre-release prisoners in Baltimore (USA)	12-months follow up completed with N=204: Arm 1: Counselling Only: counselling in prison, with passive referral to treatment upon release (n=64); Arm 2: Counselling + Transfer: counselling in prison with transfer to methadone maintenance treatment (MMT) upon release (n=69); Arm 3: Counselling + Methadone: counselling and methadone maintenance in prison, continued in the community upon release (n=71). Results: mean number of days in community-based drug abuse treatment was the highest in Counselling + Methadone followed by Counselling + Transfer and Counselling Only. Less positive heroin and cocaine test in Counselling + Methadone group. Secondary outcome: 4 people died from opioid overdoses – all from Counselling Only group	Positive for Counselling + Methadone compared to Counselling Only regarding treatment retention and heroin consumption
McKenzie et al. (2012)	3-arm RCT with 12-months follow up 90 male IDUs from Rhode Island Department of Corrections (USA) with scheduled release at least 28 days after enrolment	6-months assessment completed with N=62: Arm 1: initiation of OST pre-release with continued treatment in the inmates' methadone programme of choice and short-term payment of treatment costs (n=21); Arm 2: referral to the participants' methadone programme of choice upon release from incarceration with provision of the same short-term financial assistance (n=32); Arm 3: referral to the participants' methadone programme of choice upon release from incarceration without financial assistance (n=9). All 3 arms received HIV risk reduction and overdose prevention counselling and assistance with linkage to the methadone programme of their choice at the time of release. Results: Arm 1 participants entered treatment in the community earlier. Two participants who neither received methadone prior to release nor attended a post release programme have yet died from overdoses. Non fatal overdoses occurred equally across the 3 arms. 5 of 8 participants reporting non-fatal overdoses did not enrol in OST post-release. Lower 6-months post-release heroin and cocaine relapse rate in arm 1.	Positive for pre-release initiation of OST combined with payment assistance post-release

Source: GÖG-own presentation

3.3.2 Background articles, reports and guidelines

Although no studies on the effectiveness of prison release management exist, a lot of measures for preventing drug-induced mortality following a prison release are mentioned in several articles and reports:

- » Naloxone “take home” programmes (EMCDDA 2012b; Gould 2011; Lyons et al. 2010; Merrall et al. 2010; Wakeman et al. 2009; WHO 2010) see also chapter 2.
- » Pre-release counselling on overdose risks including risk assessments, overdose prevention training and/or training in first aid and overdose management (EMCDDA 2012b; Farrell/Marsden 2008; Lyons et al. 2010; Merrall et al. 2010; WHO 2010).
- » Optimising referral to aftercare services and into community treatment (EMCDDA 2012b; Merrall et al. 2010; WHO 2010).
- » Improved communication and cooperation of prison and community based treatment (EMCDDA 2012b; Lyons et al. 2010; WHO 2010).
- » Providing accommodation and employment (Binswanger et al. 2012; Binswanger, I. et al. 2011; Lyons et al. 2010).
- » Avoid involving the police when calling emergency ambulances (Lyons et al. 2010) as people who are on probation/parole might be discouraged when expecting to get in contact with the police.
- » Opioid maintenance treatment in prison (Farrell/Marsden 2008; Huang et al. 2011; Kinlock et al. 2009; Lyons et al. 2010; McKenzie et al. 2012; WHO 2010).

WHO (2010) indicates – except from the above-mentioned measures – the importance of “equivalence of care” in prison and community healthcare service provision and of throughcare. Throughcare means the uninterrupted professional healthcare throughout the criminal justice system and the subsequent amalgamation with community interventions. Continuity of care is also the key recommendation of the Patel report (Lord Patel of Bradford 2010). The importance of throughcare is also emphasised by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA 2012b) .

3.3.3 Models and interventions in different countries

As a model of good practice, WHO (2010) lists a programme from England and Wales, which delivers an integrated multi-entry-point throughcare model of drug treatment. EMCDDA (EMCDDA 2012b) lists the “Through the gate” scheme in Wales as example of good practice for community-based organisations that includes “in-reach”, prison gate pick-up, assertive outreach, local networking and enhanced engagement with support

services. A further model of good practice is the provision of naloxone on prison release which is available across England, Scotland and Wales' prison estates.

The Bolwara House Transitional Centre in New South Wales, Australia, provides an intensive community-based pre-release programme for women that implements throughcare principles and involves the creation of partnerships and effective working relationships with all stakeholders, including correctional and treatment staff, prisoners and external service providers (WHO 2010).

Spain provides a high standard and elaborated prison-based harm reduction programme that includes also pre-release education and post-release treatment referral to community services (WHO 2010). Good models of practice in pre-release counselling on overdose risks or overdose prevention training were identified in Belgium (Flemish prisons) and Portugal (EMCDDA 2012b).

3.4 Discussion

The literature (EMCDDA 2012b; WHO 2010) describes various possible measures to prevent fatalities due to overdoses like throughcare (continuity of treatment before, during and after prison), opioid maintenance treatment (including start of OST before release), naloxone "take home" programmes, pre-release counselling on overdose risks (including risk assessments, overdose prevention training and/or training in first aid and overdose management), optimised referral to aftercare services and into community treatment. Nevertheless, there are no available studies concerning the effectiveness of these measures in reducing post-release fatalities due to overdoses. Hedrich et al. conclude:

"The lack of research is somewhat surprising, given the evidence of raised mortality in the period immediately following release from prison. This is especially pertinent in view of evidence from a systematic review that methadone maintenance is clearly effective in reducing overall and overdose mortality." (Hedrich et al. 2011, 513)

At least the results of Kinlock et al. (2009) and McKenzie et al. (2012) indicate that OST in combination with counselling and active referral might be more effective than counselling only.

The effectiveness of naloxone peer programmes is discussed in Chapter 2. Naloxone programmes at prison release are already available in England, Scotland and Wales. Literature recommending naloxone programmes for prison release also exists (EMCDDA 2012b; Gould 2011; Lyons et al. 2010; Merrall et al. 2010; Wakeman et al. 2009; WHO 2010).

Regarding theory based validity, it makes sense to provide healthcare from the very beginning of imprisonment until reintegration in the society (“throughcare”). Many different factors may contribute to the effectiveness of throughcare so it is impossible to investigate it as a whole. Nevertheless, to enable continuity of care and treatment, stability is one of the key recommendations of the WHO (2010) concerning prevention of drug induced mortality after prison release.

In a qualitative study, Binswanger et al. (2011; 2012) describe the transitional challenges for released inmates and barriers like: access to housing, job, physical and mental healthcare and problematic conditions of parole. Further cognitive and emotional responses during the transitional period are discussed. For the future it might be useful to conduct more studies on the problems and challenges of released prisoners, as well as studies on the effectiveness of various interventions.

3.5 Conclusions and recommendations

Several measures are recommended to reduce mortality after prison release but for none of them studies on their effectiveness in reducing post-release fatalities due to overdoses are available.

- » There is evidence to suggest that OST combined with counselling and active referral to community based programmes might be more effective than pre-release counselling only. OST in prison should be expanded; a special focus could be put on the active referral into community programmes upon release.
- » Naloxone on prison release is already available in England, Scotland and Wales. It might be useful to expand these programmes to other European countries (see also chapter 2).
- » Regarding theory based validity, it makes sense to provide healthcare from the very beginning of imprisonment until reintegration in society (“throughcare”).
- » For the future, it might be useful to conduct more studies on the problems and challenges of released prisoners as well as on the effectiveness of various interventions.

4 Needle exchange programmes in prison

Is it possible to reduce HIV, hepatitis B and hepatitis C infections of opioid users by providing needle exchange programmes (NSP) in prison?

4.1 Background

Between 2001 and 2010 the prison population in the 27 EU Member States increased from 582.000 to 635.000. Offences related to use, possession or supply of illicit drugs are main reasons for imprisonment (10 % and 25 % of all sentenced prisoners). For the interpretation of these numbers it has to be taken into account that on one hand, not all of these prisoners necessarily have experience or problems with drug use. On the other hand, not all prisoners with drug use problems have been imprisoned for a drug law offence (e. g. imprisonment for other leading offences like burglary, shoplifting, etc.) (EMCDDA 2012b). Estimations suggest that about 50 percent of prisoners in the EU have a history of drug use and a high proportion of them with drug use problems (WHO 2007b). **Concerning injecting drug use (IDU), there is evidence that on one side some IDUs reduce the frequency of injection in prison, but on the other side it has also been described that due to the low availability of heroin in prison, some drug users switch to injections from other routes of administration (e. g. smoking) (EMCDDA 2010; Peña–Orellana et al. 2011).** The scarcity of injecting equipment fosters sharing networks more intensively than outside prison. Additionally, inadequate cleaning practices of the equipment used for injecting and the rent of needles and syringes in exchange for the drugs are promoted (Long et al. 2004). In addition, some prisoners start (IDU-) drug use in prison (WHO 2007b). A recent study in 31 German prisons (14.537 inmates) shows that 22 % of all prisoners are IDUs (Schulte et al. 2009). It is not surprising that various studies have shown that prison is a risk factor for HIV, HBV and HCV infections (Judd et al. 2005; Lines et al. 2006; Stark et al. 2006).

Due to these facts, it is consequent to introduce, in the prison setting, harm reduction measures that have been proven effective outside prison. In 1992 the first needle and syringe exchange programme (NSP) in prison was started on an informal basis by a physician at the Oberschöngrün men's prison. The physician ignored regulations and began distributing sterile syringes to patients he knew to be injecting drugs and sharing needles. In 1994 the first formal needle exchange pilot project was established (Lines et al. 2005). In 2012 needle and syringe exchange was available in five EU countries (Germany, Spain, Luxembourg, Portugal and Romania). But some NSP programmes were also stopped. In Portugal two programmes established in 2008 were not accepted by the inmates (EMCDDA 2012b) and in Germany 6 out of the 7 imple-

mented programmes were terminated by a newly elected government due to political reasons (Lines et al. 2005). Outside Europe NSPs in prisons are available in Armenia, Iran, Kyrgyz Republic, Moldova and Ukraine (Stöver et al. 2008). In Australia the decision was recently made to try NSP in a prison in Sydney (Sweet 2012).

Although NSP in prison shows a theory based validity (NSP has proved to be effective outside prison – why should it not work inside prison, too?) there are some hypothetic arguments against this approach based on the special features of prison settings (Lines et al. 2006). However, some of them brought to mind the discussion on NSP outside prison some decades ago:

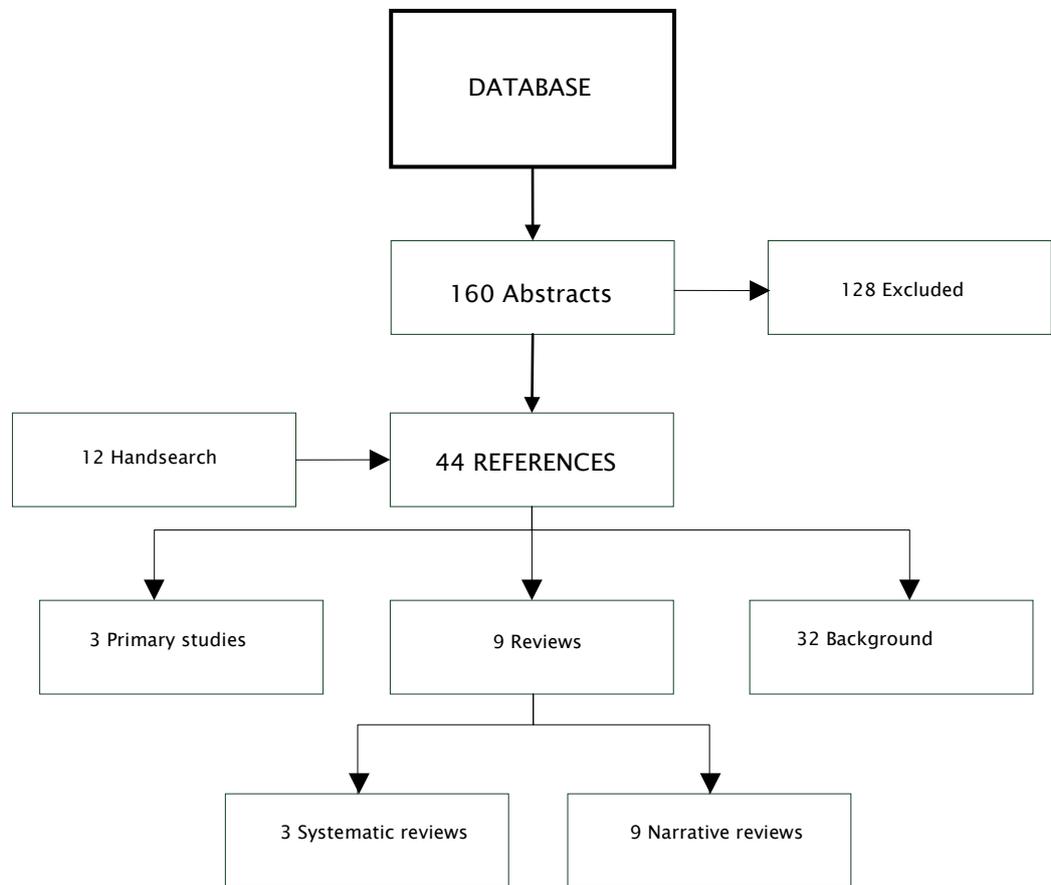
- » Prison needle exchange leads to increased violence and the use of syringes as weapons against prisoners and staff.
- » Prison needle exchange leads to an increased consumption of drugs, and/or an increased use of injection drugs among those who were previously not injecting.
- » Prison needle exchange undermines abstinence-based messages and programmes by condoning drug use.
- » The successful implementation of prison needle exchange programmes in one prison does not mean that it will be possible to implement NSPs in other prisons since existing programmes are based on specific and unique institutional environments.

4.2 Methods

A systematic literature research with predefined keywords was performed in Medline, Eric, Psycinfo, Embase and the Cochrane Library. To identify relevant publications, two keywords-clusters were connected, one with the terms prison or jail and the second with the terms needle/syringe exchange, needle-exchange programmes, supervised injecting and preventive health service (for details see search strategy in section 6).

The selection of abstracts and full-text versions was performed according to predefined selection criteria. The original plan to focus on studies including a control (comparison) group could not be followed due to the fact that no study according to this design was found. Exclusion criteria for the 160 identified abstracts were: studies not published in English or German, studies focusing on other themes than NSPs, studies conducted before the year 2000 and studies that were already included in systematic reviews that had been selected for this review.

Figure 4.1:
Identification and selection of articles for NSP in prison



Source: GÖG-own presentation

4.3 Results

No study, including some kind of comparison, has been identified. This is surprising because on a first glimpse this kind of studies seem to be easy to realise (e. g. comparison of a prison with and without NSP). Maybe such studies have not been carried out due to ethical problems or due to problems finding a prison which agreed to serve as comparison. Most evaluations available are based on a comparison of the situation before or at the beginning of the introduction of NSP and some time after. Apart from

seroconversion and the rate of needle sharing, the level of (injecting) drug use and other possible negative consequences (like using the needle as a weapon) which have been stressed as arguments against NSPs in prisons, (see section 4.1) are included in the evaluations. Another problem concerning the availability of evidence is that most evaluations are published in grey literature only. But summaries of the main results can be found in reviews. Three primary studies published after 2000 have been identified in addition.

4.3.1 Reviews and primary studies

Detailed information on the evaluation of NSP in prisons is available for 6 programmes based on a review from the National Drug and Alcohol Research Centre of the University of New South Wales (Rutter et al. 2001). Partly published in "Addiction" in 2003, (Dolan et al. 2003) – Table 4.1

Table 4.2 gives an overview about the results of evaluations in ten European prisons in three countries.

One evaluation study, published 2006, carried out in two German prisons (Lehrter, Strasse and Lichtenberg) from 1998 to 2001 involved 166 IDUs. Follow up visits were performed every four months including questionnaires and blood samples. Overall 7.954 syringes were delivered in the framework of the project. No adverse events possibly related to the project were observed (e. g. overall increase in IDU, violence involving needles against staff or other inmates). The rate of needle sharing decreased from 71 % at the baseline investigation to 11 % at the first follow up, to 2 % at the second follow up and to 0 % on the third follow up. At the baseline investigation the seroprevalence for HIV was 18 %, for hepatitis B 53 %, and for hepatitis C 83 %. Concerning HIV and HBV no seroconversion has been observed and for HCV 4 infections (one infection definitely acquired in prison). Two of eight individuals who had previously used illicit drugs by routes other than injection, started to inject during the follow-up (Stark et al. 2006).

A poster is available from a recent evaluation of NSPs in Iranian prisons only. The project, carried out in three prisons involving 341 prisoners on a voluntary basis, found an average reduction of 3,7 syringes shared per week to zero, after the implementation of the project. No infection with HIV, HCV or HBV occurred (Shahbazi et al. 2010).

Table 4.1:
Overview of evaluations on needle exchange in six European prisons in three countries

Prison (country)	Sample Size	Years studied	N of Syringes Distributed	% of Syringes Returned	Methods	Limitations	Results
Women's prison Hindelbank (Switzerland)	137	2	5.985	100	Surveys of inmates and staff, syringe distribution data, medical records and prison records	Low participation rate of staff in surveys, drug use monitored by self report	Acceptance by staff and inmates, no increase in drug use, no initiation to drug use, reduction in sharing, no increased sanctions, no attacks or inmate violations, no increase in drug-related deaths, no seroconversion for HIV or hepatitis, decrease in abscesses, lack of inmate knowledge about hepatitis
Women's prison Vechta (Germany)	169	2	16.390	98,9	Surveys of inmates and staff, syringe distribution, medical records and prison records	Drug use monitored by self report, no pre- and post-test HIV or hepatitis testing	Acceptance by staff and inmates, no attacks or inmate violations, no effect on inmates seeking drug treatment, reduction in sharing syringes, reduced overdoses, decrease in abscesses and no seroconversions
Men's prison Lingen (Germany)	83	2	4.517	98,3	Surveys of inmates and staff, syringe distribution, medical records and prison records	Drug use monitored by self report, no pre- and post-test HIV or hepatitis testing	Reluctance by inmates due to staff distribution, high acceptance by staff, no attacks or inmate violations, no effect on inmates seeking drug treatment, reduction in sharing syringes, reduced overdose and no seroconversions
Men's prison Realta/Cazis (Switzerland)	234	1	1.389	No data	Surveys of inmates and staff	Surveys after programme began, drug use & infections monitored by self report	No increase in drug use, no increase in injecting, reduction in syringe sharing, acceptance by staff and inmates
Men's prison Basauri, Bilbao (Spain)	607	1	12.500	82	Surveys of inmates and staff, syringe distribution	Drug use monitored by self report, health effects by medical staff report	Acceptance by inmates and staff, no increase in drug use, no attacks or inmate violations, reduction in sharing syringes, no seroconversions
Pamplona prison (Spain)	115	1	No data	No data	Surveys of inmates and staff, syringe distribution	Information based on self report	Conditional acceptance by inmates and staff, lack of programme knowledge among staff, reduction in syringe sharing

Source: (Rutter et al. 2001)

Table 4.2:

Overview of evaluations and epidemiological studies on needle exchange in ten European prisons in three countries

Prison (country)	Drug use	IDU	Needle sharing	Incidence of HIV/HCV
Am Hasenberg (Germany)	No increase	No increase	Strongly reduced	No data
Basauri (Spain)	No increase	No increase	No data	No seroconversion
Hannöversand (Germany)	No increase	No increase	Strongly reduced	No data
Hindelbank (Switzerland)	Decrease	No increase	Strongly reduced	No seroconversion
Lehrter Strasse (Germany)	No increase	No increase	Strongly reduced	No data
Lichtenberg (Germany)	No increase	No increase	Strongly reduced	No data
Lingen I (Germany)	No increase	No increase	Strongly reduced	No seroconversion
Realta (Switzerland)	Decrease	No increase	Single cases	No seroconversion
Vechta (Germany)	No increase	No increase	Strongly reduced	No seroconversion
Vierlande (Germany)	No increase	No increase	No change	No seroconversion

Source: (Stöver/Nelles 2003) updated from (WHO 2007a)

A long-term evaluation report is available for the NSP in the prison of Champ-Dollon (Geneva, Switzerland) covering the period 2001 to 2010. Each year from 169 to 446 syringes were distributed to between 24 and 53 IDUs. The return rate ranged from 58 to 83 %. No acts of aggression or other incidents involving the contents of injection kits (e. g. threats, aggression, injury by a syringe left in a dustbin, etc.) were reported. The programme was well accepted by the prison staff and the healthcare team (Wolff et al. 2011).

4.3.2 Different types of NSP in prison

For needle distribution, different methods with specific advantages and disadvantages are in use in different prisons. The following description follows an analysis of existing projects from Lines et al. (Lines et al. 2005).

Distribution by a medical service/unit (physician, nurse) of the prison:

Advantages: personal contact with the prisoner including the opportunity to provide counselling, contact with formerly unknown drug users, high control over access to syringes, one for one or multiple syringe distribution is possible

Disadvantages: Lower degree of anonymity and confidentiality which might reduce participation rate, limited access (syringes are available at the opening hours of the medical unit only), possibility of proxy exchanges by prisoners obtaining syringes on behalf of other prisoners

Hand-to-hand distribution by peer outreach worker:

Advantages: high acceptance by prisoners, high degree of anonymity and trust, high degree of accessibility

Disadvantages: No direct staff control over distribution, which can lead to increased fears of workplace safety among staff, one-for-one exchange is more difficult to enforce

Hand-to-hand distribution by external harm reduction organisations or health professionals:

Advantages: personal contact with the prisoner including the opportunity to provide counselling, contact with formerly unknown drug users, high control over access to syringes, one for one or multiple syringe distribution are possible, some degree of anonymity is provided (no direct interaction with prison staff)

Disadvantages: syringe availability is limited to set hours or set times per week, anonymity may be compromised by policies that require the external agency to provide information on participation to the prison administration, prison staff might show mistrust towards external workers, external workers may experience more barriers in dealing with prison bureaucracy

Automated dispensing machine:

Advantages: high degree of accessibility, anonymity and acceptance, strict one-for-one exchange

Disadvantages: machines are vulnerable to vandalism by prisoners and staff not in favour of the programme, technical problems might reduce availability, some prisons are not architecturally suited for the use of dispensing machines (lack of discrete areas freely accessible for prisoners)

Table 4.3 gives an overview about the modes of syringe distribution used in eleven prisons. The evidence from NSP evaluations shows that the actual method of syringe distribution is less important than ensuring that the programme responds to the needs of the institution, prisoner population and prison staff. One key factor in establishing trust in the NSP from the perspective of the prisoners is the issue of confidentiality which is, to some extent, contradictory to prison setting. Therefore, pragmatic approaches are necessary to ensure confidentiality to the greatest possible extent (Betteridge/Jürgens 2008; Lines et al. 2005).

Table 4.3:

Syringe exchange programmes in Europe – mode of distribution and other measures (data from 2003 or earlier)

Country	Prison	Mode of Distribution	Other Measures
Switzerland	Men's Oberschöngrün	Doctor	E,O,C
Switzerland	Women's Hindelbank	Machine	E,O,C
Switzerland	Men/Women's Champ Dollon	Doctor	No information
Switzerland	Men's Realta/Cazis	Machine	E,O,C
Germany	Women's Vechta	Machine	E,O,C, AIDS support user groups
Germany	Men's Lingen	Drug counselling service	E,O,C, AIDS support user groups
Germany	Men's Vierlande	Machine	No information
Germany	Women's Lichtenberg, Berlin	Machine	No information
Germany	Men's Lehrter Str., Berlin	Machine	No information
Germany	Men's, Fuhlsbüttel	Staff	No information
Spain	Men's Basauri, Bilbao	External staff	E,O,C, bleach, condoms, detox
Spain	Pamplona	External staff	No information

E = education, O = opioid substitution treatment, C = counselling; Source: (Dolan et al. 2003)

Another very relevant aspect regarding the implementation of NSP in prison is that (like outside prison) NSPs should always be a component of a broader, comprehensive harm reduction strategy (Lines et al. 2005). This is the case in most prisons offering NSP (see Table 4.3).

4.3.3 Guidelines and political papers

There is consensus in European policy that prisoners should have the same health support as the general population (e. g. Dublin declaration on HIV/AIDS in prisons in Europe and Central Asia, (WHO 2007b). Article 1 of the Dublin declaration on HIV/AIDS in prisons in Europe and Central Asia states: *"Prisoners have a right to protect themselves against HIV infection. Prisoners living with HIV/AIDS have a right to protect themselves from re-infection and/or co-infection with hepatitis C and/or TB. Therefore, States have a responsibility to: Ensure that HIV prevention measures available in the outside community are also available in prisons. This includes providing prisoners with free access to HIV prevention and harm-reduction measures including, but not limited to, sterile syringes and injecting paraphernalia [...]."* (Lines et al. 2004)

One chapter of the WHO status paper on prisons, drugs and harm reduction dating 2005 focuses on NSP in prison and comes to the following conclusion: *"Many countries with well-established exchange schemes in the community do not make them available*

in prisons. Evidence shows that needle-exchange programmes can be provided in prisons and that they can be safe, as effective as those outside prison schemes and acceptable to both prisoners and staff (Lines et al., 2004; Stöver & Nelles, 2003). The experience of the prisons that have successfully used this approach should be used to give guidance on the most acceptable way of exchanging the injecting equipment and of ensuring safe and effective service.”(WHO 2005, 12)

The WHO guide “Health in Prisons” a WHO guide to the essentials in prison health states: *“When prison authorities have any evidence that injecting is occurring they should therefore introduce needle and syringe programmes, regardless of the current prevalence of HIV infection”*(WHO 2007b, 103)

Recently, the UNODC policy brief “HIV prevention, treatment and care in prisons and other closed settings: a comprehensive package of interventions” (UNODC 2012) lists needle and syringe programmes as one of 15 key interventions. Prisoners who inject drugs should have easy and confidential access to sterile drug injecting equipment, syringes and paraphernalia, and should receive information about the programmes.

4.4 Discussion

Almost all studies on NSPs in prison show a dramatic decrease in needle sharing and no (or very low) seroconversion rates concerning HIV, HCV and HBV. The study designs are not the best (no comparison) – which may lie in the nature of the topic (ethical or ideological constraints to serve as a comparison prison with no NSP). This limitation can affect the generalisability of results because there might be unknown factors of influence. Nevertheless the conclusion can be drawn that the NSP in prison is an effective method to reduce risk behaviour concerning infection with HIV, HBV and HCV.

The fear that the syringes distributed will be used as weapons or lead to injuries of staff when they are carrying out their routine duties (e. g. cell searches) has to be rejected. No such event has been reported in the literature on NSPs in prison reviewed. On the contrary NSPs can be seen as a prevention measure of the latter when the NSP includes the possibility to store the syringe safely and there is no reason to hide it because hiding of syringes is one of the reasons for needle stick injuries of prison staff (Larney/Dolan 2008).

Since the evaluation reported no increase of (injecting) drug use after implementation of NSP, the fear on fostering drug use via NSP has to be rejected, too. There is only one qualitative study which dates back to 1998 which found out, that some prisoners, who had stopped using drugs, started drug use in prison again and others changed from other routes of administration to IDU. In the study it was suggested that the presence

of anonymous syringe dispensing machines might serve as temptation (Gross 1998 cited from Lines et al. (Lines et al. 2005)). In some cases, a change of the route of administration to IDU was also reported by Stark et al. (Stark et al. 2006). These concerns have been discussed in scientific literature intensively. On one hand, these phenomena have been observed in two studies for single cases only and there is no quantitative study reporting an increase of (injecting) drug use after the implementation of a NSP in prison. On the other hand, relapse to drug use and change of other routes of administration to IDU also happen in prison without NSP (Long et al. 2004; Stark et al. 2006). The hypothetical argument that prison needle exchange would undermine abstinence-based messages and programmes by condoning drug use can be objected. In most cases, NSP is part of a wider range of interventions and – like outside prison – NSP sometimes constitutes the first health-related contact with IDUs. After the introduction of NSP, an increase of treatment referrals has been observed in some prisons. NSP has successfully cohabited in prisons with other drug addiction prevention and treatment programmes (Stöver et al. 2008).

The statement against full coverage of NSP in prison states that: the successful implementation of prison needle exchange programmes in one prison does not mean that it will be possible to implement NSP in other prisons (since existing programmes are based on specific and unique institutional environments evidence). Contradictory to this statement, we realised that in different countries with various settings, NSP has been implemented successfully. The best possible example for offering NSP in prison is Spain where NSP is implemented nationwide in 41 prisons with good coverage.

4.5 Conclusions and recommendations

Based on the literature reviewed, it can be concluded that NSP in prison is an effective method to decrease the rate of needle sharing and as a consequence to avoid infection with HIV, HBV and HCV. Although, the number of countries that have implemented syringe exchange in prison is limited, these programmes have been established successfully in different settings and diverse environments. The concern over negative consequences of NSP in prison has been proven to be unfounded.

It is striking that – despite scientific evidence and numerous guidelines and political papers in favour of NSP in prison – the implementation of these programmes is restricted to five EU countries at the moment. The following conclusions can be drawn:

- » NSP as part of a comprehensive package of harm reduction and health-related measures in prison can be supported strongly.
- » As it seems that the lack of implementation is due to political reasons (Brett 2012) a strong need for political support exists. Furthermore, scientific evidence on effectiveness and models of good practice is available.

5 Review on route of administration

Which interventions focus on the route of administration (e. g. avoid shifting to injecting drug use (IDU) from other routes or promote shifting from IDU to other routes of administration)? How successful are these programmes concerning the reduction of drug-induced deaths?

5.1 Background

Data on route of administration of opioids are collected by EMCDDA in the framework of the Treatment Demand Indicator (TDI) and partly through the Problem Drug Use Indicator (PDU). The data from the TDI refer to the period before starting treatment (30 days before the start of treatment) and concern two types of pattern of drug use: the route of administration of the primary drug and the current/ever injection behaviour for any drug. This may result in quite different pictures and provides additional information on risk behaviours. Methodological limitations may originate from problems of data validity in the phase of recording the client's information and the lack of information on past drug use behaviours (the TDI reports if a person has been an injector but it is unknown for which drug). The new TDI-protocol 3.0 is tackling these problems.

A look at the data leads to the following conclusions:

- a) The three main routes of illegal administration of opioids in Europe are injection, smoking/inhaling ("chasing the dragon") and sniffing/snorting.
- b) There are significant differences in the proportion of injecting, smoking and sniffing of opioids.

Since drug-injecting is regarded as the most harmful route of administration concerning the risk of infection with drug related infectious diseases as well as fatal overdoses (Fischer et al. 2006), the differences between countries seem to be relevant.

A well researched intervention to change the route of administration of opioids from injecting to ingestion via eating/drinking is opioid substitution treatment (Bridge 2010). An overview about the respective literature can be found in the main report in section (10.2.2). The route of administration of opioids outside of OST (e. g. heroin) differs a lot between countries and regions (see Table 5.1) and there is a lot of evidence about changes in routes of administration in the course of a drug-career (de la Fuente et al. 1997). Due to these facts the assumption that there might be possibilities to influence the route of administration is plausible.

Table 5.1:

Route of administration of clients entering treatment by primary drug, 2010 or most recent year available – all opioid outpatient clients by country and usual route of administration (%)

Route of administration of opioids					
Country	Inject	Smoke/inhale	Eat/drink ¹¹	Sniff	Others
Austria	34,7	6,5	17,9	40,8	0,0
Belgium ¹	20,6	63,7	12,8	2,7	0,2
Bulgaria	81,8	4,6	0,9	7,4	5,2
Cyprus	64,1	29,9	3,2	2,8	0,0
Czech Republic	79,3	7,4	8,9	4,2	0,1
Denmark	15,6	19,5	58,8	6,1	0,0
Estonia ²	86,5	11,4	1,3	0,8	0,0
Finland	74,7	0,5	16,7	8,1	0,0
France	22,8	14,1	9,3	52,9	0,9
Germany	35,8	17,0	39,7	6,6	1,0
Greece	38,0	10,5	0,9	50,5	0,0
Hungary	69,3	15,2	11,7	3,9	0,0
Ireland	32,0	60,9	7,0	0,1	0,0
Italy ³	53,3	35,3	1,9	8,7	0,8
Latvia ⁴	93,5	0,3	5,5	0,7	0,0
Lithuania	:	:	:	:	:
Luxembourg	68,4	30,5	0,0	0,0	1,1
Malta ⁵	61,2	30,9	0,4	5,8	1,7
Netherlands ⁶	7,0	77,3	13,4	2,4	0,0
Poland ⁷	66,2	29,2	4,2	0,4	0,0
Portugal ⁸	14,5	84,1	0,9	0,4	0,1
Romania	91,4	6,9	1,0	0,8	0,0
Slovakia	78,0	12,4	3,5	6,0	0,0
Slovenia	51,9	35,0	2,5	10,6	0,0
Spain ⁹	16,4	71,1	5,1	6,0	1,4
Sweden	58,5	11,3	27,6	2,3	0,3
UK ¹⁰	33,5	54,9	10,0	0,9	0,7
Croatia	73,4	5,2	1,5	19,9	0,0

Notes:

1 – In Belgium if the exact primary drug is not known, the generic category is recorded. In 2010 there were 198 opiates, 7 cocaine, 7 stimulants, 2 hypnotics and sedatives and 1 hallucinogens clients with the exact primary drug unknown. 24 of which were new clients for opiates and 5 for stimulants. 2 – Data are from outpatient, inpatient treatment centres and prisons (aggregated data). 3 – In 2010 around 29 % of all clients and 30 % of new clients were registered as not known / missing for the primary drug category. Caution should be made when comparing data over time. 4 – In 2010 Latvia submitted a new dataset with a more precise TDI EMCDDA definition. Caution should be made when comparing data with previous years. 5 – Data refer to outpatient and inpatient treatment centres, low-threshold services and prisons (aggregated data). 6 – Data are from outpatient, inpatient treatment centres and low-threshold services (aggregated data). 7 – Data are from 2009. Double counting is not eliminated in data from outpatient centres. Caution should be made when interpreting the data. Heroin includes both heroin and so called "kompot" (heroin gained from the poppy straws). 8 – In 2010 a new national information system implying methodological changes particularly in the registration criteria has been implemented. 9 – Data are from 2009. Data are from outpatient treatment centres and some treatment units in prison (aggregated data). 10 – Data are from 1st of April 2009 to 31st of March 2010.

11 – data on eat/drink as route of administration has to be interpreted very cautiously because sometimes clients name substances prescribed for substitution treatment as their primary drug (e.g. if a client has been in a stable substitution treatment – with no use of any other opioids than the prescribed substitution medication for 10 years – starts a new outpatient treatment episode).

Source: EMCDDA Statistical Bulletin 2012 – TDI-17/2

In addition there are some well documented transitions of whole groups of drug users over a rather short time period from one route of administration to another. The most prominent example is the decrease of injecting as the dominant route of administration, from two thirds to one third in the Netherlands, from the mid 1980s to the mid 1990s (van Ameijden/Coutinho 2001). The complex background of this change is discussed by Grund and Blanken (Grund/Blanken 1997). Routes of administration can be seen as a cultural ritual, which is influenced by many factors. Two of them were important ecological aspects: On the one hand in the “Chinatowns” of Amsterdam and Rotterdam a well established community of opium smokers existed since the 1960s and on the other hand the street market was dominated by dealers from Surinam with a cultural “needle taboo”. These two factors lead to a stigmatisation of injecting drug use that had come to the Netherlands in the 1970s in the context of the “protest culture” originating from the US. Other supporting factors have been the early implementation of low threshold methadone programmes and HIV-prevention programmes.

It is important to note that individual changes in the route of application are not single irreversible events. A lot of drug users change their predominant route of administration several times in the course of their drug-career (Bravo et al. 2003).

5.2 Methods

A systematic literature research with predefined keywords was performed in Medline, Eric, Psycinfo, Embase and the Cochrane Library. To identify relevant publications, three keywords-clusters were connected; one with the terms opioids/opiates, the second with route of administration and third with change/switch/shift/transition. For details see search strategy in section 6.

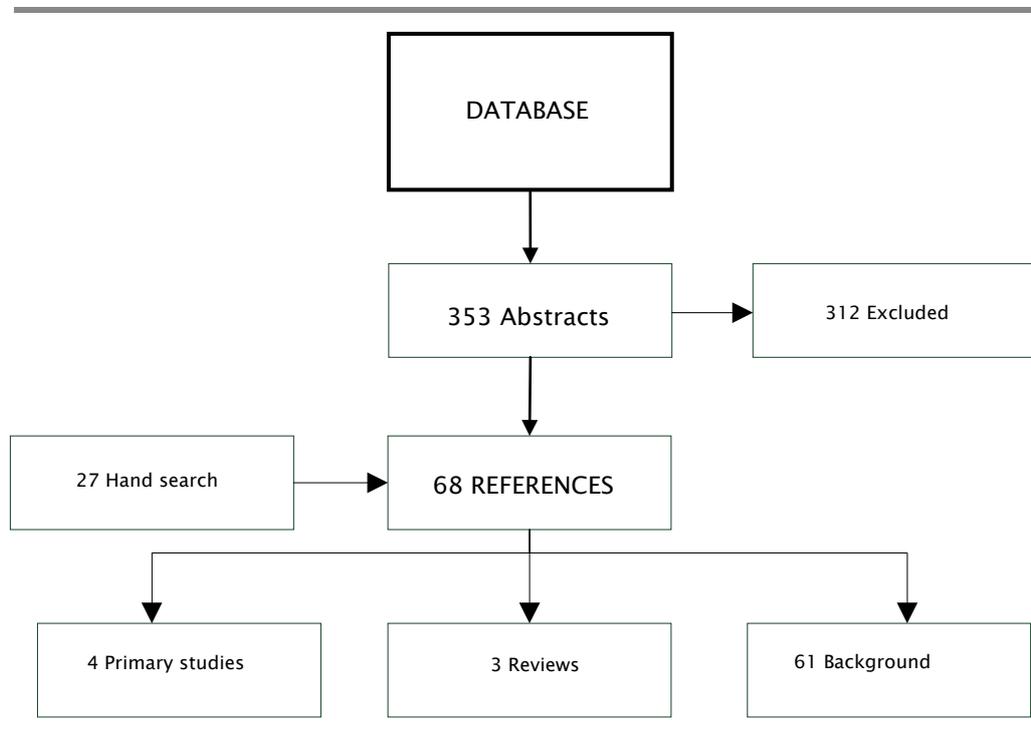
The selection of abstracts and full-text versions was performed according to predefined selection criteria. The original plan to focus on studies on interventions had to be broadened due to the fact that very few studies on interventions have been found. In addition, studies on factors which might influence the route of administration have been included. Exclusion criteria for the 353 identified abstracts were: studies not published in English or German, studies focusing on other themes than route of administration of opioids and studies conducted before the year 2000.

In addition a hand search was conducted based on citations found in the systematic literature review. Furthermore, literature used for a recently published article on route of administration by the authors (Busch/Eggerth 2010) and a diploma thesis on predictors of transition and interventions supervised by EMCDDA (Stellamanns 2008) were included.

5.3 Results

No study that investigates the primary outcome “reduction of drug-induced deaths” has been identified. Two reviews and two studies focusing on route transition interventions published after 2000 have been identified. Due to the lack of recent studies, all evaluations mentioned in the reviews (one randomised controlled trial and one longitudinal study) and another review dating back to before 2000 were included too. Studies focusing on factors influencing transitions in route of administration have been included in the background literature (see Figure 5.1).

Figure 5.1:
Identification and selection of articles for route of administration



Source: GÖG-own presentation

5.3.1 Interventions to influence route of administration

There are just four different forms of interventions to promote non-injecting routes of administration (NIROA) described in literature:

Motivation and information:

The “chasing campaign” in the UK has been developed by the Healthy Option Team, London, in partnership with the Respect Users Union to promote heroin “chasing” as an alternative route of drug administration for injectors. The campaign was based on a social marketing approach and presented arguments concerning the relative benefits of “chasing”, along with detailed technical guidance aimed at injecting drug users who lack the skills or inclination to use the technique (Hunt et al. 1999). No evaluation is available.

Provision of equipment for NIROA:

In Australia, the Netherlands, Spain and the UK some needle exchange programmes provide sheets of aluminium foil for people who want to smoke or “chase” their drugs. In the Netherlands, foil is distributed in all 22 safer injecting facilities (Bridge 2010). Only one evaluation study on this kind of intervention has been identified.

Evaluation: Specially produced foil packs to promote a transition from heroin injecting to inhalation together with information and counselling have been provided to attendees of four needle and syringe exchange sites in South-West England. Out of 320 attendees between October 2006 and August 2007, 54 % took the offered foil packs. In addition, 32 new people, who “chased” heroin but did not inject, attended the service. More detailed data based on a baseline and a follow up questionnaire are available for one NSP-site only (48 recent injectors who took foil). Prior to the introduction of the foil packs, 46 % of this sub-group reported “chasing” heroin in the previous four weeks. At follow up, 85 % reported using the foil to “chase” heroin on occasions when they would otherwise have injected. Among the people who took the foil pack, client satisfaction with the quality and size of the foil packs was good and respondents viewed its availability as a valuable extension to the NSP's services (Pizzey/Hunt 2008).

Discussion: Although there is only one poor quality evaluation-study (no comparison), foil distribution has been implemented in some countries. Further evaluation is necessary, but the above reported first results are promising. No final evidence statement can be derived.

Prescription of “heroin reefers”:

Heroin reefers have occasionally been prescribed to drug users in the UK but no data have been published to allow this technique to be assessed (Hunt et al. 1999).

Training programmes to prevent transitions to injecting:

The “Sniffer” programme for intranasal heroin users in New York, based on social learning principles, challenged positive myths about IDU, reinforced motives for avoiding injecting and developed coping skills (Bridge 2010).

Evaluation: 104 subjects (eligibility criteria: administration of heroin predominantly sniffing, no more than 60 drug injections in the last two years, HIV and hepatitis B antibody negative) have been recruited via advertisements, in treatment centres and via snowballing. They were offered a \$20 payment for participation in the study. Data were collected using a questionnaire at baseline and a follow-up questionnaire after a mean of 8,9 months (range from 5 to 21 months). Subjects were randomly assigned to the intervention group and the control group. The intervention group received presentation of didactic materials, group discussions, role playing of critical situations but also information on safer injecting. The control group received HIV counselling at baseline only. At follow up, it was possible to interview 83 subjects (80 % of the sample at baseline). 15 % (6 of 40) of the persons assigned to the intervention group injected during the follow up period compared to 33 % (14 of 43) in the control group ($\chi^2 = 3,5$, $p < ,05$ one-tailed testing) (des Jarlais et al. 1992).

A brief intervention for use with current injectors has been developed in UK (“Break the Circle”). The intervention aimed to increase contemplation about injecting, reduce injection in presence of non-injecting users and reduce talk about injection with non-injecting users (behaviours hypothesised to promote injecting and encourage initiation requests). The intervention was also the basis for a “Prevention of Transition to Injecting” project in Australia (Bridge 2010).

Evaluation: The intervention lasted for around one hour and consisted of five main sections: the participants own initiation, the initiation of others in the past, the risks from initiation, identification of behaviour that may inadvertently promote injecting and common initiation scenarios. Follow-up data were available for 73 of original 86 participants and (self-reported) changes in the desired direction were found. Injection in presence of non-injecting users decreased from 97 to 49 injections in front of non-injecting drug users in comparison to the three months period before the training. The number of requests for initiation from non-injecting drug users decreased from 36 to 15 requests and the initiations from six to two. But the number of non-injectors with whom injection was discussed did not change. In addition significant reduction of willingness to initiate (scale based on a questionnaire) and a significant increase of awareness of risks from initiating were observed (Hunt et al. 1999; Hunt et al. 1998).

In Australia a five session programme was developed for people who inject drugs to promote transitions to NIROA. The intervention included components of motivational enhancement therapy with a focus on negative aspects of injection and benefits of NIROA, a video, goal-setting discussion, written material on NIROA, cognitive restructuring (challenging unrealistic beliefs and expectancies about injecting) and behavioural skills training as well as relapse prevention.

Evaluation: It was possible to follow 10 of originally 42 subjects who had started the training for 6 months (3 months 21). For these ten subjects a significant reduction of injection frequency and syringe sharing was observed (Dolan et al. 2004).

Discussion: One evaluation of training programmes follows the RCT-approach and shows significant improvement. The others included no comparison and are based on low sample size. The study of Dolan et al. faced a high drop-out rate which leads to a high bias risk. Although some of the results are promising no final evidence statement can be derived.

5.3.2 Factors influencing the route of administration

A lot of factors influencing route transition have been described in the literature. Important **risk factors for shifting from NIROA to IDU** are for example: depression (Cepeda et al. 2012), longer drug-career (many drug users start with NIROA and change to IDU when their drug addiction gets heavier) (Malekinejad/Vazirian 2012), homelessness (Roy et al. 2007), poly-drug use (Emmanuel/Attarad 2006), lifetime history of sexual violence (Cheng et al. 2006), an injecting partner (Sherman et al. 2002), many IDUs in the social network (Koram et al. 2011), younger age at first heroin use (Neaigus et al. 2006), school drop-out (Fuller et al. 2002), belief that injection is more efficient route than smoking or sniffing (Bravo et al. 2003) and prison (Long et al. 2004). Important factors associated with **shifting away from injecting to non-injecting routes** of administration are: opioid substitution treatment (Hunt et al. 2005) concerns about health (Des Jarlais et al. 2007), social stigmatisation of injecting (Des Jarlais et al. 2007), vein problems (Bravo et al. 2003) – more details and overview (Hunt et al. 2005; Roy et al. 2007; Stellamanns 2008).

The availability of different kinds and purity of heroin or opioids might also play a role in the frequency of different routes of application. In Spain the predominance of brown and white heroin in different regions showed a relation to the predominant route of administration. A study showed that while in Barcelona three quarter of heroin users injected, in Madrid and Seville less than one quarter injected and the predominant route of administration was smoking. These regional differences showed a strong relation to the seizures of brown and white heroin. There were more seizures of brown heroin in regions where smoking prevailed (de la Fuente et al. 1997; de la Fuente et al.

1996). Since brown heroin volatilises at a low temperature it is more appropriate for smoking than white heroin which burns before volatilisation (Hunt et al. 2005).

A more recent example for a shift in the other direction is the recent development in Iran where an increase of injection of heroin and a decrease of opium smoking can be observed. Reasons discussed for this shift are the appearance of a cheap, white powdered, more potent form of heroin locally known as “Kerack”. “Kerack” is reported as easier to prepare for injection, being soluble in water without acid based materials or heating. “Kerack” was also reported to produce withdrawal symptoms more rapidly, thereby requiring more frequent injection.

Based on this correlation between different kinds of opioids available and routes of administrations some authors propose to try to indirectly influence the ingestions routes via manipulating the drug market. This could be done for example by concentration of criminal justice efforts on sectors of the black market dealing with injectable drugs like white heroin (Hunt et al. 1999). This proposal has never been realised, possibly due to legal problems. Another aspect which might be relevant and where manipulation is much easier is the medicines used for medical treatment (e.g. pain treatment, opioid substitution treatment). A recent study based on 59.792 patients entering treatment for substance use disorders in 464 treatment centres in the USA shows, that – when a medication is abused – the risk of injecting the medication varies for different medicines. In particular for the compounds/formulations with morphine and hydromorphone a higher risk for injecting drug use was found (Butler et al. 2011).

5.4 Conclusions

Although the importance of the route of administration for prevention of infectious diseases as well as for prevention of drug-induced deaths has been reported in literature for 20 years, interventions as well as research on interventions to influence route of administration of opioids other than OST are scarce. Foil distribution in needle exchange facilities is the only measure that has been implemented in some countries, but only one evaluation, showing promising results, is available (from the UK).

An indirect way to influence the route of administration discussed in the literature is manipulating the drug market. This approach has never been realised, possibly due to legal reasons. Since it is unavoidable that a part of the medication (pain relievers, medications for opioid substitution treatment) spreads to the black market, this could be used in avoiding prescription of medicines that can easily be misused via injection.

One way to gather more insight into factors influencing the route of administration would be to analyse differences in route of administration between countries.

6 Search strategies

Search strategy naloxone distribution

Database: Embase <1988 to 2012 Week 46>

Search Strategy:

-
- 1 (peer* adj3 program*).ti,ab.
 - 2 (peer* adj5 administration).ti,ab.
 - 3 self administration.ti,ab.
 - 4 first aid training.ti,ab.
 - 5 (naloxone adj5 distribution).ti,ab.
 - 6 1 or 2 or 3 or 4 or 5
 - 7 Naltrexone.ti,ab.
 - 8 naloxone.ti,ab.
 - 9 exp *Naloxone/
 - 10 7 or 8 or 9
 - 11 6 and 10
 - 12 (opioid or opiate).ti,ab
 - 13 opiate addiction/ or opiate substitution treatment/
 - 14 12 or 13
 - 15 11 and 14
 - 16 limit 15 to human
 - 17 limit 16 to (english or german)

Database: PsycINFO <1806 to November Week 3 2012>

Search Strategy:

-
- 1 (peer* adj3 program*).ti,ab.
 - 2 (peer* adj5 administration).ti,ab.
 - 3 self administration.ti,ab.
 - 4 first aid training.ti,ab.
 - 5 (naloxone adj5 distribution).ti,ab.
 - 6 1 or 2 or 3 or 4 or 5

- 7 Naltrexone.ti,ab.
- 8 naloxone.ti,ab.
- 9 exp *Naloxone/
- 10 7 or 8 or 9
- 11 6 and 10
- 20 (opioid or opiate).ti,ab.
- 21 11 and 20
- 22 limit 21 to (english or german)

Database: Ovid MEDLINE(R) 1946 to Present with Daily Update

Search Strategy:

-
- 1 (peer* adj3 program*).ti,ab.
 - 2 (peer* adj5 administration).ti,ab.
 - 3 self administration.ti,ab.
 - 4 first aid training.ti,ab.
 - 5 (naloxone adj5 distribution).ti,ab.
 - 6 1 or 2 or 3 or 4 or 5
 - 7 Naltrexone.ti,ab.
 - 8 naloxone.ti,ab.
 - 9 exp *Naloxone/
 - 10 7 or 8 or 9
 - 11 6 and 10
 - 12 limit 11 to humans
 - 13 limit 12 to (english or german)

Search strategy prison release management

Database: PsycINFO <1806 to December Week 3 2012>

- 1 prisons/
- 2 (prison\$ or jail\$).ti,ab.
- 3 1 or 2
- 4 (opioid or opiate).ti,ab.
- 5 exp opiates/
- 6 4 or 5
- 7 3 and 6
- 8 release\$.ti,ab.
- 9 7 and 8
- 10 limit 9 to (english or german)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)
<1946 to Present>

- 1 Prisons/
- 2 prison\$.ti,ab.
- 3 1 or 2 (14088)
- 4 (opioid or opiate).ti,ab.
- 5 exp opioid-related disorders/
- 6 4 or 5
- 7 3 and 6
- 8 release\$.ti,ab.
- 9 7 and 8
- 10 limit 9 to (english or german)

Database: Embase <1988 to 2012 Week 50>

- 1 prison/
- 2 (prison\$ or jail\$).ti,ab.
- 3 1 or 2
- 4 (opioid or opiate).ti,ab.

- 5 opiate addiction/
 - 6 opiate/ae, do, it, to [Adverse Drug Reaction, Drug Dose, Drug Interaction, Drug Toxicity]
 - 7 4 or 5 or 6
 - 8 3 and 7
 - 9 release\$.ti,ab.
 - 10 8 and 9 (61)
 - 11 limit 10 to (english or german)
-

Database: ERIC <1965 to November 2012>

Search Strategy:

- 1 (prison\$ or jail\$).ti,ab.
 - 2 (opioid or opiate).ti,ab.
 - 3 exp Drug Addiction/ or exp Drug Abuse/ or exp "Drug Use"/
 - 4 2 or 3
 - 5 1 and 4
 - 6 release\$.ti,ab.
 - 7 5 and 6
-

Search strategy needle exchange in prison

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

- 1 Needle-Exchange Programs /
- 2 (Supervised adj3 Inject\$.ti,ab.
- 3 ((needle\$ or syringe\$) adj3 exchange\$.ti,ab.
- 4 ((needle\$ or syringe\$) adj3 (change\$ or replace\$)).ti,ab.
- 5 1 or 2 or 3 or 4
- 6 prisons/
- 7 (prison\$ or jail\$.ti,ab.
- 8 6 or 7
- 9 5 and 8
- 10 limit 9 to (english or german)

Database: EBM Reviews – Cochrane Database of Systematic Reviews <2005 to November 2012>, EBM Reviews – ACP Journal Club <1991 to November 2012>, EBM Reviews – Database of Abstracts of Reviews of Effects <4th Quarter 2012>, EBM Reviews – Cochrane Central Register of Controlled Trials <December 2012>, EBM Reviews – Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews – Health Technology Assessment <4th Quarter 2012>, EBM Reviews – NHS Economic Evaluation Database <4th Quarter 2012>

- 1 (Supervised adj3 Inject\$.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
- 2 (Supervised adj3 Inject\$.ti,ab.
- 3 ((needle\$ or syringe\$) adj3 exchange\$.ti,ab.
- 4 ((needle\$ or syringe\$) adj3 (chang\$ or replac\$)).ti,ab.
- 5 1 or 2 or 3 or 4
- 6 (prison\$ or jail\$.ti,ab.
- 7 prisons/
- 8 6 or 7
- 9 5 and 8

Database: Embase <1988 to 2012 Week 50>

-
- 1 preventive health service/
 - 2 (Supervised adj3 Inject\$.ti,ab.
 - 3 ((needle\$ or syringe\$) adj3 exchange\$.ti,ab.
 - 4 ((needle\$ or syringe\$) adj3 (change\$ or replace\$)).ti,ab.
 - 5 2 or 3 or 4
 - 6 prison/
 - 7 prisoner/
 - 8 (prison\$ or jail\$.ti,ab.
 - 9 6 or 7 or 8
 - 10 5 and 9

Database: PsycINFO <1806 to December Week 3 2012>

-
- 1 exp Needle Exchange Programs/
 - 2 (Supervised adj3 Inject\$.ti,ab
 - 3 ((needle\$ or syringe\$) adj3 (chang\$ or replac\$)).ti,ab.
 - 4 ((needle\$ or syringe\$) adj3 exchange\$.ti,ab.
 - 5 1 or 2 or 3 or 4 (805)
 - 6 (prison\$ or jail\$.ti,ab.
 - 7 prisons/
 - 8 6 or 7
 - 9 5 and 8
 - 10 limit 9 to (english or german)

Database: ERIC <1965 to November 2012>

-
- 1 ((needle\$ or syringe\$) adj3 exchange\$.ti,ab.
 - 2 ((needle\$ or syringe\$) adj3 (chang\$ or replac\$)).ti,ab.
 - 3 (prison\$ or jail\$.ti,ab.
 - 4 1 or 2
 - 5 3 and 4 (0)

Search strategy 4: route of administration

Database: PsycINFO <1806 to October Week 4 2012>

Search Strategy:

- 1 ((substance* or drug*) adj4 (inject* or intravenous)).ti,ab.
- 2 (opiat* adj4 (inject* or intravenous)).ti,ab.
- 3 ((opiate or opioid) adj3 (substitut* or misus* or addict* or use* or depend*)).ti,ab.
- 4 1 or 2 or 3
- 5 ((route* or way* or mode*) adj5 administ*).ti,ab.
- 6 ((route* or way* or mode*) adj5 drug use*).ti,ab.
- 7 ((route* or way* or mode*) adj5 consumption).ti,ab.
- 8 ((route* or way* or mode*) adj5 intake).ti,ab.
- 9 5 or 6 or 7 or 8
- 10 (alter* or chang* or switch* or shift* or transition).ti,ab.
- 11 9 and 10
- 12 ((chang* or switch* or shift* or transition) adj6 non-inject*).ti,ab.
- 13 11 or 12
- 14 4 and 13
- 15 limit 14 to (english or german)

Database: Embase <1988 to 2012 Week 43>

Search Strategy:

- 1 ((substance* or drug*) adj4 (inject* or intravenous)).ti,ab.
- 2 (opiat* adj4 (inject* or intravenous)).ti,ab.
- 3 ((route* or way* or mode*) adj5 administ*).ti,ab.
- 4 ((route* or way* or mode*) adj5 drug use*).ti,ab.
- 5 ((route* or way* or mode*) adj4 consumption).ti,ab.
- 6 ((route* or way* or mode*) adj4 intake).ti,ab.
- 7 3 or 4 or 5 or 6
- 8 (alter* or chang* or switch* or shift* or transition).ti,ab.
- 9 ((chang* or switch* or shift* or transition) adj6 non-inject*).ti,ab.
- 10 7 and 8
- 11 9 or 10

- 12 exp *drug administration route/
- 13 1 or 2 or 12
- 14 11 and 13
- 15 limit 14 to humans
- 16 limit 15 to (english or german)
- 17 limit 16 to yr="2008 -Current"
- 18 limit 16 to medline
- 19 16 not 18

Database: Ovid MEDLINE(R) 1946 to Present with Daily Update

Search Strategy:

-
- 1 ((substance* or drug*) adj4 (inject* or intravenous)).ti,ab.
 - 2 opioid-related disorders/
 - 3 Opiate Substitution Treatment/
 - 4 (opiat* adj4 (inject* or intravenous)).ti,ab.
 - 5 Substance Abuse, Intravenous/
 - 6 1 or 2 or 3 or 4 or 5
 - 7 ((route* or way* or mode*) adj5 administ*).ti,ab.
 - 8 ((route* or way* or mode*) adj5 drug use*).ti,ab.
 - 9 ((route* or way* or mode*) adj4 consumption).ti,ab.
 - 10 ((route* or way* or mode*) adj4 intake).ti,ab.
 - 11 7 or 8 or 9 or 10
 - 12 (alter* or chang* or switch* or shift* or transition).ti,ab.
 - 13 ((chang* or switch* or shift* or transition) adj6 non-inject*).ti,ab.
 - 14 11 and 12
 - 15 13 or 14
 - 16 6 and 15
 - 17 limit 16 to humans
 - 18 limit 17 to (english or german)
 - 19 limit 17 to yr="2008 -Current"

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <October 26, 2012>

Search Strategy:

- 1 ((substance* or drug*) adj4 (inject* or intravenous)).ti,ab.
- 2 (opiat* adj4 (inject* or intravenous)).ti,ab.
- 3 ((opiate or opioid) adj3 (substitut* or misus* or addict* or use* or depend*)).ti,ab.
- 4 1 or 2 or 3
- 5 ((route* or way* or mode*) adj5 administ*).ti,ab.
- 6 ((route* or way* or mode*) adj5 drug use*).ti,ab.
- 7 ((route* or way* or mode*) adj5 consumption).ti,ab.
- 8 ((route* or way* or mode*) adj5 intake).ti,ab.
- 9 5 or 6 or 7 or 8
- 10 (alter* or chang* or switch* or shift* or transition).ti,ab.
- 11 9 and 10
- 12 ((chang* or switch* or shift* or transition) adj6 non-inject*).ti,ab.
- 13 11 or 12
- 14 4 and 13
- 15 limit 14 to (english or german)

Abbreviations

ACMD	British Advisory Council on the Misuse of Drugs
AIDS	acquired immune deficiency syndrome
CPR	cardiopulmonary resuscitation
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EU	European Union
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HTA	Health Technology Assessment
IDU	injecting drug user, injecting drug use
MMT	methadone maintenance treatment
NIROA	non injecting route of administration
NSP	needle (and syringe) exchange programme
OST	opioid substitution treatment
PDU	problem drug use
PICO	population–intervention–comparison–outcome
RCT	randomised controlled trial
UK	United Kingdom
WHO	World Health Organization

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