



European Monitoring Centre
for Drugs and Drug Addiction



TECHNICAL REPORT

Systematic review on the prevention and control of blood-borne viruses in prison settings

Prevention and control of communicable
diseases in prison settings

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Abbreviations

Ab	Antibodies
AGREE	Appraisal of Guidelines for Research and Evaluation
AIDS	Acquired immune deficiency syndrome
ALT	Alanine aminotransferase
ART	Antiretroviral therapy
BBVs	Blood-borne viruses
CD4	Cluster of differentiation 4
DAA	Direct-acting antivirals
DOT	Directly observed therapy
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFTA	European Free Trade Association
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EU	European Union
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HWBs	Health Without Barriers
IFN	Interferon
NICE	National Institute for Health and Clinical Excellence
MSM	Men who have sex with men
NR	Not reported
NSP	Needle and syringe programme
OST	Opioid substitution treatment
PEG-IFN	Pegylated interferon
PEP	Post-exposure prophylaxis
PICO	Population-Intervention-Comparison-Outcome
PLHIV	People living with HIV
PrEP	Pre-exposure prophylaxis
PWID	People who inject drugs
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
RBV	Ribavirin
RCT	Randomised controlled trial
RNA	Ribonucleic acid
SSTI	Skin and soft tissue infection
SVR	Sustained viral response
TB	Tuberculosis
UNISS	Università degli Studi di Sassari
UK	United Kingdom
USA	United States of America
WHO	World Health Organization

Glossary

Acceptability	How acceptable a given intervention is to the target population in relation to the effect of the intervention
Accessibility	How accessible a given intervention is to the target population (availability of good health services within reasonable reach and when needed) [1]
Correctional facility	All institutions where a state holds people deprived of their liberty (e.g. prison or jail), excluding migrant centres and police detention rooms
Directly observed therapy (DOT)	An approach which seeks to improve treatment adherence by active monitoring and recording of the consumption of each and every drug dose by an 'observer' acceptable to the patient and the health system [2]
Feasibility	Whether it is feasible to implement an intervention in terms of time, money, or other circumstances
Jail	Locally-operated, short-term facilities that hold people awaiting trial or sentencing or both, and people sentenced mostly to a term of less than one year
Prevention, care and treatment of HIV (macro area 4)	All public health measures to prevent HIV and minimise HIV transmission within the prison environment and in the community, including mother-to-child transmission and post-exposure prophylaxis
Prevention, care and treatment of viral hepatitis (macro area 5)	All public health measures to prevent viral hepatitis and minimise viral hepatitis transmission within the prison environment and in the community, with a focus on hepatitis C treatment
Prevention and control of injecting-related infections among PWID (macro area 6)	All public health measures to prevent injecting-related infections and minimise transmission of these infections among current or former drug users within the prison environment and the community
Prison	All institutions where a state holds adults deprived of their liberty (e.g. prison or jail), either sentenced or on pre-trial detention (remand), excluding migrant centres, and police detention rooms, and other facilities such as juvenile prisons or secure training centres for children and young people.
Prison population	Adult individuals aged 18 and older detained in prison for custody, remand or awaiting trial. In certain instances, the term may include individuals visiting correctional facilities, intervening in various capacities or prison staff working also in various capacities. This population includes vulnerable groups, i.e. men who have sex with men (MSM), transgender, people who inject drugs (PWID), foreign-born persons, homeless people, people with mental health and/or substance misuse needs (including alcohol) and others.
Problem drug use	Injecting drug use or long-duration/regular use of opioids, cocaine and/or amphetamines
Service model	An operational approach to deliver an intervention, defined by descriptors such as time (e.g. at entry, during stay, at release), target population (e.g. universal), modality of offer/service delivery (e.g. healthcare provider, setting), etc.
Throughcare	It entails continuity of care when transitioning from the community to prison settings, as well as from prison settings back into the community. The latter covers both interventions starting in prison settings aimed at prevention of blood-borne viruses (BBVs) post-release, as well as interventions starting in prison settings to increase linkage to care for BBVs or drug addiction post-release.
Transition planning	It entails the planning for continuity of care when transitioning from the community to prison settings, as well as from prison settings back into the community. Transition planning may also include a broad range of individual needs such as housing, social support and re-integration

Executive summary

Compared with the general public, people in prisons have a higher prevalence of infection with blood-borne viruses (BBVs) such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV). This is recognised as a major issue for the health of people in prisons, as well as the general population, because the majority of people who have been incarcerated will subsequently return to their communities.

The objective of this report was to systematically review data on prevention and control of BBVs in prison settings, with a focus on the countries of the European Union (EU) and the European Economic Area (EEA).

A systematic literature review was performed in PubMed and Embase from 1990 onwards and in Cochrane Library from 1980 onwards (search date 12 January 2017). No language or geographical limits were applied. In addition, the following sources were searched through a predefined website list search, including the websites of the main international organisations (last search date 8 May 2017) and a call for papers from experts (last call date 7 July 2017): conference abstracts (2010 or newer), unpublished research reports, protocols and guidelines (2005 or newer). A total of 66 primary articles were included from the peer-reviewed literature. In addition, 20 conference abstracts/unpublished research reports and 18 guidelines were identified from the grey literature.

Five peer-reviewed articles (none from the EU/EEA) and one conference abstract were included covering BBV prevention through health promotion interventions, condom distribution and safe tattooing programmes in prison settings. A range of 11–28% of inmates used condoms through condom provision programmes, but not necessarily for sex, and 55–84% supported condom distribution. In a US study condom provision was considered to be cost-saving, but concerns were raised over a possible increase in sexual activity, including non-consensual intercourse, and the inconsistent message of condom availability with the prohibition of sexual activities in prison. Safe tattooing in prison was shown to be acceptable for people in detention in one study, however no infection-related outcomes were reported to assess the effectiveness in reducing infection transmission. Two randomised controlled trials (RCTs) investigated a combination of health promotion and skills-building interventions, and showed conflicting results. Five additional peer-reviewed articles (two from the EU/EEA) and one conference abstract were included reporting prevention interventions targeting people who inject drugs (PWID) in prison settings. Two comparative studies on opioid substitution therapy (OST) found no difference in HIV and HCV seroconversions between the OST and control groups. Periods of imprisonment <2 months were significantly associated with increased risk of HCV seroconversion, and compared to community settings, OST dropout risk was higher in prison during short sentences (≤ 1 month) and lower during longer (>4 months) sentences. An OST programme in prison was no more costly than community-based programmes. HCV seroconversions were reported in one of the three studies on a needle and syringe programme (NSP) and were attributed to sharing of injection paraphernalia; no HIV or HBV seroconversions were reported. In a country-wide study, a reduction in HCV and HIV prevalence in the prison population over a period of more than 15 years was documented, which coincided with the introduction of a wide range of harm reduction measures in the community and prison, including a prison needle and syringe programme. However, prison staff and, to a lesser extent, people in detention, reported concerns about prison security following the distribution of sterile syringes and needles and were not persuaded of the need for such a measure.

Provision of HIV treatment in prison settings was reported in sixteen peer-reviewed articles (seven from the EU/EEA) and five conference abstracts. Two comparative studies found no significant difference in adherence and viral suppression between self-administered therapy (SAT) and directly observed therapy (DOT), while one study showed a higher proportion of viral suppression among individuals receiving DOT for HIV. A sizeable proportion of patients voluntarily transitioning from SAT to DOT modality of treatment provision was registered in one study. In another, a significant increase in the likelihood of achieving viral suppression was found in a telemedicine group compared to conventional care. Overall, all studies reported sufficiently high ranges of treatment adherence and levels of viral suppression when treatment was provided in prison settings, and the proportion of HIV treatment acceptance among those eligible was reasonably high (73–80%).

While no study was retrieved reporting on HBV treatment in prison settings, twenty-one peer-reviewed articles (seven from the EU/EEA), eleven conference abstracts and two unpublished research reports were included on HCV treatment. The majority of the included studies described provision of interferon-based regimens, and focussed on implementation modalities. Two comparative studies found no significant difference in treatment completion and sustained viral response (SVR) between SAT and DOT models of HCV care provision. Two economic evaluation studies from USA concurred that performing a liver biopsy before starting interferon-based treatment is likely to be more cost-effective approach than treating all patients. Two comparative studies found no significant difference between the main outcomes of HCV treatment completion and SVR in prison versus community, unless patients were released or transferred from prison while on treatment. Similarly, release or transfer was reported as a major predictor of treatment discontinuation in several studies.

There have been rapid developments in the management of chronic HCV infection with a new generation of medications, called direct-acting antiviral drugs (DAAs), which are now used alone or in combination with PEG-

IFN/RBV. As a result of the higher effectiveness and reduced side effects of DAAs, the use of interferon-based treatment regimes has declined. According to conference abstracts and grey literature reports, the proportion of detained patients achieving SVR was much higher with DAA-based than with interferon-based treatment. Finally, another US cost-effectiveness study suggests that HCV treatment with DAAs is more cost-effective for incarcerated persons than no treatment or treatment with older regimens, provided that it is affordable.

Many intervention studies among prison populations showed high attrition rates due to prison transfer or release, and the improvement of continuity of care between different prisons and upon release from prison – otherwise known as 'throughcare' – to reduce dropout was identified as an important issue. Thus, nineteen peer-reviewed articles (none from EU/EEA) were included reporting on the transitioning of individuals from detention into the community (throughcare); no studies were found on the transition from community into prison. Comparative studies reported the impact of behavioural and skills-building interventions aimed at improving BBVs prevention post-release. In most cases the interventions resulted in greater improvement in relation to several behavioural outcomes, such as occurrence of unprotected sexual intercourse, compared to conventional care. However, this was not the case for all measured outcomes, including some specifically relevant ones such as the sharing of used drug injecting equipment. In general, interventions were well accepted with low rates of refusal. Linkage to care post-release interventions that were investigated ranged from individual education and skills-building programmes to active referral to intensified case management. A study describing the latter (being met at the gate by a case manager) showed a significantly higher likelihood of participation in drug/alcohol treatment and significantly less engagement in sex exchange and street drug use compared to those not being met at the gate. No significant difference was reported in access to HIV care or substance abuse services, and adherence to HIV treatment post-release between intervention and control groups in the other studies. Other observational studies described conventional care approaches such as active referral to community healthcare services including provision of drug prescription to the patient upon release. For PWID receiving ART, provision of OST before release and retention on OST community programme was associated with higher likelihood of viral suppression in one study. Finally, three studies showed that initiation of OST during incarceration significantly increases the likelihood of enrolment and retention in OST community programmes.

Overall, there is considerable heterogeneity between studies in the peer-reviewed and grey literature, making comparisons difficult. A large proportion of the studies included originate from the USA prison setting, raising concerns regarding the generalisability of the findings to the situation in the EU/EEA. Overall, the level of evidence derived from the studies included is quite low; most studies had a descriptive and observational design and were conducted in single institutions with relatively small sample sizes. Moreover, study characteristics, interventions and outcomes were often poorly described.

Evidence available on interventions for prevention and control of BBVs in correctional facilities is limited, especially with regard to prevention interventions targeting PWID. More comparative studies and operational research are needed on the effectiveness and impact of interventions in correctional facilities within the EU/EEA.

In conclusion, the findings from this systematic review reveal a wide variety of interventions that use a range of prevention measures, treatment service models and linkage to care interventions directed at the prison setting, as well as predictors of intervention uptake and barriers to their implementation. Most notably, release or transfer from prison was identified as the main factor hampering adherence and/or completion of treatment for HIV, HCV and OST. These findings are crucial to informing and supporting the design of evidence-based public health interventions to increase coverage and uptake of BBV prevention measures and to scale up BBV treatment in prison settings in the EU/EEA.

1. Background

Worldwide, more than ten million people are held in prison, either as pre-trial detainees/remand prisoners or as convicted and sentenced inmates. On 1 September 2015, just over 600 000 persons were being held in prisons within the European Union/European Economic Area (EU/EEA), with considerable variation among countries [3]. The median imprisonment rate varied from 21.3 prisoners per 100 000 general population in Liechtenstein, to 53 per 100 000 in the Netherlands and 277.7 per 100 000 in Lithuania. When considering the whole European region, the median age of the prison population was 35 years, and the average length of stay seven months [3]. Across the Member States of the Council of Europe, on average, 17.3% of inmates were sentenced for drug offences, followed by 16.8% who committed theft and 12.9% robbery. The main offence of 14.9% of prisoners was attempted or perpetrated homicide, 9.4% were convicted for battery and assault, and 7.6% for sexual crimes [3].

Prisons pose particular challenges to reducing the burden of infectious diseases. In part, this is the result of prison settings being a high-risk environment, and also because people entering prison settings may already have elevated levels of infection. Compared with the general public, people in jails or prisons have a high prevalence of infection with human immunodeficiency virus (HIV), hepatitis B, hepatitis C, syphilis, gonorrhoea, chlamydia and tuberculosis (TB) [4]. Those who are healthy on entry are at greater risk of exposure to communicable diseases such as HIV or viral hepatitis in prison and are more likely to develop drug addiction problems or mental illnesses over their lifetime than the general population [5,6].

Most people in European prisons are from poor communities and vulnerable social groups and an increasing proportion of people have migrant or minority ethnic backgrounds [7]. Drug users form a large part of the imprisoned population and international studies show that a large sub-group of people in prisons have used illicit drugs at some point in their lives, with many chronic users and problematic drug use patterns, such as the injection of drugs, being common [8]. Data on drug use among prison populations in Europe show that 12–43% have used heroin; 9–42% cocaine and 2–29% amphetamines [9].

Several communicable diseases are more common among people in prison than among the general population, mainly as a result of unsafe drug injection practices - e.g. the prevalence of blood-borne virus (BBV) infections is high among current and former drug users entering prison settings. The main risk factors linked with increased transmission rates inside prison settings seem to be proximity (aggravated by overcrowding), high-risk sexual behaviour, practices of injecting drugs with shared, unclean equipment, and unsafe tattooing and piercing [10,11]. The problem can be aggravated by lack of awareness of infection status, and possibly substandard healthcare. Primary, secondary and tertiary prevention offered in prison settings, especially with adequate linkage to care, could be effective in lowering infection rates [5,12].

A recent briefing on prison conditions in the Member States by the European Parliament's policy department on citizens' rights and constitutional affairs addresses the issue of healthcare in prison. It states that the 'general principle is that prisoners should enjoy an equivalent standard of care to persons outside prisons, yet their needs tend to be greater than those of free persons, as they often lead a marginalised life before entry to prison and as imprisonment may put a strain on their mental health and physical well-being'. This underlines the need for an up-to-date guidance on prison health.

1.1.1 Guidance on communicable diseases in prison settings

In 2015, the European Centre for Disease Prevention and Control (ECDC) launched a project to develop evidence-based guidance on the prevention and control of communicable diseases in prisons, jails and other custodial settings, with a special focus on EU/EEA countries. ECDC collaborated closely with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in order to explore drug use as a risk factor for the transmission of communicable diseases in prison settings and to take into account the high prevalence of people who inject drugs (PWID) among prisoners in the EU/EEA. This collaborative ECDC/EMCDDA project, the first of its kind by the two EU agencies, involved the development of joint evidence-based guidance for the control of communicable diseases in prison settings in the EU/EEA.

During the scoping phase, evidence published from 2000 to 2014 on the burden of communicable diseases, preventive measures and associated costs in prison settings in the EU was assessed, and knowledge gaps on communicable diseases in prison settings were identified. An evidence mapping tool was developed, and findings were supplemented with information from EU/EEA experts in order to define thematic areas to be addressed by the guidance document. This guidance document will be developed as a series of guidance modules on specific thematic areas (macro areas). The following macro areas will be covered:

- Macro area 1: Active case finding for selected communicable diseases on admission and during prison stay
- Macro area 2: Vaccination strategy, including vaccination at entry and vaccination in outbreak situations
- Macro area 3: Diagnosis, treatment, care and prevention of TB
- Macro area 4: Prevention, care and treatment of HIV, including throughcare

- Macro area 5: Prevention, care and treatment of viral hepatitis, with a focus on treatment for hepatitis C, including throughcare
- Macro area 6: Prevention and control of injecting-related infections among current or former drug users, including throughcare.

This systematic review report focuses on macro areas 4, 5 and 6 (i.e. prevention and control of HIV, viral hepatitis and injecting-related infections).

1.1.2 Blood-borne viruses and burden of disease in prison settings

BBVs are those viruses that can be spread through contamination by blood or other body fluids [NICE, Physical health, 2016], namely HIV, HBV and HCV for the purpose of this report. People in prisons are at increased risk of hepatitis B, hepatitis C and HIV, due to a combination of factors such as high prevalence of infection during incarceration and high prevalence of risk behaviour during detention (e.g. injecting drug use with unclean equipment, sex between men, tattooing) compounded by the characteristics of the prison environment [4,5].

Human immunodeficiency virus

HIV is a virus with a long incubation period that attacks the immune system and when untreated causes a severe, lifelong illness. The end-stage of the infection, acquired immunodeficiency syndrome (AIDS), results from the destruction of the immune system. HIV is transmitted when infected blood, semen, vaginal fluids or breast-milk enter another person's body [7,13].

Prevalence estimates for HIV among the prison population are reported as part of the monitoring of the Dublin Declaration. In 2016, 15 EU/EEA countries reported estimates ranging from 0.2% to 15.8%, with Estonia, Italy, Spain and Latvia reporting a prevalence above 5% [14]. According to a recent study assessing the global burden of HIV infection among the prison population, HIV prevalence in western Europe is estimated to be 4.2% (95% CI 2.7-6.1) [4]. While there is an overall lack of published research, available data confirm high variability of HIV prevalence among people in prisons with a history of injection drug use. Studies among this group conducted in prisons in Hungary (2008), Ireland (2010), Latvia (2010, 2011) and Sweden (2007–2010, 2012, 2013) found HIV prevalence ranging between 0% (Hungary) and 18% (Latvia) [15].

Viral hepatitis

Hepatitis B is primarily a liver disease that results from being infected with the hepatitis B virus (HBV). The symptoms can vary greatly and many of those acutely infected are asymptomatic. The infection may resolve or become chronic, with the latter being a more frequent outcome in younger age groups (from >30% among children to <5% among adults) [APHA, 2015]. Chronic hepatitis B may result in serious health outcomes such as liver cirrhosis (25%) and liver cancer (5%). Chronically infected patients may act as a reservoir for onward disease transmission [16].

In a recent systematic review of the literature coordinated by ECDC, HBV prevalence estimates that were considered representative for people in prisons were available for 12 countries, ranging from 0.3% to 25.2%, compared to a prevalence range of 0.1–4.4% in the general population [17]. Countries with the highest HBV prevalence in prison settings were Bulgaria (25.2%), Portugal (10.8%), Luxembourg (7.0%) and Italy (6.7%) [17]. According to a recent study assessing the global burden of infection among the prison population, HBV prevalence in western Europe was estimated to be 2.4% (95% CI 1.6-3.3) [4].

Hepatitis C is a liver disease caused by infection with the hepatitis C virus (HCV). HCV can cause both acute and chronic hepatitis. Most people with acute HCV infection do not have any symptoms. It is estimated that 75–85% of infections become chronic, and these are often asymptomatic until decades after infection when symptoms develop secondary to serious liver damage. Reinfection with HCV may occur among people with previously resolved infections or among chronically infected patients [7,18,19].

In many EU/EEA countries, more than half of those who inject drugs have been infected with HCV, and those who currently inject drugs or have done so in the past constitute the largest risk group for HCV transmission in the region [20,21]. In a recent systematic review of the literature coordinated by ECDC, HCV prevalence estimates considered representative for people in prisons were available for 11 countries. These estimates ranged from 4.3% to 86.3%, as compared to a prevalence range of 0.1–5.9% in the general population [17]. According to a recent study assessing the global burden of infections among the prison population, the estimated HCV prevalence among prison populations in western Europe is 15.5% (12.2–19.1), which was much higher when only looking at imprisoned PWID [4]. Even though the prison setting – together with drug treatment centres and other settings – is included in prevalence studies among PWID in several countries, research exclusively conducted in the prison setting is very limited, and those studies available are sometimes based on small samples. Available studies from Hungary (2008, 2009, 2011), Ireland (2010), Latvia (2010) and Sweden (2007-2010, 2012, 2013) among PWID found anti-HCV prevalence ranging from 12% (Hungary) to 97% (Sweden) [15].

1.1.3 Drug use and drug-related infections among prisoners

According to a recently published systematic review, substance use disorders are highly prevalent in people in prisons and much more common than in the general population [8]. The pooled prevalence estimate for drug use disorders (i.e. substance abuse and/or dependence, excluding nicotine-related disorders) in male prisoners was 30% (95% CI 22–38; $I^2 = 98\%$; 13 studies; range 10–61%) and in female prisoners it was 51% (95% CI 43–58; $I^2 = 95\%$; 10 studies; range 30–69%). Data reported to EMCCDA showed large variations in the proportion of people in prisons with experience of drug use, depending on the country and on the substance [9]. In particular, people in prisons differ greatly from the general population in their reported experience with heroin and cocaine. In recent studies, lifetime prevalence levels among prisoner populations ranged between 12% and 43% for heroin and between 9% and 42% for cocaine, versus less than 1% and less than 2% respectively for the general population having used these drugs. Harmful drug use patterns are common among people in prisons, with between 6% and 48% of detainees reporting injecting drug use prior to imprisonment [9].

Studies among problem drug users show that many have spent time in prison - between one-third and three quarters of the samples of opioid, cocaine and amphetamine users and PWID had been incarcerated [22]. Problem drug use and drug dependence increase the risk of imprisonment, due to the illegality of the drugs market and high cost of drugs. Incarceration and problem drug use patterns are intertwined and result in overlapping vulnerability, increased risks of infection with communicable diseases and worse health outcomes [14,22].

As noted above, prevalence of BBVs among PWID and people in prisons are many times higher than in the general population. PWID are also at increased risk of bacterial skin and soft tissue infections (SSTIs). Although SSTIs pose significant health risks, little is known about their prevalence and characteristics in this population, and even less in prison sub-populations. Furthermore, cases of injection-related botulism have been reported among PWID in the community, possibly related to contamination of the injecting substance [23].

1.1.4 Prevention of blood-borne viruses

Studies show that prevalence of BBVs is high when entering prison [24]. As risk behaviour for BBV transmission in prison settings is common, there is considerable potential for implementing prevention measures to control onward transmission among the prison population.

PWID and other drug users are overrepresented in prison. Despite being illegal, drugs are reported as being available and in use among the incarcerated population [14,22]. Sex is a major taboo in prison settings, however consensual and non-consensual sexual intercourses may occur; with the latter increasing the risk of transmission due to trauma. Tattooing or piercing is highly prevalent in prison settings and closely linked to the prison sub-culture. Research has demonstrated that PWID tend to get tattooed in prison settings more frequently than other people in prisons. Sharing tattooing or piercing equipment which has not been appropriately sterilised is considered to be one of the main transmission routes for BBVs in prison settings, as is the sharing of equipment for snorting drugs, such as straws or rolled notes. In addition, the potential for transmission through medical procedures should be considered, as well as vertical transmission for incarcerated pregnant women [7].

The similarities in modes of transmission of BBVs mean that prevention measures are virtually all valid for the three diseases in focus (HIV, hepatitis B and C) [7]. A solid evidence base exists for a number of public health interventions to reduce and control BBV infections in the community. HIV Pre-Exposure Prophylaxis (PrEP) is the latest addition to the existing basket of prevention options. Other prevention measures include health education; vaccination (hepatitis B only); active case finding and subsequent treatment; condoms and lubricants; use of sterile syringes, needles and other drug injecting equipment; safe tattooing and piercing programmes; post-exposure prophylaxis (HIV only); prevention of mother-to-child transmission; universal precautions for safe workplaces and health services, and reducing the sharing of everyday items (WHO, Prisons and Health, 2014; UK Dep 2011 a&b; ECDC/EMCCDA guidance 2011) [23]. However, data on the coverage of such interventions in EU/EEA prison settings are currently scarce. According to the 2016 Dublin Declaration monitoring, only six EU/EEA countries attribute high priority to HIV prevention targeting prison populations [14]. In 2016, although 12 EU/EEA countries reported having laws or policies in place that authorise the provision of condoms in prison settings, 15 countries reported that they had implemented condom distribution and promotion programmes. In contrast, lubricant promotion and distribution programmes were reported by five EU/EEA countries only. HIV PrEP was reportedly implemented in prison settings in one country, while HIV Post-Exposure Prophylaxis (PEP) was implemented in 13 countries. Half of the countries reported having health promotion or behaviour change programmes in place [14].

Prevention of injection-related infections

As injecting drug use is one of the most important types of risk behaviour for BBV infection in prison settings, measures specifically aiming to prevent injection-related infections are of the utmost importance. A solid evidence base exists for a number of cost-effective public health interventions to reduce and control infections among drug users in the community [25]. These include testing, vaccination and treatment of infections, as well as harm reduction interventions aiming to reduce drug use and injection-related risk behaviour, ranging from health

promotion and drug dependence treatment to needle and syringe programmes (NSPs) [25]. The principle that people in prison should enjoy an equivalent standard of care to that available to people outside of prison, includes the care associated with problem drug use and drug dependence among people in prison. Accordingly, various drug treatment options, in particular opioid substitution therapy (OST) have been introduced in the penitentiary systems of most European countries. In some countries, NSP have been set up as part of a comprehensive range of measures to respond to problem drug use and reduce drug-related harms in prisons. Furthermore, links between prison health services and drug treatment and rehabilitation programmes in the community aim to increase the effectiveness of services by creating a continuum of care [9,26].

However, the coverage of harm reduction interventions is low in prison settings [14,21,22,27]. Although in principle OST is reported to be widely available in EU/EEA prisons (except in Lithuania and the Slovak Republic¹ [9,21,27]), levels of provision do not match those in the community, and often those entering prison are subjected to detoxification treatment while on OST. NSPs are far less available in prisons; only three EU/EEA countries (Spain, Luxembourg and Germany) report NSP availability in all or some prisons, while Romania reports no use of the available prison NSP [14,27]. Specialised harm reduction programmes for people who inject non-opioid drugs were also available in seven EU/EEA countries. In some prison systems, disinfectants are made available for any equipment that comes into contact with blood² [27].

1.1.5 Treatment of blood-borne viruses

Human immunodeficiency virus

Nowadays, treatment with combination antiretroviral therapy (ART) enables people with HIV infection to live a long, healthy and productive life. Early treatment of HIV infection has been associated with both clinical benefits to individual patients and a dramatic decrease in the risk of transmission to sexual partners [28,29]. The effectiveness of HIV treatment as prevention (TasP) depends on starting treatment early and adhering to it. Retention in care is an essential component of HIV care, to correctly monitor treatment and to provide for other health issues such as co-morbidities, mental health, etc.

In the past few years, an increasing number of countries in the broader European region have eliminated CD4 cell count thresholds altogether or have introduced higher thresholds for starting ART. This is consistent with the European AIDS Clinical Society guidance, recommending immediate ART initiation among persons found to be HIV positive, regardless of CD4 cell count (i.e. 'test and treat') [30]. The number of countries reporting that HIV treatment is initiated regardless of CD4 cell count has increased from four in 2014 to 30 in 2016 [31]. Still, the proportion of all people estimated to be living with HIV in the EU/EEA and receiving HIV treatment is low. Based on reporting by 19 countries that had data in 2016, it is estimated that 69% of all people currently living with HIV are on treatment. However, the viral suppression rate among those who are on ART is estimated to be as high as 89%, suggesting a good level of care with successful retention strategies in place [27,31]. Based on this assumption, correctional facilities may offer a suitable platform to scale-up diagnosis and treatment among higher-risk population groups, and contribute to reaching underserved and marginalised communities bearing a disproportionate burden of HIV infection (e.g. PWID, sex workers). However, data on ART initiation and treatment coverage in prison settings in the EU/EEA are currently not available.

Barriers still exist limiting ART coverage and uptake in the EU/EEA and broader European region, including unfavourable laws and policies. More specifically, criminalisation of drug use is reported to be a potential barrier to treatment access or uptake in one particular EU/EEA country [27]. Half of the countries in the EU/EEA do not provide HIV treatment for undocumented migrants. While 15 countries provide ART for undocumented migrants on the same basis or at the same cost as for others in the country, 15 countries do not. In many of the latter, undocumented migrants are only entitled to emergency healthcare and cannot access longer-term HIV treatment, in the absence of legal residence status and/or health insurance [27,31].

Viral hepatitis

The release of new direct active antivirals (DAAs) for the management of HCV has opened new avenues for the treatment and cure of the infection. Evidence is accumulating on the high rates of safety, tolerability and efficacy of DAA regimens for the treatment of HCV-infected and HIV-HCV co-infected patients compared with interferon/ribavirin (IFN/RBV) [32,33]. IFN-free regimens with new DAAs are considered best treatment options, because of their virological efficacy, ease of use and tolerability. Since contraindications to the use of interferon include severe psychiatric illness, particularly depression, which is not uncommon among people who use drugs, the new medications represent the first real treatment option for many of them.

¹ No data available for Lichtenstein

²² European Monitoring Office for Drugs and Drug Addiction. Reitox national reporting 2016, - Prison workbooks

However, affordability remains a substantial barrier to the scale-up of DAA treatment in the EU/EEA. Limited data are currently available on the extent of DAA coverage in the EU/EEA region, based on reported consumption of HCV antivirals. In 2015, 25 of the 27 EU/EEA countries reported at least some consumption of DAAs, with great variations in relation to RBV. PWID with hepatitis C and people in prisons have been identified as a priority group for HCV treatment due to the fact that they are likely to constitute important transmission groups [34]. However, HCV testing, linkage to care, and treatment of these groups remain low, due to various barriers [35]. A review of data on treatment and prevention of HCV infection among PWIDs in Europe found high levels of undiagnosed HCV infection, and a low proportion of treatment initiation among those diagnosed [36]. The proportion of PWID with diagnosed chronic HCV infection entering antiviral treatment was found in this systematic review of 26 studies to range between 1% and 19% (median 9.5, IQR 3.5-15) in six non-clinical observational studies (four EU/EEA countries, total n=3,017). Moreover, three observational studies with non-clinical recruitment settings provided estimates of the proportion of diagnosed PWID referred to a specialist for treatment evaluation: median 57%, range 9.0–59 (3 EU/EEA countries, total n=2 958). Although access to DAAs is restricted in most EU/EEA countries, data on DAA coverage in prison settings across the EU/EEA are currently not available. A recent survey among 168 prison health units in France (response rate 38%, representing 39% of the prisoner population), reported that 70% systematically offered HCV screening to prisoners and 60% had introduced at least one DAA treatment, with 130 patients treated during 2015 [37].

However, according to guidelines from the European Association for the Study of the Liver [34], HCV treatment with new DAAs should be considered without delay in individuals at risk of transmitting HCV, including active PWIDs, MSM with high-risk sexual practices, and incarcerated individuals.

Treatment for chronic HBV infection is also available. However, there is currently no cure and the main endpoint of all current treatment strategies is the long-term suppression of HBV DNA levels. Treatment outcomes have improved over the past few decades, with the use of conventional and then pegylated interferon, and more recently with the advent of nucleos(t)ides analogues [38-40]. Similarly, as for HCV, no European level data are available on the coverage of HBV treatment in prison settings.

1.1.6 Throughcare

Transition planning to prepare for release from prison has long been identified as the weakest link in the effective re-entry of incarcerated individuals with substance use disorders, or with special health needs (e.g. chronic diseases, TB treatment, HIV treatment, mental disorders) into the community. This is especially relevant in the context of prevention and control measures for BBV infections to ensure continuity of and adherence to treatment for HIV, HBV and drug addiction (i.e. OST). While HCV treatment with DAAs may be less important, given its limited duration, HBV vaccination may require long-term follow-up and boosters when administered according to the rapid and very rapid schedules. The long-term efficacy of healthcare interventions and programmes for risk reduction are greatly diminished if intervention and care provision are terminated or disrupted when the individual transitions from one institution to another, or from a custodial institution back into the community. Many factors may contribute to such situations. For example, limited budget and resources, including staff and infrastructure, separate sphere of influence and institutional responsibility over prison and community health, and challenges in inter-sectorial cooperation [41].

For the purposes of this report, throughcare entails both continuity of care from the community to prison settings, as well as from prison settings back into the community. The latter covers both interventions starting in prison settings aimed at prevention of BBVs post-release, as well as interventions starting in prison settings to increase linkage to care for BBVs post-release.

1.2 Scope and objectives

The objective of this systematic review was to gain insight into the evidence base for the prevention and control of HIV, viral hepatitis and injecting-related infections in prisons, jails and other custodial settings.

This systematic review aims at collating and synthesising all relevant evidence (peer-reviewed as well as grey literature) with regard to prevention and control of HIV, viral hepatitis and injecting-related infections (see specific research questions in the methodology section). This report does not include BBV active case finding and HBV vaccination as these topics are covered by separate systematic reviews [24]. Assuming there are no plausible biological reasons for differences in the effectiveness of HIV and viral hepatitis treatment inside or outside prison settings, the focus of this systematic review is on treatment models of care and service delivery rather than on treatment regimens, as the latter is already extensively covered in existing and well-established guidance documents [30,34,38,42].

2. Review methods

This systematic review applies a rigorous high-quality methodology, adhering to international methodological standards as established by Cochrane [43] and PRISMA [44]. It also uses the same methodology employed by ECDC during the scoping phase of the project for the systematic reviews targeting the other macro-areas [11,24].

The screening and selection phases of the systematic review were carried out jointly for the three macro areas (i.e. HIV prevention and care, viral hepatitis prevention and care, and prevention and control of infections among PWID). This section summarises the methodology relevant to these macro areas. For a detailed overview of the overall process used for the three macro areas, please see Annex 1.

2.1 Review questions

The following objectives, questions, populations and settings were defined for the systematic review:

Review objectives:

- To gain insights into the evidence base (peer-reviewed and grey literature) for the prevention, care and treatment of HIV in prison settings, including throughcare.
- To gain insights into the evidence base (peer-reviewed and grey literature) for the prevention, care and treatment of viral hepatitis in prison settings, with a focus on treatment of hepatitis C, including throughcare.
- To gain insights into the evidence base (peer-reviewed and grey literature) for the prevention and control of injecting-related infections among current drug users in prison settings, including throughcare.

The objectives do not include active case finding and vaccination as these topics are covered by separate systematic reviews [24].

The PICOS (Population-Intervention-Comparison-Outcome-Settings) method was used to develop specific research questions from these review objectives (Table 1).

Table 1. PICO table

Prevention, care and treatment of HIV	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention, care and treatment of HIV
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in HIV incidence or prevalence, number of people who adhered to treatment, number of people who are linked to care – including community care after release) • Cost-effectiveness (based on study-specific metrics)
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)
Prevention, care and treatment of viral hepatitis	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention, care and treatment of viral hepatitis
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in hepatitis incidence or prevalence, number of people who have completed treatment, number of people who are linked to care – including community care after release) • Cost-effectiveness (defined based on study specific metrics)
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)
Prevention and control of injecting-related infections among PWID	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention and control of injecting-related infections among former/current PWID
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in BBVs incidence or prevalence) • Cost-effectiveness (defined based on study specific metrics)
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)

Review questions:

- Which prevention interventions for BBVs and injecting-related infections are effective in prison settings?
- Which care and/or treatment interventions aimed at control of BBVs and injecting-related infections are effective in prison settings?
- Which service models for prevention, care and/or treatment of BBVs and injecting-related infections are effective in prison settings?
- Which service models for prevention, care and/or treatment of BBVs and injecting-related infections are cost-effective in prison settings?
- What is the acceptance/uptake/coverage of prevention, care and/or treatment of BBVs and injecting-related infections in prison settings?
- How can the acceptance/uptake/coverage of prevention, care and/or treatment of BBVs and injecting-related infections be improved in prison settings?
- Who should be targeted for prevention, care and/or treatment of BBVs and injecting-related infections in prison settings?

2.2 Search and selection strategy

The search and selection phases were done jointly for the three macro areas; see Annex 1 for a detailed description of the process. A brief description of the strategies and specific issues can be found below.

2.2.1 Search strategies for peer-reviewed articles

A peer-reviewed literature search was carried out on 12 January 2017 (PubMed, Embase and Cochrane Library). The search included search strings relevant for all three macro areas (Annex 1). Two search limits were applied: a time limit and a geographical limit. Literature published from 1990 onwards was searched in PubMed and Embase, while literature published in 1980 and later was searched in the Cochrane Library on account of the difference in scope and breadth of the three databases. The literature searches in PubMed and Embase were further limited to include only literature from EU/EEA/EFTA countries or EU candidate countries and other western countries (i.e. USA, Canada, Australia and New Zealand, see Annex 1).

2.2.2 Selection of peer-reviewed articles

Articles were screened by title and abstract, and if considered possibly relevant, in full text. Further scrutiny of the articles during the extraction phase could have led to exclusion. Inclusion and exclusion criteria by study design/type, study quality, study population, geographical area, comparison and specific outcomes are described in detail in Annex 1. Meta-analyses and systematic reviews were checked for any relevant primary articles, and included if necessary (i.e. not already included and of sufficient methodological quality). No data extraction was performed for meta-analyses or systematic reviews.

2.2.3 Critical appraisal for peer-reviewed articles

During the selection process, the methodological quality of the articles that appeared to present relevant data for the review was critically appraised using standardised evidence-based medicine checklists in order to identify quality issues.

For this review, the National Institute for Health and Clinical Excellence (NICE) checklists were used for selection purposes as they cover tools for both quantitative and qualitative checklists. NICE checklists³ are available for the following study designs: systematic reviews and meta-analyses, randomised controlled trials (RCTs), cohort studies, case-control studies, diagnostic accuracy studies, economic evaluations and qualitative studies. Each study is awarded an overall study quality grading for internal validity and a separate one for external validity:

++: all or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter;

+: some of the checklist criteria have been fulfilled, where they have not been fulfilled, or are inadequately described, the conclusions are unlikely to alter;

-: few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

If an article received a score of '-' for both the internal and external validity, the article was excluded (exclusion reason 'insufficient methodology', see Annex 5). If methods and/or results were unclear, articles were excluded. Otherwise, articles were included and limitations, if present, were described in the data extraction tables.

³ National Institute for Health and Clinical Excellence. The guidelines manual: Appendices B-I. London: NICE; 2012. Available from: <https://www.nice.org.uk/process/pmg6/resources/the-guidelines-manual-pdf-3304416006853>

Relevant publications in the field of infectious disease also include outbreak investigations, surveillance studies or other observational studies. For these types of studies no standardised checklists are available, and therefore quality was assessed based on relevant aspects of the existing NICE checklists, supplemented with questions concerning the study design (e.g. whether – in a cross-sectional study – the study population is a representative sample of the source population). See Annex 3 for a complete list of questions on study design. Predefined aspects of a study were qualitatively scored using - - or -, +/-, + or ++. The checklist was not designed to calculate a total quality score to assess quality differences between studies. The final decision on whether the quality of a study was sufficient for inclusion was taken by the reviewer, based on his/her expertise and knowledge.

2.2.4 Search strategies for grey literature documents

A grey literature search with a focus on EU/EEA countries was performed to complement the peer-reviewed literature. Articles, abstracts, reports, case studies, service models, guidelines and protocols which focused on prisons and people in prisons were recovered. The search was conducted through a pre-defined list of websites and a call for papers/experts input. More details can be found in Annexes 1 and 7.

2.2.5 Selection of grey literature documents

Documents were included if the reported information was relevant and of sufficient quality. Inclusion and exclusion criteria by period of publication, type of document, document quality, population, subject of the study, geographical area, and specific outcomes of interest are described in Annex 1. If prison-focused guidelines could not be retrieved/were not available, guidelines with a relevant section on prisoners were searched for in order to complement the data. If these were lacking, general population guidelines were reviewed (i.e. without a section on prisoners).

2.2.6 Critical appraisal for grey literature

Only grey literature documents with clearly-stated methods for compiling data and/or with clear data sources/references were included. The following document types were identified (in order of quality, highest quality first):

Conference abstracts and unpublished research reports

Conference abstracts were checked against included peer-reviewed literature in order to avoid duplication; if duplication was found, the full-text article from the peer-reviewed literature was preferred. Conference abstracts and unpublished research reports focussing on prison settings were included if they contained information relevant to the review objectives. They were screened using the same inclusion/exclusion criteria as the peer-reviewed literature.

Guidelines

The following types of guidelines were identified (highest quality first):

- Evidence-based: largely based on the scientific literature. Good clinical practices or expert opinions could be used to supplement the scientific literature
- Practice-based: reflecting expert opinion or information derived from good clinical practices; some literature references (not systematic) possibly included.

Relevant guidelines were critically appraised with a selection of criteria derived from the AGREE instrument:

- The overall objectives of the guidelines are described in detail
- Systematic/clearly-stated methods were used to compile the data, and/or data sources/references were given
- The recommendations are specific and unambiguous.

Each of the three criteria were qualitatively scored on a 5-tier scale: - -, -, 0, +, ++. The final decision whether the quality of a guideline was sufficient for inclusion in the evidence base was taken by the reviewer, based on his/her expertise and knowledge.

Case studies/service models

Case studies/service models were included to provide insights into the way specific interventions are implemented in a given setting. Case studies/service models were only included when at least both of the criteria (a AND b) were met:

- a) Clearly described accounts of their intervention/service model related to the relevant macro area;
- b) Elements of monitoring or evidence of success (e.g. pre- and post- intervention testing positivity rate for case finding interventions).

2.3 Data extraction

2.3.1 Data extraction for peer-reviewed articles

All relevant information from included articles was summarised in a standardised evidence table. The evidence tables contain the following information:

- Bibliographic reference: author, year, journal, country
- Study characteristics: study design, study period, follow-up, prison setting, study objective
- Study population: population description, inclusion and exclusion criteria, sample description: sample size, gender, age, risk groups
- Data sources and definitions: description of data source/s and relevant definitions
- Macro area-specific methods: methods for prevention, care and treatment of HIV/viral hepatitis, methods for prevention and control of injecting-related infections among PWID
- Macro area-specific outcome results: prevention, care, and treatment of HIV/viral hepatitis, prevention and control of injecting-related infections among PWID
- Reviewer comments, limitations and level of evidence: any additional information which was relevant for interpreting the study results, major issues with regard to the critical appraisal, and the final level of evidence based on these considerations.

2.3.2 Data extraction for grey literature documents

Included documents were collated into evidence tables. The evidence tables contain information on the following topics:

- Bibliographic reference: title, year, place of publication
- Source: institute/company, etc. that prepared the document
- Type of document: conference abstract, guideline, etc.
- Setting and population: country, prison setting, risk groups, etc. to which the results apply
- Intervention: type of intervention and brief description
- Results: relevant results on the objectives given in the document, by objective
- Comments: any additional information which is relevant for interpreting the results.

2.3.3 Level of evidence peer-reviewed literature

The included studies showed a large degree of heterogeneity, therefore the strength of evidence was not assessed beyond individual studies. For the studies included in the review, the level of evidence per individual article was determined based on the study design and the risk of bias, following the GRADE approach criteria (Grading of Recommendations Assessment, Development and Evaluation).

For RCTs, the following aspects were included to assess the risk of bias:

- Randomisation
- Allocation concealment
- Blinding
- Loss to follow-up
- Intention to treat
- Other limitations (e.g. non-validated method to assess the outcome).

For observational studies, the following aspects were included to assess the risk of bias:

- Appropriateness of eligibility criteria (e.g. the study population is not a representative sample of the source population; selection of exposed and unexposed individuals in cohort studies from different populations)
- Measurement of exposure and outcome (e.g. not measured in a standardised, valid and reliable way or not clearly described; differences in measurement in exposed and non-exposed populations or measurement of the outcome while not blinded/with knowledge of the exposure)
- Control for confounding (e.g. degree of accuracy when measuring relevant confounders or adjustment in statistical analyses)
- Follow-up (e.g. no follow-up, short follow-up or different follow-up for exposed and non-exposed populations)
- Other limitations (e.g. participants and non-participants differ regarding relevant characteristics).

For cost-effectiveness studies, the following aspects were included to assess the risk of bias:

- Nature of health condition reflected by the model
- Time horizon
- Perspective
- Discount rate
- Relevant health outcomes and costs
- Sources used for model input
- Reporting of incremental cost-effectiveness ratio
- Sensitivity analyses
- Other limitations.

In general, this led to the following levels of evidence for individual studies (based on study design and methodological quality; see risk of bias criteria above):

- High (i.e. high quality RCTs)
- Moderate (i.e. lower quality RCTs; high-quality cohort/case-control studies, and cost-effectiveness studies)
- Low (i.e. lower quality cohort/case-control studies and cost-effectiveness studies, cross-sectional studies with comparison, high-quality surveillance studies)
- Very low (i.e. low-quality surveillance or other observational studies, outbreak studies, cross-sectional studies without comparison).

2.4 Evidence summary

Separate summary tables were created for effectiveness outcomes, acceptability/barriers outcomes, and cost-effectiveness outcomes. Rather than structuring the evidence summary per macro area, a categorisation by overlapping topics was used, namely: BBVs prevention, prevention of injecting-related infections, HIV treatment, viral hepatitis treatment, and BBVs throughcare (see Annexes 9-12).

The effectiveness summary tables contain the following information:

- Region (EU/EEA or non-EU/EEA) and source (peer-reviewed literature or grey literature)
- Bibliographic reference, country, study design
- Setting (e.g. jail, prison), time period, sample description and size
- Methods: description intervention/model of care, eligibility, comparator
- Results:
 - BBV prevention: BBV prevalence/incidence, other outcomes of interest, sub-group considerations
 - PWID: seroconversion, adverse events, other outcomes of interest
 - HIV care and treatment: viral load, CD4 count, treatment adherence, linkage to care post-release, other outcomes of interest, sub-group considerations
 - HCV care and treatment: SVR, predictors of SVR, treatment completion, linkage to care post-release, other outcomes of interest, sub-group considerations
 - Throughcare:
 - Prevention: BBV prevalence/incidence, other outcomes of interest, sub-group considerations
 - Linkage to care: viral load, CD4 count, treatment adherence, linkage to care post-release, other outcomes of interest, sub-group considerations
- Level of evidence.

The acceptability/barriers summary tables contain the following information:

- Region (EU/EEA or non-EU/EEA) and source (peer-reviewed literature or grey literature)
- Bibliographic reference, country, study design
- Setting (e.g. jail, prison), sample description and size, time period
- Methods: description intervention/model of care
- Results:
 - BBV prevention: eligibility/access, acceptance, intervention adherence, attrition, other outcomes of interest, sub-group considerations
 - PWID: eligibility/access, acceptance, attrition, sub-group considerations
 - HIV care and treatment: eligibility/access, acceptance, treatment discontinuation/non-adherence, attrition, other outcomes of interest, sub-group considerations
 - HCV care and treatment: eligibility/access, treatment discontinuation/non-adherence, attrition, other outcomes of interest, sub-group considerations
 - Throughcare:
 - Prevention: eligibility/access, acceptance, intervention adherence, attrition, other outcomes of interest, sub-group considerations
 - Linkage to care: eligibility/access, acceptance, treatment discontinuation/non-adherence, attrition, other outcomes of interest, sub-group considerations.
- Level of evidence.

The cost-effectiveness summary tables contain the following information:

- Region (EU/EEA or non-EU/EEA) and source (peer-reviewed literature or grey literature)
- Bibliographic reference, country, study design
- Setting (e.g. jail, prison), sample description and size
- Methods: perspective, time horizon, scenarios
- Results: cost-effectiveness results/conclusions, sub-group considerations
- Level of evidence.

Guidelines, protocols and service models were summarised in the narrative sections only.

2.5 Quality control

During the review process, the following quality control measures were used to search and select peer-reviewed literature:

- Peer-review of the search strings by ECDC librarians and expert panel members.
- Selection based on title and abstract performed by two independent researchers. All hits that could be excluded for clearly explicable reasons (inclusion/exclusion criteria) were excluded. When in doubt, the title and abstract were assessed by two researchers and discussed. All articles cited by these two researchers (including articles when doubts remain) were checked by another researcher with expertise in the field of prison health, who then took the final decision on inclusion or exclusion.
- Duplicate screening and critical appraisal of 50% of the full-text articles was performed by two independent reviewers to refine inclusion/exclusion criteria in order to minimise inconsistencies among reviewers. The results were compared and discussed early in the review process, and any disagreements were adjudicated by a third reviewer. Any doubts arising during the screening of the remainder of the full-text articles were discussed in the project team.
- Evidence tables were compiled by two researchers (not in duplicate), and all evidence tables were reviewed by an independent researcher.

The following quality control measures were applied to search and select grey literature:

- Evidence tables were compiled by a researcher and reviewed by a second researcher of the project.
- Early in the process, a senior researcher also checked a sample of 10% of the articles included in the evidence tables to allow for refinement of data extraction.
- Critical appraisal of the guidelines was performed by a researcher and reviewed by a second researcher.

2.5.1 Role of the ad-hoc scientific panel

As part of the project, a multi-disciplinary expert panel was consulted. The panel members were selected based on their expertise in prison health, prevention and control of communicable diseases and evidence-based public health. The experts came from a variety of organisations, such as clinical professional associations, public health institutions, ministries, EU-funded initiatives, international agencies, and civil society organisations. Experts were based in the Czech Republic, France, Germany, Italy, Portugal, Romania, Spain, Switzerland and the UK. ECDC and EMCDDA staff members were also on the expert panel, adding further areas of expertise (e.g. disease-specific knowledge, preparedness, social sciences, health determinants). See Annex 4 for a complete list of expert panel members. The panel members were involved in the prioritisation of the systematic review topics, methodology and evidence gathering.

3. Review results

In the peer-reviewed article search, the PubMed search returned 4 405 hits, the Embase search 4 921 hits, and the Cochrane Library search 62 hits. Following the removal of duplicates and the addition of 12 items after a manual search, 6 119 unique hits remained. After screening the titles and abstracts, a total of 329 articles were selected. The main reasons for the exclusion of articles during the title and abstract screening were:

- Incorrect setting (not in prison setting)
- Ineligible health outcomes (cancer, mental disease, etc.)
- Non-pertinent publication types (e.g. news, letter to the editor, editorial).

After reviewing the full text of the selected articles, 246 articles were excluded. Articles excluded and reasons for exclusion during the full-text selection step can be found in Annex 5. Additionally, a total of 17 articles could not be retrieved and could therefore not be assessed (see Annex 6).

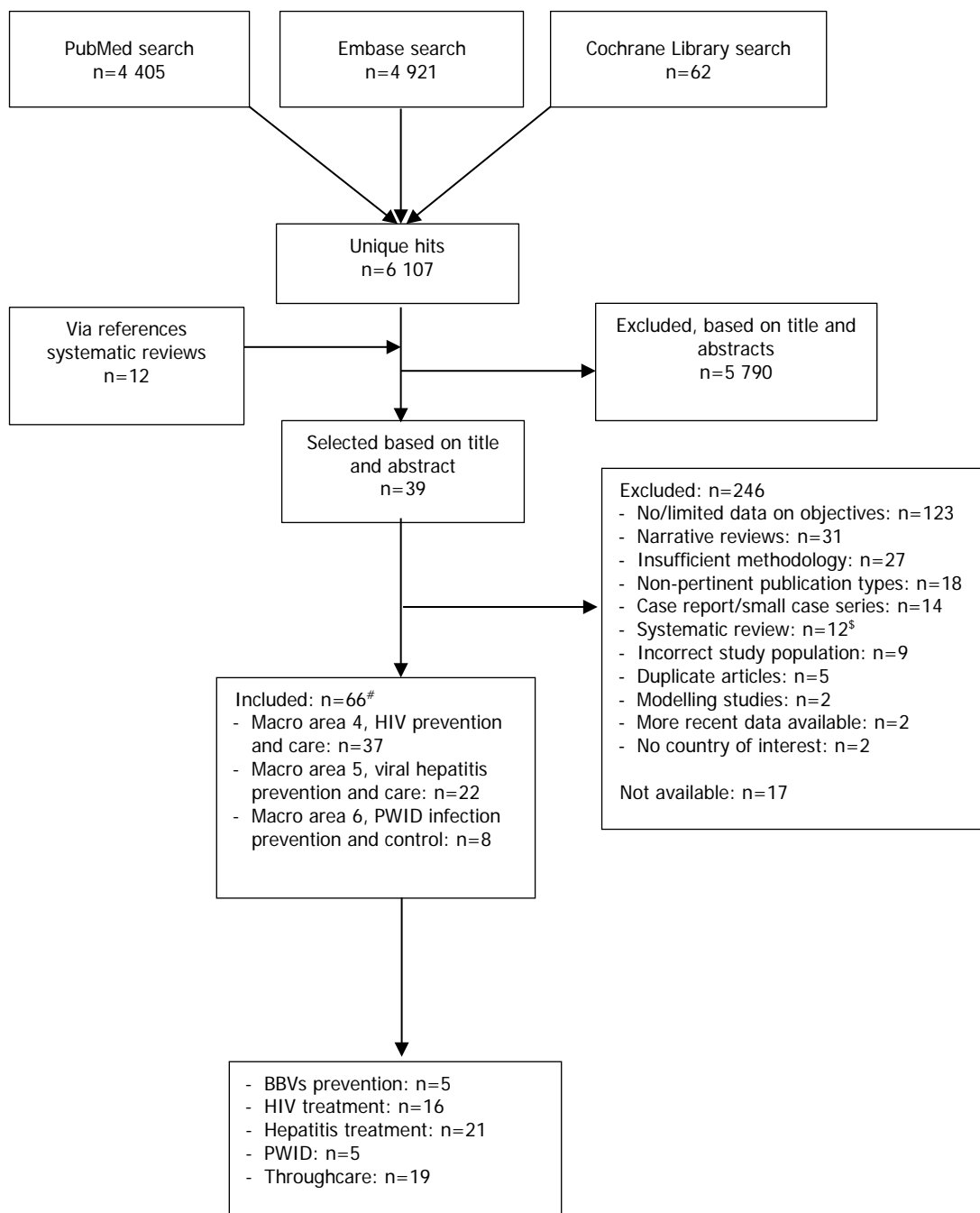
In total, 66 articles were included, of which 36 reported on prevention, care and treatment of HIV (macro area 4), 21 were on prevention, care and treatment of viral hepatitis (macro area 5), one was on both HIV and viral hepatitis, and eight dealt with prevention and control of injecting-related infections among PWID (macro-area 6). When stratifying by topics of interest, of the 66 included articles, five reported on BBV prevention, 16 were on HIV treatment, 21 were on HCV treatment, five dealt with PWID, and 19 reported on throughcare. Figure 1 shows a flowchart of the selection process. It is worth noting that the searches were conducted for the three macro areas combined, and therefore no complete macro area-specific flowchart could be developed. The majority of these studies was conducted in the USA, while only 16 (24%) came from the EU/EEA region.

The grey literature search focused solely on the EU/EEA; a pre-defined website search returned 13 documents, and a call for papers yielded 109 documents. The grey literature gathering process using a call for papers is detailed in Annex 7.

Documents received from field researchers were screened based on title and content, and a total of 84 documents were excluded. Articles excluded during this selection step can be found in Annex 8. Exclusion reasons were:

- Not relevant for the review objective = 74
- No country of interest = 7
- More recent documents available = 1
- Duplicate with included peer-reviewed literature article = 1
- Outside date range = 1.

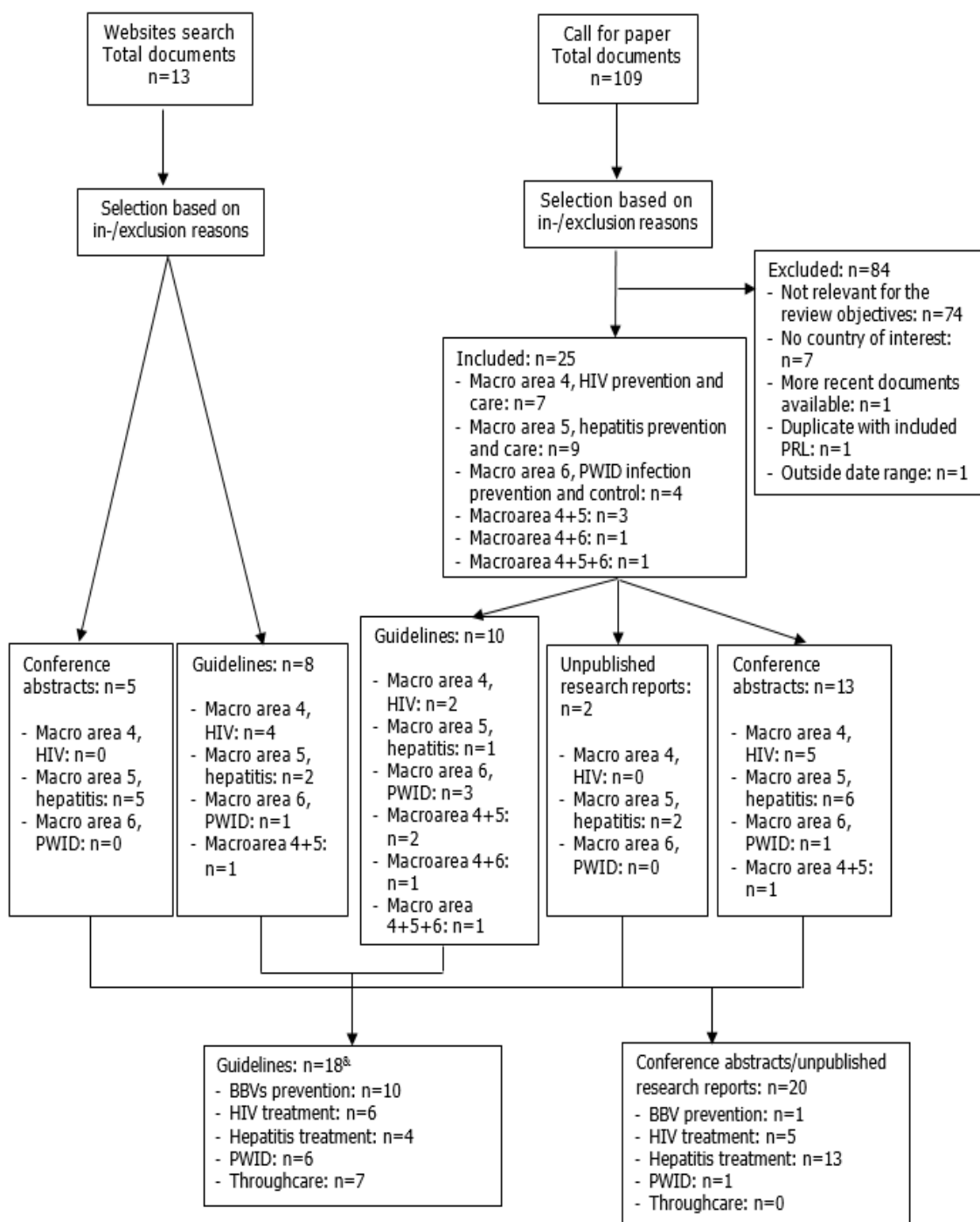
Overall, a total of 38 documents met the pre-defined inclusion criteria, including 20 conference abstracts/unpublished research reports and 18 guidelines. Of the conference abstracts/unpublished research reports, five reported on HIV treatment, 13 were on treatment of viral hepatitis, one reported on BBV prevention and one dealt with prevention and control of injecting-related infections among PWID. Six of the guidelines reported on treatment of HIV, four were on treatment of viral hepatitis, 10 dealt with BBV prevention, six dealt with prevention and control of injecting-related infections among PWID, and seven reported on throughcare. Several guideline documents reported on more than one topic. Figure 2 presents a flowchart of the selection process. Of note, the searches were conducted for all the three macro areas, and therefore no complete macro area-specific flowchart could be developed.

Figure 1. Flowchart selection process peer-reviewed literature

[#] One article contained relevant data for two macro areas

[§] Systematic reviews were checked for relevant individual articles that were possibly missed.

Figure 2. Flowchart selection process for the grey literature



Some documents included data on more than one macro area
 & Some documents included data on more than one topic.

3.1 Prevention of transmission of blood-borne viruses

The combined findings from the systematic review on prevention of BBVs (peer-reviewed and grey literature) are summarised below. Results are presented separately for general BBV prevention and prevention of injecting-related infections among PWID. See Annex 9 for a more detailed summary of relevant information.

3.1.1 Prevention of transmission of blood-borne viruses

Five studies from the peer-reviewed literature, all from outside the EU/EEA, and one conference abstract reported on prevention of BBVs in prison settings and were included [45-50]. Overall the quality of the included studies from the peer-reviewed literature was low to very low.

Effectiveness

Four of the six included studies reported on effectiveness of interventions to prevent BBV infection in prison settings (see Table 2) [45-47,50]. None of these studies reported on the primary effectiveness outcome (i.e. seroconversion after the introduction of a BBV prevention intervention.)

One cross-sectional study reported on a free condom distribution programme in prison, where 150 condom vending machines were installed, dispensing boxes containing one sachet of lubricant, one sealable disposal bag, and an information card [45]. Overall, 28% of inmates used the condom machine. Of those, 40% used it for sex, 25% for self-masturbation, and 19% used the sealable disposal bags for storage of substances. During the study period, 24 571 condoms were dispensed per month.

A conference abstract reporting on a safe tattooing programme in prison (not further defined), found that 66% of inmates requested safe tattoos, 68% of whom underwent safe tattooing [46].

In a randomised controlled trial (RCT) comparing a group behaviour intervention, using six weekly one-hour interactive group sessions, with usual care where inmates received didactic lectures, a greater improvement in the intervention group was found for all five measured outcomes: HIV knowledge confidence, avoiding risky sex, avoiding risky drug use, HIV services and testing, and risk reduction skills [47].

In another RCT comparing six weekly group sessions using skills training to six weekly group sessions using unstructured discussion, those in the skills building intervention showed greater improvements in acknowledging a partner's request and in condom application skills, while those in the discussion intervention group showed greater improvements in commitment to change [50]. However, there were no significant differences for many other outcomes, such as refusing unprotected sex or the sharing of used drug injecting equipment and intention to use condoms.

Table 2. Evidence base for the effectiveness of interventions to prevent BBVs in prison settings

Intervention description	Studies included	Outcome 1: Sero-conversion	Outcome 2: behaviour change	Other outcomes	Level of evidence
Condom distribution	N=1 study; cross-sectional [45], sample size [606] EU/EEA (0)	NR	Frequency of condom use among sexually active inmates for anal and oral intercourse was every time (52%, 28%), often (7%, 2%), sometimes (16%, 22%), never (21%, 44%) and no sex since condom availability (4%, 4%).	294,853 condoms dispensed during study period; 24,571 per month Use condom machine: 28% 40% used condoms for sex, 25% for self-masturbation, 19% used the sealable disposal bags for storage of substances.	Very low
Safe tattooing programme	N=1 study; conference abstract [46], sample size [86] EU/EEA (1)	NR	68% of those who requested, performed safe tattooing (69.5% had previously been tattooed, mostly using uncontrolled equipment and often during imprisonment)	66% requested safe tattoos	NA
Group behaviour intervention vs. usual care	N=1 study; RCT [47], follow-up [one week post-intervention], sample size [1257] EU/EEA (0)	NR	Greater improvement in intervention group and higher mean score at post-test in intervention group than control group for: HIV knowledge confidence, avoiding risky sex, avoiding risky drug use, HIV services and testing, and risk reduction skills.	NR	Low
Group skills-building intervention vs. discussion intervention.	N=1 study; RCT [50], follow-up [6 months post-intervention], sample size [90]: EU/EEA (0)	NR	Skills building intervention: greater improvements in acknowledging a partner's request and condom application skills. Discussion intervention: greater improvements in commitment to change.	NR	Very low

NR: not reported, RCT: randomised controlled trial.

Acceptability and barriers

Three of the six included studies reported on acceptability and barriers, with a focus on condom distribution and safe tattooing programmes [45,46,49].

In a cross-sectional study, inmates and staff were asked about experiences with condom vending machines [45]: 84% of inmates, 85% of commissioned/senior officers, and 43% of prison officers supported condom provision. Of the inmates, 68% did not experience harassment for obtaining condoms, while 15% experienced harassment by other inmates and 7% by officers. Of the inmates, 14% believed condom availability would increase the occurrence of rape. In a cross-sectional study examining condom provision during weekly health education classes, HIV test counselling or upon request, 11% of inmates had been given a condom while in jail [49]. Overall, 55% of inmates and 64% of staff reported that distributing condoms is a good idea as condoms are an effective and low-risk method to prevent the transmission of HIV or STIs. Those objecting mentioned: concern of institutional and personal safety; perception of the intervention as an endorsement of same gender relationships; inconsistent message of condom availability given that sexual activity is prohibited by institutional policy. Among inmates, 42% believed condoms would increase likelihood of sex in jail, and 13% of staff reported occurrence of problems caused by condom distribution (not further defined). Both studies reported no major incidents comprising prison safety.

In the conference abstract reporting on a safe tattooing programme in prison, 32% of those who requested safe tattooing were reported not to have successfully received tattoos under the programme because of lack of money (50%) or release from prison (50%) [46].

Cost-effectiveness

One cost-effectiveness study was included, focusing on condom distribution (see Table 3) [48]. In this study, staff visited an MSM unit once a week, at which time inmates could receive one single condom. According to the model and compared with usual care, this programme resulted in 25% of HIV transmissions averted, reducing the number of new infections from 0.8 to 0.6 per month, and in cost savings over the next 32 years of almost USD 75 000.

Table 3. Evidence base for the cost-effectiveness of interventions to prevent BBVs in prison settings

Intervention description	Studies included	Scenarios	Conclusions	Level of evidence
Condom distribution vs. no condom distribution.	N=1 study [48], perspective [societal], time horizon [32 years] EU/EEA (0)	Condom distribution: staff visit the unit once a week, at which time inmates line up and may receive a single condom vs. no condom distribution.	- 25% of HIV transmissions averted, reducing the number of new infections from 0.8 to 0.6 per month - Cost savings over the next 32 years of USD 74 777.	Low

Guidelines

Ten guidelines reporting on BBV prevention were included, eight of which were specific to prison settings (four supranational and four national guidelines) and two were supranational but not specific to prison settings (Table 4). See Annex 9 for a more detailed summary of relevant information. In short, the guidelines set out the recommendations below which were of interest for this project:

Table 4. Guidelines providing recommendations on prevention of BBVs in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	All information on blood-borne diseases that is available to the community should be tailored to the needs, cultural and educational backgrounds and languages of the prison population, both staff and prisoners. The preferred strategies to reduce BBV transmission include: <ul style="list-style-type: none"> – Provision of condoms and lubricants – Safe tattooing and piercing equipment – Prevention of mother-to-child transmission – Universal precautions and safe health services – Post-exposure prophylaxis.
UNAIDS, 2014 [51]	Condoms need to be easily and discreetly available, ideally in areas such as toilets, shower areas, waiting rooms, workshops or day rooms where prisoners can pick up a condom without being seen by others. Condoms should be provided free of charge, and can be made available to all prisoners in a health kit given to them upon entry to the facility. The proper (correct) and consistent (every time) use of condoms for sexual intercourse, vaginal, anal or oral can greatly reduce a person's risk of acquiring or transmitting sexually transmitted infections, including HIV infection. New infections can be prevented by providing easy, anonymous access to condoms and lubricants. Preventing the transmission of blood-borne diseases through tattooing requires efforts at individual, institution and population level.
UNODC, 2013 [52]	It is essential to provide HIV interventions in these (prison) settings, both for prisoners and for those employed by prison authorities. <p>The comprehensive package includes 15 key interventions:</p> <ol style="list-style-type: none"> 1. Information, education and communication 2. Condom programmes 3. Prevention of sexual violence 4. Drug dependence treatment, including opioid substitution therapy 5. Needle and syringe programmes 6. Prevention of transmission through medical or dental services 7. Prevention of transmission through tattooing, piercing and other forms of skin penetration 8. Post-exposure prophylaxis 9. HIV testing and counselling 10. HIV treatment, care and support 11. Prevention, diagnosis and treatment of tuberculosis 12. Prevention of mother-to-child transmission of HIV 13. Prevention and treatment of sexually transmitted infections 14. Vaccination, diagnosis and treatment of viral hepatitis 15. Protecting staff from occupational hazards.
WHO, 2007 [53]	The proper (correct) and consistent (every time) use of condoms for sexual intercourse, vaginal, anal or oral can greatly reduce a person's risk of acquiring or transmitting sexually transmitted infections, including HIV infection. Preventing new infections can be achieved through providing easy, anonymous access to condoms and lubricants. Preventing the transmission of blood-borne diseases through tattooing requires efforts at individual, institution and population level.
<i>Specific to prison setting – national guidelines</i>	
NICE, 2016 [54]	Ensure that people in prison have discreet access to condoms, dental dams and water-based lubricants without the need to ask for them
UK Department of Health, 2011_a [55]	HIV prevention advice for prisoners: <ul style="list-style-type: none"> – Always use a condom during sex. – Never share tattooing or body piercing equipment. – Use disinfecting tablets to clean injecting equipment, razors, etc. – Post-exposure prophylaxis.

Guideline	
UK Department of Health, 2011_b [56]	Prevention <ul style="list-style-type: none"> – Condoms should be used for all sexual contact with a partner whose HIV status is unknown. – Individuals who undergo body piercing/ tattooing should ensure that disposable sterile needles are used. – Sharing of personal items like toothbrushes, injecting equipment and razors should be avoided. – Post-exposure prophylactic antiviral drugs begun within hours (and certainly no later than 48 to 72 hours after exposure) of a significant exposure to HIV virus may prevent infection occurring.
SIMIT/Minist ero della Salute (Italy), 2016 [57]	In order to reduce HIV transmission the panel recommends: <ul style="list-style-type: none"> – Free distribution of sterile tattooing equipment. – Free distribution of condoms and condoms vending machines in freely accessible but reserved areas within the prison. – Provide pre-exposure prophylaxis by the prison infectious disease specialist, if needed. – Assure the continuation of Opioid Substitution Treatment since it is highly effective in reducing HIV transmission among PWID.
Other guidelines – supranational guidelines	
WHO, 2016 [58]	In addition to the recommended interventions for people in the community, interventions relevant to closed settings include: <ul style="list-style-type: none"> – Prevention of HIV transmission through medical and dental services. – Prevention of transmission of HIV and other blood-borne diseases through tattooing, piercing and other forms of skin penetration – The correct and consistent use of condoms with condom-compatible lubricants is recommended for all key populations to prevent sexual transmission of HIV – Oral pre-exposure prophylaxis (containing tenofovir disoproxil fumarate) should be offered as an additional prevention choice for key populations (including prisoners) at substantial risk for HIV infection as part of combination prevention approaches – PEP given to reduce the likelihood of acquiring HIV infection after possible exposure.
European AIDS Clinical Society, 2017 [30]	Effective measures to reduce sexual transmission of HIV include: <ul style="list-style-type: none"> – Male condom or female condom use – Post-exposure prophylaxis – Pre-exposure prophylaxis – ART for HIV-positive partner.

3.1.2 Prevention of injecting-related infections among people who inject drugs

Five peer-reviewed literature studies and one conference abstract reported on prevention of injecting-related infections among people who inject drugs in prison settings and were included [Stark, 2006; Heinemann, 2001; Dolan, 2003; Dolan, 2005; Arroyo, 2015; Warren, 2006]. Three studies were from the EU/EEA. Overall the quality of the included studies from the peer-reviewed literature was low to very low.

Effectiveness

Five of the six included studies reported on the effectiveness of interventions to prevent injecting-related infections among PWID in prison settings (see Table 5) [59-63]. Three studies reported on needle and syringe programmes (NSPs), and two on opioid substitution treatment (OST).

One study examined NSPs in one female and one male prison. Automatic dispensers were used in the female prison, while in the male prison used material was exchanged for sterile material through social workers three times a week [62]. The investigators found no HIV and HBV seroconversions and a seroconversion incidence rate of 18/100 person-years for HCV during the study period. All four HCV seroconverters denied tattooing, piercing, sexual risk behaviour, sharing syringes in prison, but three out of four reported front-loading or sharing of spoons for drug preparation prior to seroconversion. The other study reporting on an NSP based on the installation of syringe vending machines, found no seroconversions during the intervention period and no adverse events were reported [61]. Almost all subjects in the latter study reported frequency of sharing used injecting equipment as unchanged or only slightly decreased. Arroyo reported on the implementation and impact of a nation-wide NSP in the Spanish prison system in a longitudinal study [63], during which the number of participating prisons increased from one (in 1997) to 38 (in 2003), before declining again to 22 (in 2014). The prevalence of HCV infection in the Spanish prison system decreased from 48.6% in 1998 to 20% in 2014, and the prevalence of HIV infection from 12.1% in 2003 to 5.8% in 2014. The decrease in prevalence of HCV and HIV among people in prison in Spain reflects the introduction of a range of effective harm reduction measures, including OST, NSP and ARV in the community and in prisons, which coincided with a decline at national level of injecting drug use and a reduction in new injecting-related infections.

One RCT comparing introduction of an OST programme to usual care (no OST) found no difference in HIV and HCV seroconversion between the OST and the control group after four months [59]. In a follow-up study of the above mentioned RCT, all participants were offered OST after four deferral period months and were followed up for approximately four years [60]. A seroconversion incidence rate of 21/100 person-years was found for HCV, and of 0.28 per 100 person-years for HIV. Individuals incarcerated for less than two months and those on OST for less than five months had a significantly increased risk of HCV seroconversion [60].

Table 5. Evidence base for the effectiveness of interventions to prevent injecting-related infections among PWID in prison settings

Intervention description	Studies included	Outcome 1: seroconversion	Outcome 2: adverse events/attrition ¹	Other outcomes	Level of evidence
NSPs	N=3 studies; 2 longitudinal studies [61,62], follow-up [NR; median 12 months], sample size [231, 174] 1 conference abstract [63], follow-up [18 years], sample size [NR] EU/EEA (3)	<i>Median 12 months follow-up:</i> - HIV: 0 - HBV: 0 - HCV: four out of 22 HCV seronegative at baseline (IR 18/100 person-years) - 12 HBV and 11 HCV between M0 (1-12 weeks before intervention start) and M1 (1-10 months after intervention start), at least five HBV and two HCV seroconversions probably occurred during imprisonment - No seroconversions were observed during the intervention period - Prevalence of HCV infection in Spanish prison system decreased from 48.6% in 1998 to 20% in 2014 - Prevalence of HIV infection in Spanish prison system decreased from 12% in 1998 to 5.8% in 2014.	No adverse events possibly related to the programme (n=1 study) Attrition: 28.7%	-3 383 – 10 439 syringes exchanged; in one study the number of syringes exchanged rose from 2 582 to nearly 23 000 in 2004 and decreased since then to 4 393 in 2014 - All seroconverters denied tattooing, piercing, sexual risk behaviour, sharing syringes in prison, but three reported front-loading ² or sharing of spoons for drug preparation prior to seroconversion (1 study) - Almost all subjects reported frequency of sharing of injecting equipment as unchanged or only slightly decreased (1 study)	All very low
Opioid substitution treatment	N=2 studies; 2 RCTs [59,60], follow-up [four months; four years], sample size [both studies 191 OST, 191 control] EU/EEA (0)	<i>~4 months follow-up:</i> - HIV: 0 at baseline and follow-up - HCV: four out of 32 OST and four out of 35 control HCV-negative subjects at baseline (12.5% and 11.4%, resp., p=ns) <i>Median 4.2 years follow-up:</i> - HCV: 39 of 95 HCV-negative subjects (IR 21.3/100 person-years, 95% CI 15.6-29.2), p=ns between original RCT groups - HIV: two (seronegative at baseline NR; IR 0.276/100 person-years, 95% CI 0.033-0.996)	Adverse events: NR Attrition: - 22.5% in OST and 26.6% in control group - 80.6% dropped out of their first OST episode over 436 person-years at risk (attrition rate 63.1 per 100 person-years, 95% CI 56.1-71.0)	Significant association with increased risk of HCV seroconversion (n=1 study): periods of imprisonment of <2 months (p≤0.001), OST periods of <5 months (p=0.01)	All very low

HBV: hepatitis B virus, HCV: hepatitis C virus, HIV: human immunodeficiency virus, IDU: injecting drug user, IR: incidence rate, NR: not reported, ns: not significant, NSP: needle and syringe programme, OST: opioid substitution treatment, RCT: randomised controlled trial

¹ Proportion lost to follow-up during study

² Dividing up drug doses between ≥2 IDUs involving a used syringe.

Acceptability and barriers

Four of the five included studies reported on acceptability and barriers to NSP and OST programmes in prison settings [59-62].

In a German longitudinal study reporting on an NSP, the loss to follow-up was primarily due to pre-term release or transfer of people in prison [62]. Another German longitudinal study reported that over 90% of the NSP users reported unreliability of syringe vending machines [61]. Additional reported challenges by the two studies were: not enough syringes provided, insufficient anonymity, poor supply of dummies, and lack of special injecting paraphernalia (no percentages reported). The acceptance (not defined in the study) of the overall project among incarcerated PWID was significantly higher than among non-injectors (p-value not reported). Furthermore, the two studies reported a similar proportion (58-61%) of prison employees who evaluated the programme as 'bad' or 'very bad'. At the end of the study period, the majority of the employees were still not convinced of the need for an NSP.

Two studies from Australia reported on an OST programme in prison [59,60]. Among the intervention group who were offered OST immediately and were followed up for four months, 9.3% did not start treatment (reasons not reported) [59]. In the four-year follow-up study of this RCT, where the control group received OST after a four-month delay, 97% of all original intervention and control subjects had received OST at some time during the complete study period [60]. According to the studies, the loss to follow-up was due to release from prison. The OST dropout risk was ten times higher during short prison sentences (≤ 1 month) compared to when subjects were in the community ($p < 0.001$), although after four months, imprisonment proved significantly effective against OST dropout ($p \leq 0.002$) [60].

Cost-effectiveness

One cost-effectiveness study was included that assessed the impact of a one-year OST programme compared with usual care (see Table 6) [64]. According to the study, the introduction of the OST programme resulted in an incremental cost per additional heroin-free day of AUD 38, per death avoided of almost AUD 460 and per HCV case avoided of approximately AUD 40 000. The authors concluded that an OST programme in prison was no more costly than analogous community programmes.

Table 6. Evidence base for the cost-effectiveness of interventions to prevent injecting-related infections among PWID in prison settings

Intervention description	Studies included	Scenarios	Conclusions	Level of evidence
Opioid substitution treatment	N=1 study [64], perspective provider/funder of prison services, time horizon NR EU/EEA (0)	OST programme for one year vs. no OST programme	<ul style="list-style-type: none"> - Incremental cost per additional heroin-free day: AUD 38 - Incremental cost per death avoided: AUD 458 074 - Incremental cost per HCV case avoided: AUD 40 428. - OST programme in prison is no more costly than community programmes. 	Low

AUD: Australian dollar, HCV: hepatitis C virus, NR: not reported, OST: opioid substitution treatment.

Supplementary evidence

The systematic review of the evidence on prevention interventions for injecting-related infections yielded a very limited body of evidence. Most of the studies identified through the search reported on indirect outcome measures (e.g. change in drug-injecting behaviour) rather than on infection-related outcomes. The project team decided to integrate the available evidence through a pragmatic approach, along the dimensions of analogy (i.e. evidence reporting on prevention intervention targeting PWID in the community) and of proxy measures (i.e. indirect outcome measures within the group of PWID in prison settings). The relevant evidence was sources taken from the EMCDDA best practice portal (http://www.emcdda.europa.eu/best-practice/answer-sheets/prison_en).

Guidelines

Six guidelines on prevention of BBV infection in PWID were included, three of which were specific to the prison setting (two supranational and one national guideline), and the other three were supranational guidelines not specific to the prison setting (Table 7). See Annex 9 for a more detailed summary of relevant information. In short, these guidelines set out the following recommendations of interest for this project:

Table 7. Guidelines providing recommendations on prevention of injecting-related infections among PWID in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	Different modalities have been adopted in several countries to make safe injection equipment available in prisons through health staff, by peers or through dispensing machines. There is evidence that these programmes are effective and not the source of security problems. Drug dependence treatment, including opioid substitution therapy for maintenance, is an essential component of the prevention of transmission through injection equipment.
WHO, 2007 [53]	Prevention is based on blocking transmission caused by using contaminated syringes. The individual drug user should avoid sharing injecting equipment and, when needle and syringe programmes are available, take part.
<i>Specific to prison setting – national guidelines</i>	
UK Department of Health, 2011 [55]	Never share injecting drug equipment; this includes syringes, filters, spoons, tourniquets, swabs and water, as well as needles. Use disinfecting tablets to clean injecting equipment, razors, and any other items that may have come into contact with blood or body fluids.
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	All people from key populations who are dependent on opioids should be offered opioid substitution therapy in keeping with WHO guidance (strong recommendation, low quality of evidence), including those in prison and other closed settings. People in prisons should have access to the same evidence-based treatment options for substance dependence as people in the community.
ECDC/EMCDDA, 2011 [25]	Based on the most robust evidence available, expert opinion, and best practice used within the EU/EEA, the following key intervention components should be applied and, if possible, be combined to achieve the maximum prevention effect through synergy: <ul style="list-style-type: none"> – Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes, free of charge, as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes. – Opioid substitution treatment and other effective forms of drug dependence treatment; – Vaccination: Hepatitis A and B, tetanus, influenza vaccines, and, in particular for HIV-positive individuals, pneumococcal vaccine. – Testing: Voluntary and confidential testing with informed consent for HIV, hepatitis C (hepatitis B for unvaccinated) and other infections, including TB, should be routinely offered and linked to referral to treatment. – Infectious disease treatment: Antiviral treatment based on clinical indications for those who are HIV-, hepatitis B- or C-infected. Anti-tuberculosis treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated. – Health promotion: Health promotion focused on safer injecting behaviour; sexual health including condom use; and disease prevention, testing and treatment. – Targeted delivery of services: Services should be combined and organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed sites offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.
EMCDDA, 2010 [65]	Technical guidelines for a wide range of health service providers to PWID, recommending comprehensive health examination, testing and counselling in different health settings including primary healthcare, special health services for PWID, low threshold service centres visited by PWID, rehabilitation centres, dedicated sexually transmitted infections (STI) clinics and prison healthcare facilities.

3.2 Modes of care for HIV treatment

A total of 21 studies reporting on HIV treatment provision in prison settings were included. Fifteen were peer-reviewed articles and five were conference abstracts, of which eleven were from the EU/EEA. Overall the quality of the included peer-reviewed literature studies was very low. See Annex 10 for a more detailed summary of relevant information.

Effectiveness

Overall, 19 of the 21 included studies reported on the effectiveness of different models of care to achieve retention and adherence to HIV treatment in prison settings (see Table 8). Thirteen studies were descriptive studies of usual models of care. Six reported on self-administered therapy (SAT) [66-71] and seven reported on a combination of directly observed therapy (DOT) and SAT [72-78]. In three studies a DOT-based HIV treatment approach was compared to a SAT-based approach [79-81]. In addition, one study reported on a telemedicine intervention to improve HIV quality of care [82], another investigated a clinical pharmacist-led HIV treatment approach [83], and one conference abstract reported on a monthly nurse evaluation intervention [84].

Adherence to HIV treatment was reported in ten studies [68-70,72,73,76,77,79,80,83]. It ranged from 42% to 72% in studies reporting on usual care with SAT, from 62% to 94% in studies reporting on usual care with a combination of DOT and SAT, and was 73% in the clinical pharmacist-led treatment study. The studies comparing DOT with SAT reported a median adherence range of 90%-100% in the SAT group and 82%-100% in the DOT group (depending on definition used), with no significant difference between the two approaches.

Viral suppression as the main treatment endpoint was reported by thirteen studies [66,67,69-71,73-75,78,79,82-84]. The proportion of patients achieving viral suppression ranged from 46% to 83% in studies reporting on usual care with SAT, and from 23% to 62% in studies reporting on usual care with a combination of DOT and SAT. Five studies reporting on usual care examined whether viral suppression from start of treatment improved significantly. Three studies found a significant improvement, two measured at release and one measured six months after start of treatment. The other two studies did not find a significant improvement in viral suppression after start of treatment, one after 24 weeks and one after 12 months. One study comparing DOT with SAT reported viral suppression rates of 53% and 56% for DOT and 32% and 44% for SAT, at 24 weeks and 48 weeks, respectively, with no significant difference between the two approaches. The study reporting on the telemedicine approach found a significant increase in the likelihood of achieving viral suppression in the telemedicine group compared to the usual care group (OR 7.0, 95% CI 5.1–9.8; $p < 0.001$).

Attrition was reported in six studies and ranged from 4% to 52% [68-70,73,79,80]. Possible factors associated with it are presented below.

Table 8. Evidence base for the effectiveness of different care models to achieve retention of and adherence to HIV treatment in prison settings

Intervention description	Studies included	Outcome 1: Adherence ¹	Outcome 2: Viral suppression ²	Attrition ³	Level of evidence
Usual care - SAT	N=6 studies; 2 longitudinal [68,70], follow-up [6 months; 12 months], sample size [75; 281]; 1 cross-sectional [69], sample size [50], 3 conference abstracts [66,67,71], sample size [102; 600; 144] EU/EEA (6)	42%-72% No significant changes over time reported in n=2 studies	46%-82.8% No significant changes over time reported in n=1 studies on people on ART; significant decrease in viral load in n=1 study on people started on ART.	4%-45%	All very low
Usual care - Combination of DOT and SAT	N=7 studies; 3 longitudinal [73,75,78], follow-up [24 weeks; until release; until release], sample size [108; 882; 1099]; 3 cross-sectional [72,76,77], sample size [205; 102; 177] 1 conference abstract [74], sample size [170] EU/EEA (2)	62%-94%	23%-62% Significant decrease in viral load in n=2 studies, decrease without reported significance in n=1 study, from baseline to follow-up	6%	All very low
Comparison DOT vs. SAT	N=3 studies; 2 longitudinal [80,81], follow-up [3-4 months; 16-19 months], sample size [31; 84]; 1 RCT [79], follow-up [48 weeks], sample size [43] EU/EEA (1)	No significant difference between DOT and SAT [measured by electronic monitoring, pill-count or self-reported].	No significant difference between DOT and SAT. 62.1% of patients in DOT group had viral load <400 copies/ml vs 34% in the non-DOT group ($p=0.01$)	5%-52%	All very low
Telemedicine with HIV specialist	N=1 study; 1 comparative [82], sample size [1201], follow-up [18 months] EU/EEA (0)	NR	Significant increase in likelihood of achieving viral suppression in telemedicine group.	NR	Very low
Clinical pharmacist-led treatment	N=1 study; 1 longitudinal [83], follow-up [NR], sample size [135] EU/EEA (0)	73%	Increased from 32% to 66% following intervention (significance NR)	NR	Very low
Monthly nurse evaluation	N=1 study; 1 conference abstract [84], follow-up [NR], sample size [54]	NR	Decreased from 8 341.57 to 4 040.31 copies/ml following intervention (significance NR).	NR	NA

ART: antiretroviral therapy, DOT: directly observed therapy, NR: not reported, RCT: randomised controlled trial, SAT: self-administered therapy

¹Adherence defined as self-reported adherence measure according to study specific methodology

²Viral suppression defined as viral load <50 copies/ml unless otherwise specified

³Proportion lost to follow-up during study.

Acceptability and barriers

Fifteen of the 21 included studies reported on the acceptability and barriers to HIV treatment in prison settings [66,68-77,79,80,85,86].

Acceptance

The proportion of treatment acceptance among those eligible was reported in three cross-sectional studies reporting on HIV usual care and ranged from 73.0% to 80.0% [72,76,77]. Two studies reported having trust in the physician and in the medication as significant predictors of treatment acceptance [72,76]. Another study compared individuals who refused ART to those either eligible or on treatment. Those refusing ART were characterised by a higher proportion being on OST, using heroin/cocaine in prison, having HCV co-infection, worse self-perceived health, viral load >50,000 copies/ml, and a lower mean CD4 count [85].

Two studies reporting on the combination of SAT and DOT modalities of treatment administration registered a proportion of patients transitioning from DOT to SAT (1.6% and 13.5%) much lower than that of those transitioning from SAT to DOT reported in one study (23.5%) [74,75].

Discontinuation/adherence

Causes of HIV treatment discontinuation and non-adherence were reported in five [68,71,73,74,85] and two studies [77,86], respectively. In addition to clinical reasons such as adverse effects of treatment and virological failure, personal reasons varied: forgetfulness, having exhausted medication or not having medication at hand, problems with dispensing or confusion, feeling nervous or depressed, feeling tired or being ill.

Significant predictors of adherence were reported in six studies [68,69,72,76,77,86] and were classified as personal, clinical or environmental/structural factors:

- Personal: good general/medication management, perception of the benefits of ART and acceptance of treatment, no depression, no fatigue, higher academic background, no IDU as risk factor for HIV transmission
- Clinical: good CD4 level/viral load, absence of HIV-related symptoms, no treatment-related side effects
- Environmental: active occupation inside prison, having flexible prison officials who would open the cell to make it possible to take medication when needed, having a social network, including having support outside prison and receiving visits, reliance on doctor and other healthcare staff.

Attrition

Reasons for loss to follow-up/attrition were reported in four studies and was mostly due to environmental reasons, i.e. transfer or release [69,70,79,80].

Opinions and beliefs: healthcare services in prison settings

Of those inmates treated in a longitudinal study on usual HIV care, 60% reported having received limited support from healthcare staff [68].

In two cross-sectional studies on usual care using a combination of DOT and SAT (one conducted in three prisons in 2002, the other in two of these prisons in 2000), 86.8% and 87.0% respectively had trust in treatment, 68.7% and 55.9% had trust in doctors, 57.7% and 57.7% received necessary help from doctors, and 44.4% and 43.5% received support in prison from professionals, other inmates, or non-governmental organisations/others [77,86].

In another cross-sectional study on usual care with DOT and SAT [76], 29% of inmates believed that healthcare offered to all inmates is excellent-outstanding, approximately half of them (55%) believed the HIV-related healthcare they received was excellent-outstanding, 71% that the HIV doctor always listens to them, and three in five patients (59%) thought that the HIV doctors always understands what they are saying.

Finally, in a cross-sectional study on usual care with DOT and SAT, 82% of females and 65% of males had high level of trust in their current HIV doctor, 55% of females and 72% of males had high level of trust in current HIV nurse, only 16% believed that taking medications for HIV was most essential for remaining healthy, but 83% had high level of trust in HIV medications [72].

Cost-effectiveness

No studies were found on the cost-effectiveness of care models for HIV treatment in prison settings.

Guidelines

Six guidelines on HIV treatment were included, four of which were specific to prison settings (two supranational and two national guidelines), and the other two were supranational guidelines not specific to prison settings (Table 9). See Annex 10 for a more detailed summary of relevant information. In short, these guidelines set out the following recommendations which are of interest for this project:

Table 9. Guidelines providing recommendations on HIV treatment in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	There is evidence that ART is feasible in prison settings. One of the problems of ART is resistance. In addition, specific attention should be paid to adherence to the treatment. Clinical and laboratory follow-up is needed to monitor the response to treatment. Prevention of opportunistic infections is part of the treatment for HIV.
WHO, 2007 [53]	Providing access to ART for those in need in the context of prisons, particularly in resource-constrained settings, is a challenge, but it is necessary and feasible. Studies have shown that when prisoners are provided care and access to ART, they respond well.
<i>Specific to prison setting – national guidelines</i>	
UK Department of Health, 2011 [55]	All prisoners with HIV will require referral for specialist care. ART is the main type of treatment for HIV.
SIMIT/Ministero della Salute (Italy), 2016 [57]	ART should be offered to every HIV-infected prisoner, independently of CD4 cell count. Early treatment, apart from individual benefit, could result in better linkage to care of the prisoner and the HIV RNA reduction lowers the possibility of HIV transmission during prison stay and after release. ART should be provided according to the specialist prescription and as Directly Observed Therapy (DOT).
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	The use of ART for HIV in key populations should follow the same general principles and recommendations as for all adults. Special consideration should be given to ensuring that pregnant female prisoners have ready access to PMTCT services, as women often face greater barriers to HIV testing, counselling, care, and treatment in prison than outside prison.
European AIDS Clinical Society, 2017 [30]	ART is recommended in all adults with chronic HIV infection, irrespective of CD4 counts. ART should always be recommended irrespective of the CD4 count, but the lower the CD4 count, the greater the urgency to start ART immediately.

3.3 Models of care for viral hepatitis C treatment

A total of 34 studies reporting on HCV treatment provision in prison settings were included. Twenty-one were peer-reviewed articles, of which seven came from the EU/EEA, eleven were conference abstracts and two were unpublished research reports. Of these, twenty studies reported on INF-based treatment, and the remainder on DAAs. No studies were retrieved reporting on HBV treatment in prison settings. The quality of the included peer-reviewed literature studies was mostly very low. See Annex 11 for a more detailed summary of relevant information.

Effectiveness

Twenty-nine of the 34 studies reported on the effectiveness of different models of care to achieve sustained viral response (SVR) and completion to HCV treatment [87-115]. Of the twenty studies on INF-based regimens using ribavirin (RBV) and interferon (IFN), 15 studies were descriptive studies on usual care models [87,89-94,96,99,102,103,105,110-112], including DOT, SAT or a combination. Two were comparative studies assessing DOT-based treatment versus SAT-based treatment [108,109]. One study reported on a telemedicine intervention to support treatment provision in prison settings [98]. Finally, two studies compared community-based treatment to prison-based treatment outcomes [88,107]. Nine studies, none from the peer-reviewed literature, reported descriptive data on DAA treatment in prison settings (see Table 10) [95,97,100,101,104,106,113-115].

Among studies investigating the older treatment regimens, the proportion achieving an SVR ranged from 28% to 67% in studies on SAT-based usual care, from 29% to 50% in studies on the combination of DOT and SAT, and was 44% in the telemedicine study. The studies comparing DOT with SAT reported an SVR rate of 62%-64% with no significant difference between DOT or SAT models of care. The studies comparing prison-based treatment to community-based treatment reported an SVR rate ranging from 38% to 63% with no significant difference in achieving SVR between the two settings. Among studies investigating DAAs, the proportion achieving an SVR was higher and ranged from 85% to 95%.

Among studies investigating the INF-based regimens, the proportion achieving HCV treatment completion ranged from 47% to 91% in studies on SAT-based usual care, from 46% to 98% in studies on the combination of DOT and SAT, and was 69% in the telemedicine study.

Among studies investigating DAAs, the proportion of HCV treatment completion was higher and ranged from 88% to 96%.

Attrition in these studies varied broadly and ranged from 6% to 50%.

Table 10. Evidence base for the effectiveness of different care models to achieve sustained viral response and HCV treatment completion in prison settings

Intervention description	Studies included	Outcome 1: SVR ¹	Outcome 2: Treatment completion ²	Attrition ³	Level of evidence
Usual care – SAT ⁴ IFN+RBV	N=11 studies; 7 longitudinal [89,91-94,110,112], follow-up [all 24 weeks/6 months after end treatment], sample size [79; 71; 431; 114; 90; 32; 268] 1 cross-sectional [102], sample size [162] 1 nested case-control [90], follow-up [NR], sample size [185] 2 conference abstract [99,105], sample size [513; 41], EU/EEA (5)	27.6%-67.1%	46.5%-91.4%	5.8%-50.0% before SVR assessment	All very low
Usual care - Combination of DOT and SAT IFN+RBV	N=4 studies 4 longitudinal [87,96,103,111], follow-up [12 months; 24 weeks; 6 months; 24 weeks after end treatment], sample size [90; 50; 68; 59], EU/EEA (1)	28.9%-50.0%	45.6%-98.3%	13.6%-14.4% before SVR assessment	All very low
Comparison DOT vs. SAT IFN+RBV	N=2 studies 1 RCT [109], follow-up [24 weeks after end of treatment], sample size [244] 1 conference abstract [108]; follow-up [24 weeks after end of treatment], sample size [244], EU/EEA (2)	Overall: 63.5%, 62.2% - DOT: 60.6%, 58.5% - SAT: 65.9%, 65.9% No significant difference in SVR between DOT and SAT in both studies.	Overall: 83.0%, 79.8%	4.9% before completion of treatment	Very low
Telemedicine IFN+RBV	N=1 study 1 longitudinal [98], follow-up [24 weeks after end of treatment], sample size [108], EU/EEA (0)	43.5%	69.4%	26.9% before SVR assessment.	Very low
Comparison community-based vs. prison-based treatment IFN+RBV (+ or – a protease inhibitor in n=1 study)	N=2 studies 1 matched cohort [88]; follow-up [24 weeks after end of treatment], sample size [1428] 1 comparative [107], follow-up [≥24 weeks after end of treatment], sample size [553], EU/EEA (1).	- Inmates: 42.9%-73.6% - Community: 38.0%-62.9% No significant difference in SVR between inmates and community members in n=2 studies.	- Inmates: 75.0%-73.5% - Community: 86.6% No significant difference in completion between inmates and community members in n=1 study.	NR	Moderate; low
Provision of first generation DAAs	N=2 studies 2 conference abstracts [100,101]; follow-up [NR; NR], sample size [24; 32], EU/EEA (2)	62.5% eRVR (time period NR), 85.7% (as treated, time period NR).	87.5%	NR	NA
Provision of second generation DAAs	N=7 studies 5 conference abstracts [95,97,104,106,113], follow-up [12 weeks after end of treatment in n=4; NR in n=1], sample size [83; 50; 40; 142; 207] 2 unpublished research reports [114,115], follow-up [12 weeks after end of treatment: NR], sample size [141; 23], EU/EEA (7)	85.0%-98%	90.0%-95.5%	10% (time period NR)	NA

DAAs: Direct-acting antiviral agents; DOT: directly observed therapy, eRVR: extended rapid virological response⁴, IFN: interferon, NR: not reported, RBV: ribavirin, SAT: self-administered therapy, SVR: sustained viral response

¹ Proportion achieving undetectable viral load at 24 weeks/6 months after treatment completion or – in case of DAAs – 12 weeks/3 months after DAAs therapy completion

² Proportion completing the treatment course

³ Proportion lost to follow-up during study

⁴ If studies on usual care did not report the use of DOT, it was assumed treatment was SAT only.

⁴ eRVR indicates an undetectable viral load at week 4 of treatment and maintenance of viral load suppression through week 12

Acceptability and barriers

Twenty-nine of the 34 included studies reported on the acceptability and barriers to HCV treatment in prison settings [87-113,116,117].

Acceptance

Nine studies on HCV usual care with the INF-based regimens (some with partly DOT) reported on the proportion initiating treatment among HCV-positive evaluated inmates to range from 25.8% to 68.6% [87,90,92,94,96,103,110-112]. Compared to treated patients, untreated patients were more likely to be PWID in the community or to be co-infected with HBV [90].

In an RCT comparing INF-based treatment where RBV was administered via DOT or SAT, 7.4% of participants randomly allocated to DOT transitioned to SAT modality of treatment administration [109].

In a comparative study of HCV INF-based treatment outcomes for incarcerated versus non-incarcerated HCV-positive patients, there was no difference in the likelihood of being started on treatment between the two groups (60.3% vs. 61.2%) [107]. Substance abuse, medical and psychiatric issues and patient refusal were reported significantly less as a reason for not initiating treatment among inmates compared to community patients.

In a longitudinal study where nurses independently performed triage on patients for treatment and asked for specialist support either via discussion only, through a teleconference, or a face-to-face assessment, the shortest lead time from assessment to treatment initiation was found among those patients who needed a discussion with the specialist only (no p-value reported), indicating that nurse-led treatment may speed up treatment initiation for uncomplicated cases [98].

Reasons for not initiating treatment were reported in eleven studies on IFN-based regimens only [87,90,94,96,98,103,107,109,110,112,116], and were categorised as personal, clinical or environmental/structural factors:

- Personal: lack of motivation/awareness, fear of adverse events, influence by relatives/others, lack of confidence in health professionals, preference to be treated after release, medical and/or psychiatric contraindications including hepatic decompensation, uncontrolled HIV or diabetes disease, patient deemed to be non-compliant, drug use.
- Clinical: normal transaminases, normal/mild liver biopsy.
- Environmental: release, transfer, delays in laboratory work-up, lack of material resources.

Discontinuation/adherence

Causes of HCV treatment discontinuation were reported in sixteen studies covering the IFN-based regimens [87,89,91-94,96,98,99,102,103,105,108-110]. In addition to clinical reasons, such as treatment side effects and non-response to therapy, a number of personal reasons were reported: voluntary patient withdrawal/gave up, drug use/addiction relapse/drug overdose, non-compliance, tuberculosis relapse, mental health issues, deceased. Environmental factors were frequently reported to be release or transfer. In the longitudinal study of De Juan et al., 2014, most treatment discontinuations occurred in the first trimester of treatment, and release from prison was the most frequent cause for treatment discontinuation during all trimesters except the first, where the main cause was lack of motivation [92]. Studies on DAAs did not report on any additional factors for adherence/discontinuation. On the contrary, fewer reasons were reported (i.e. release, adverse events, non-response and voluntary withdrawal) [60,97,100,101,106,113,117].

Significant predictors of discontinuation of INF-based treatment regimens were personal reasons: injecting drug use in and out of prison ($p=0.006$) and having cirrhosis ($p=0.03$), and environmental reasons – e.g. transfer ($p=0.05$) or release ($p<0.01$) [88,102].

Attrition

Reasons for loss to follow-up were only environmental, namely release or transfer [90,98,102,112].

Predictors of sustained viral response

Three studies reported on various predictors of an SVR apart from having a low viral load [88,93,109]. These were classified as personal and environmental factors. Significant personal predictors of achieving an SVR were no IDU, and having no HIV infection. Not being released from prison during treatment was a significant predictor of achieving an SVR.

Cost-effectiveness

Three cost-effectiveness studies were found on HCV treatment delivery in prisons, two of moderate quality and one of low quality (see Table 11).

In a US study comparing no HCV treatment to a 2-drug INF-based regimen and a 3-drug treatment with DAAs (sofosbuvir), the latter was likely to be cost-effective (based on incremental cost per QALY gained) for incarcerated

persons. However, given the high market price of sofosbuvir at the time of the analysis, affordability was flagged as an important consideration by the authors [118].

In two US cost-effectiveness studies, a strategy in which inmates with chronic HCV undergo liver biopsy and only those with a histologically significant liver disease undergo treatment with standard IFN and RBV was overall cost-effective (based on incremental cost per SVR and incremental cost per QALY gained) compared to treating all inmates without a biopsy or elevated liver enzyme ALT [119,120]. However, the findings from these studies may have limited relevance now, in the light of the technological advances on non-invasive diagnosis methods and the advent of DAAs.

Table 11. Evidence base for the cost-effectiveness of models of care for HCV treatment in prison settings

Intervention description	Studies included	Scenarios	Conclusions	Level of evidence
No treatment vs. 2 drug therapy vs. 3- drug therapy	N=1 study; [118], perspective [societal], time horizon [lifetime] EU/EEA (0)	No treatment vs. 2-drug therapy (pegylated IFN + RBV for 48 weeks) vs. 3- drug therapy with either boceprevir or sofosbuvir (4 weeks of pegylated IFN + RBV followed by 24 weeks of triple therapy)	<i>Short sentences (<1.5 years)</i> - Sofosbuvir 3-drug therapy costs \$25,700 per QALY gained compared with no treatment <i>Long sentences (≥1.5 years)</i> - Sofosbuvir 3-drug therapy dominated other treatments, costing \$28,800 per QALY gained compared with no treatment Sofosbuvir-based treatment is cost-effective for incarcerated persons. Given the high price of sofosbuvir, affordability is an important consideration	Moderate
Treatment with or without elevated ALT or liver biopsy	N=1 study; [119], perspective [Virginia Department of Corrections], time horizon [until 24 months after end of treatment] EU/EEA (0)	Treating (IFN + RBV) all patients without a liver biopsy vs. treating (IFN + RBV) only those with elevated ALT without performing a liver biopsy vs. liver biopsy and examination of liver histology to define sufficient liver injury from chronic HCV (Knodell score <5 and no fibrosis) to warrant treatment (IFN + RBV)	- Cost savings biopsy-directed strategy: USD 124 700 for 100 patients; incremental cost associated with treating all patients: 3 334 for each additional SVR. Cost savings would increase to USD 408 857 when only those with fibrosis were treated (69% of the cohort) - Cost savings ALT-directed strategy: USD 870 191 for the 100 patients; incremental cost associated with treating all patients: USD 0 for each additional SVR A strategy in which inmates with chronic HCV undergo liver biopsy and only those with a histologically significant liver disease undergo therapy with standard IFN and RBV is cost-effective compared to treating all inmates without a biopsy or elevated ALT.	Low
Treatment with or without liver biopsy	N=1 study; [120], perspective [US prison healthcare system], time horizon [lifetime] EU/EEA (0)	No liver biopsy prior to starting treatment (pegylated IFN + RBV) vs. liver biopsy prior to beginning therapy (pegylated IFN + RBV) in order to determine stage of fibrosis.	- Treatment was cost-effective based on cost per QALY gained compared to no treatment in prisoners of all age ranges and genotypes when liver biopsy was not a prerequisite to starting ART - Treatment after pre-treatment biopsy was cost-effective compared to no treatment in prisoners of all age ranges and genotypes with portal fibrosis, bridging fibrosis or compensated cirrhosis Pegylated IFN and RBV combination therapy is cost-effective in the prison population based on incremental cost per QALY gained. The strategy with pre-treatment biopsy was the most cost-effective, however not for inmates between 40 and 49 years old with genotype 1 and no fibrosis.	Moderate

ALT: alanine transaminase, IFN: interferon, QALY: quality-adjusted life year, RBV: ribavirin, SVR: sustained viral response

Guidelines

Four guidelines on HCV treatment were included, three of which were specific to prison settings (one supranational and two national guidelines), and the other one was a supranational guideline not specific to prison settings (Table 12). See Annex 11 for a more detailed summary of relevant information. In short, these guidelines and documents set out the following recommendations which are of interest for this project:

Table 12. Guidelines providing recommendations on HCV treatment in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	Diagnosis and treatment for HCV are expensive and not available in all countries. Assessment for HCV is very similar to assessment for HBV. In addition to assessment of the severity of liver disease, it includes the determination of the genotype of the virus. Both components are critical to treatment decisions.
National Hepatitis C Strategy 2011-2014 (Ireland) [121]	The principle that treatment should be available in an equitable manner for all those infected with HCV. Improving access to treatment and supporting patients through treatment will reduce the progression from viral infection to liver damage for many patients. It should also contribute to a reduction in the prevalence of HCV infection, thus reducing the associated clinical and social burden of the disease.
Technical Group of Italian experts on Hepatitis management (Italy), 2009 [122]	It is advisable to take advantage of a prison stay as a unique occasion to provide information on health and hepatitis in a population which is 'hard-to-reach' when outside the prison walls. It is advisable to start antiviral therapy using DOT only in prisoners with an imprisonment duration that allows the completion of treatment or when the linkage and continuity of care is guaranteed. It is also advisable to start or maintain OST with methadone or buprenorphine in active PWID in order to limit hepatitis transmission and reinfection.
<i>Other guidelines – supranational guidelines</i>	
European Association for the Study of the Liver (EASL), 2016 [34]	The goal of therapy is to cure HCV infection to prevent hepatic cirrhosis, decompensation of cirrhosis, hepatocellular carcinoma (HCC), severe extrahepatic manifestations and death. In 2016 and onwards, IFN-free regimens are the best options in treatment-naïve and treatment-experienced, DAA-naïve patients with compensated and decompensated liver disease, because of their virological efficacy, ease of use and tolerability. Treatment should be considered without delay in individuals at risk of transmitting HCV (active injection drug users, men who have sex with men with high-risk sexual practices, women of child-bearing age who wish to get pregnant, haemodialysis patients, incarcerated individuals).

However, more EU/EEA countries may have or be in the process of developing policies, strategy documents or guidelines covering prevention of HCV in prison settings and the above list may therefore not be exhaustive.

3.4 Throughcare

3.4.1 Throughcare at prison entrance

No studies were found on throughcare at prison entrance (i.e. from the community to prison settings).

3.4.2 Throughcare on release from prison

Nineteen studies were included which reported on throughcare models of care upon release from prison. Results are presented separately for interventions aimed at prevention of BBVs post-release, and interventions aimed at linkage to care post-release. Most interventions were focused on HIV. See Annex 12 for a more detailed summary of relevant information.

3.4.3 Prevention of blood-borne viruses post-release

Eight studies reporting on prevention of BBV infections post-release were included from the peer-reviewed literature, all from outside the EU/EEA [123-130]. No conference abstracts were found on this topic. The study quality of the peer-reviewed literature was mostly low to very low, even though most studies were RCTs.

Effectiveness

All eight included studies reporting on effectiveness of interventions to prevent BBVs post-release (see Table 13). The included studies investigated a range of different interventions, with three studies covering more individually-oriented interventions [123,126,130], and five covering group-oriented interventions [124,125,127-129]. The interventions were multifaceted and included counselling, case management, peer- or regular education, skills building, social support, and relationship-focused contents. As there was considerable heterogeneity between these interventions, and different comparison groups were used, it was not possible to group the studies or perform a meta-analysis.

Overall, none of the studies included reported on seroconversion after the introduction of a BBV prevention intervention as a study outcome. Studies investigated a range of different behaviour outcomes, while similar behaviour outcomes were often investigated differently between studies. Overall, in all but one comparative study, the interventions resulted in greater improvements for several of the measured behavioural outcomes compared to usual care. However, this was not the case for all measured outcomes. In general, in almost all comparative studies, unprotected sexual intercourse was less frequent in the intervention group than in the control group, while

generally no difference was found in drug-injecting behaviour and likelihood of sharing injecting equipment between intervention and control groups. One study did not find a significant difference between the intervention group and control group in any of the outcomes [129]. In this study, which is quite old, the intervention group consisted of four educational group sessions before release while the control group received no education at all.

Attrition in these studies ranged from 17% to 49% in intervention groups, and from 18% to 56% in control groups.

Table 13. Evidence base for the effectiveness of interventions to prevent BBVs post-release

Intervention description	Studies included	Outcome 1: sero-conversion	Outcome 2: behaviour change	Attrition ¹	Level of evidence
Individual counselling and case management services (7 modules before release)	N=1 study; Longitudinal study [123], follow-up [NR], sample size [745], EU/EEA (0)	NR	Significant improvement after intervention in: attitude towards condoms, self-efficacy to use condoms, self-efficacy to reduce IDU and other substances risk, safe sex intentions and likelihood having HIV/AIDS.	NR	Very low
Individual 30-minute peer-education session before release vs. no intervention	N=1 study; RCT [126], follow-up [2 weeks after release], sample size [404] EU/EEA (0)	NR	After release, intervention group significantly more condom use during first time sex after release compared to control, but no significant difference in drug use, IDU and sharing injecting equipment since release	- Intervention: 42.5% - Control: 42.0%	Very low
Individual enhanced multisession intervention (2 before, 4 after release) vs. individual single-session intervention (before release)	N=1 study; RCT [130], follow-up [24 weeks after release], sample size [522] EU/EEA (0).	NR	24 weeks after release, significantly less unprotected sex with any partner, main partner, and at-risk partner, but not with non-main partner in enhanced intervention compared to single-session intervention group. No significant differences at 1 and 12 weeks post-release.	- Single session: 17.8% - Other: 16.7%	Low
Group sessions skills building and social support intervention (16 before, 6 after release) vs. standard care (3 AIDS information group sessions before release)	N=1 study; RCT [124], follow-up [1 month after release], sample size [145], EU/EEA (0)	NR	Significantly greater improvement post-release in the intervention group compared to standard care in safer sex behaviour, coping skills, and perceived emotional support, but no significant difference between groups in perceived vulnerability to HIV, sexual self-efficacy and AIDS knowledge	- Intervention: 26.9% - Control: 33.3%	Very low
Group sessions behavioural intervention (9 before, 3 short phone calls after release) vs. standard care (single STI education in 1 st 3 months of incarceration).	N=1 study; RCT [125], follow-up [6 months after release], sample size [521] EU/EEA (0).	NR	Significantly more improvement post-release in intervention group compared to standard care in HIV knowledge, health-protective communication, motivational barriers to condoms, physical spousal abuse (all at 3 months after release), and unprotected vaginal sex outside monogamous relationships, condom use during sex with main partner, HIV knowledge, motivational, partner and physical effect barriers to condom use, and tangible support (all at 6 months after release). See summary table for non-significant differences.	- Intervention: 40.4% - Control: 44.5%	Moderate

Intervention description	Studies included	Outcome 1: sero-conversion	Outcome 2: behaviour change	Attrition ¹	Level of evidence
Group sessions relationship-focused intervention (5 before, 1 after release) vs. standard care (short HIV/AIDS information video)	N=1 study; RCT [127,128], follow-up [90 days], sample size [378/344] EU/EEA (0)	NR	Intervention group reported post-release significantly fewer past-month unprotected sexual behaviours than control group; greater improvement in intervention group in overall HIV knowledge of HIV risk behaviours, self-esteem, sexual relationship power, relationship control, specific HIV risk knowledge items, and specific myths. See summary table for non-significant differences.	9%	Low
Group educational sessions intervention (4 before release) vs. standard of care (no health education)	N=1 study; Comparative [129], follow-up [median 7months after release], sample size [101] EU/EEA (0)	NR	No significant difference at post-release between both groups in drug injection, needle/syringe sharing and sterilisation, heroin use, crack use, multiple sexual partners, high-risk sexual partners, condom use, and enrolling or remaining in drug dependency treatment. Being in drug dependency treatment at the time of follow-up was associated with reductions in heroin use and drug dealing	- Intervention 48.5% - Control: 55.6%	Very low

NR: not reported, RCT: randomised controlled trial

¹Proportion lost to follow-up during study.

Acceptability and barriers

Seven of the eight studies included reported on barriers and acceptance to the prevention interventions [123-128,130].

In a longitudinal study evaluating an individual counselling and case management intervention, completion rates per mandatory module varied from 21.2% to 95.8%, and 88% of participants completed ≥ 2 mandatory modules, but only 39% completed three or four modules [123]. Despite the goal of individualised attention, participants completed more modules and spent more programme time in group sessions.

In an RCT comparing an individual 30-minute peer-education session to no session, 19% refused to participate (reasons not reported), and only 60.3% of those randomised to the intervention group, received the intervention [126]. Reasons for this were: failure to appear for their intervention appointment (not further specified), unable to attend due to institutional lock-downs, or unexpectedly paroled (percentages not reported).

In an RCT comparing an enhanced individually-focused intervention (two sessions before release and four after release) to a single-session intervention before release, 5.2% refused to participate (reasons not reported) [130]. Attendance of the enhanced intervention sessions was 88.6%-98.5% for the pre-release sessions and 65.8%-79.8% after release; 18.6% chose to receive additional sessions. Attendance was 94.2% for the one session in the single-session intervention.

El Bassel et al. 1995 compared a skills building and social support group intervention (16 sessions before release, six sessions after release) with an information group intervention (three sessions before release) [124]. In the skills building and social support group intervention 52.2% attended ≥ 13 sessions, 28.4% 4-12 sessions, and 19.4% attended ≤ 3 sessions. In the information group intervention 85.9% attended all three sessions.

Fogel et al. 2005 compared a behavioural group sessions intervention (nine sessions before release, short phone calls after release) to standard care (STI education in first three months of incarceration), and found that 12.0% refused to participate (reasons not reported), and 12.8% of participants did not attend any of the behavioural group sessions [125].

In an RCT comparing a relationship-focussed group sessions intervention (five sessions before release, one after release) with standard care (short HIV/AIDS informational video), 4.3% of screened women refused to participate (reasons not reported) [127,128].

Although most studies reported attrition during the study, none reported the corresponding reasons.

Cost-effectiveness

No studies were found on the cost-effectiveness of interventions to prevent BBVs post-release.

Guidelines

No specific guidelines have been found on BBVs prevention post-release.

3.4.4 Linkage to care post-release

Eleven studies reporting on linkage to care post-release were included from the peer-reviewed literature, all from outside the EU/EEA. No conference abstracts were found on this topic. The study quality of the peer-reviewed literature was mostly low to very low, even though half were RCTs. All but three studies focused on HIV.

Effectiveness

Eight included studies reported on effectiveness of interventions to increase linkage to care post-release for HIV treatment (see Table 14) [131-138]. As a large heterogeneity exists between these interventions, and different comparison groups were used, it was not possible to group the studies nor to perform a meta-analysis.

One RCT compared an ecosystem intervention with an individually focused intervention. The participants in the ecosystem group were significantly less likely to be taking anti-HIV medication and to be adherent at four months post-release, but no significant difference was observed in groups and between groups at eight and twelve months post-release [134]. No significant difference was observed in sexual behaviour after release in the two groups.

Two studies compared an individual-level intervention with usual care, one focusing on education and skills building [133] and the other on intensive case management [136]. The two studies did not find significant differences between intervention and control groups in adherence to HIV treatment, accessing HIV and outpatient substance abuse services in the community after release. Moreover, no significant difference between both groups was found on sexual behaviour, STIs occurrence and injecting drug use after release.

One comparative study assessed the impact of a multifaceted intervention involving education, individual counselling, discharge planning, and being met at the gate or soon after release by a case manager [132]. Those being met at the gate by a case manager were significantly more likely to access drug/alcohol treatment in the community and engaged significantly less in sex exchange and street drug use, compared to those not being met at the gate. Another comparative study assessed the impact of retention in OST for PWID on ART after release. Those on OST (with buprenorphine) were significantly more likely to achieve viral suppression than the other groups [138].

In a descriptive study of usual care, inmates were actively referred to community health care services and received a medication supply prescription at release. However, only 71% of those who were given a prescription collected it before release. A follow up among those individuals subsequently re-jailed showed that 46% had accessed HIV care services in the community [135]. In another descriptive study of usual care, 58% were linked to care in the community [131]. No significant association was found between length of incarceration and linkage to care. Another descriptive study [137] reported similar proportion of HIV visit attendance post-release. Retention in care post-release was higher among male individuals having an HIV care provider before incarceration and receiving individual support services before release (e.g. disease management session and discharge planning) and in the community (e.g. needs assessment, HIV education, and transportation assistance).

Finally, three similar RCTs assessed the impact of induction on OST during imprisonment on linkage and retention in drug-dependence community programmes [139-141]. The studies concurrently reported a significantly higher likelihood of enrolment and retention in OST programmes for those who received OST while in prison.

Attrition in these studies ranged from 3% to 46%.

Table 14. Evidence base for the effectiveness of interventions in increasing linkage to care post-release

Intervention description	Studies included	Outcome 1: Linkage to care	Outcome 2: Behaviour change	Attrition ¹	Level of evidence
HIV treatment					
Ecosystem vs. individually focused (both medication supply at release)	N=1 study; 1 RCT [134], follow-up [12 months post-release], sample size [151] EU/EEA (0).	Ecosystem significantly less likely to be taking anti-HIV medications and to be adherent at four months post-release (both groups significant decrease vs. baseline), but no significant difference in groups and between groups at eight and 12 months post-release.	No significant difference between both groups in sexual behaviour after release.	15%	Moderate
Individual-level educational and skills-building intervention vs. usual care (medication supply at release NR).	N=1 study; 1 RCT [133], follow-up [3 months post-release], sample size [73], EU/EEA (0).	No significant change in taking HIV medication from time of release to three months post-release in both groups and between groups. Intervention recipients reported a statistically significant increase in receiving healthcare at HIV clinics at 3-month post-release (62.5–84.4 %); no significant difference between groups.	No significant change in unprotected vaginal or anal sex, IDU, and STI diagnosis from three months pre-incarceration to three months post-release between groups.	14%-25%	Low
Individual-level intensive case management vs. usual care (both 30-day medication supply at release).	N=1 study; 1 RCT [136], follow-up [48 weeks post-release], sample size [89], EU/EEA (0).	No significant difference between both groups in % medical care access \geq once, median time to clinic access, mean number of clinic visits, rate of hospitalisations, ER or urgent care centre visits, and outpatient substance abuse care post-release.	NR	40%-46%	Low
Being met at the gate vs. not being met at the gate, (both education, counselling and discharge planning, medication supply on release NR).	N=1 study; 1 comparative [132], follow-up [6 months post-release], sample size [226], EU/EEA (0)	Those being met at the gate participated significantly more in drug/alcohol treatment after release than those not met at the gate.	After release those met at the gate were significantly less engaged in sex exchange and use of street drugs than those not met at the gate.	35%	Very low
Provision of OST for PWID on ART vs. no OST (ART administered either DOT or SAT).	N=1 study; 1 comparative [138], follow-up [6 month post-release], sample size [94], EU/EEA (0).	Retention on OST (buprenorphine) was significantly associated with increased likelihood of achieving viral suppression (<50 copies/ml) ($p=0.03$), receiving DOT or methadone were not associated with viral suppression post-release.	NR	8%	Low
Usual care (active referral after release, with or without medication supply).	N=2 study; 2 longitudinal [135,137], follow-up [NR, 6-month], sample size [77; 867], EU/EEA (0).	In total, 69% received 3-day supply prescription, of whom 71% picked it up; 46% of those re-jailed received HIV medications in community. In total, 61% had an appointment with a community HIV care services; 58% attended HIV care in the first 3 months; 475 in the second 3 months post release; 38% attended twice in 6-month period.	NR	NR	Very low
Usual care (referral after release only, unclear if active or passive)	N=1 study; 1 longitudinal [131], follow-up [NR], sample size [64], EU/EEA (0).	In total, 58% linkage to care No significant association between length of incarceration and linkage to care.	NR	NR	Very low

Intervention description	Studies included	Outcome 1: Linkage to care	Outcome 2: Behaviour change	Attrition ¹	Level of evidence
Opioid Substitution Treatment					
No OST in prison without (Group 1)/with (Group 2) referral to community OST vs OST in prison and referral.	N=1 study; 1 longitudinal [139], follow-up [12-month], sample size [204], EU/EEA (0)	-Group 1:25% enrolled in care; 0% were on OST at 12-month -Group 2: 53.6% enrolled in care; 17.3% were on OST at 12-months. -Group 3: 70.4% enrolled in care; 36.7% were on OST at 12 months. Pair-wise comparison all significant (p<0.01)	Positive urine test for opioid at 12-month post-release: -Group 1: 65.6% -Group 2: 48.7% -Group 3: 25% Group 3 significantly less as compared to Group 1 & 2.	3.3%	Low
No OST in prison with referral to community OST vs OST in prison and referral.	N=1 study; 1 RCT [140], follow-up [12-month], sample size [211], EU/EEA (0).	Participants in the in-prison BPN group were significantly more likely (p=0.012) to enrol into community OST programmes (47.5% vs. 33.7%).	No statistically significant difference for days of heroin use and crime, and opioid and cocaine positive urine screening test results (all Ps>0.14)	NR	Low
OST in prison and financial support (Arm 1) vs. no OST in prison with (Arm 2)/without (Arm 3) financial support. All participants received referral.	N=1 study; 1 RCT [141], follow-up [6-month], sample size [90], EU/EEA (0).	Participants on OST prior to release were significantly more likely to enter treatment post release (P < 0.001). Among participants who enrolled in community OST, those who received OST in prison did so within fewer days (P =0.03).	Participants on OST prior to release reported less heroin use (P = .008), other opiate use (P = .09), and injection drug use (P = .06) at six months.	30%	Very Low

BNP: Buprenorphine, ER: emergency room, OST: Opioid Substitution Treatment, NR: not reported, RCT: randomised controlled trial

¹Proportion lost to follow-up during study.

Acceptability and barriers

Among the four studies reporting on attrition, only two reported the relevant reasons, which were release/transfer and loss to follow-up (not further specified) [132,136].

In two intervention studies, the intervention did not proceed according to plan. In the RCT comparing an ecosystem intervention to an individually focused intervention, 28% of those in the ecosystem group did not succeed in identifying a support person to participate in the intervention [134]. In the comparative study, where the protocol indicated that a case manager meets the inmate soon after release, only 46% were successfully met at the gate (reasons not reported) [132].

In a longitudinal study, 72% of those eligible for HIV treatment, were on treatment in jail, while 15% refused therapy (reasons not reported), 6% were scheduled for release before receiving therapy, and an additional 7% did not receive the treatment for unreported reasons [White, 2001]. A total of 29% of those on treatment at the time of release did not receive a prescription as per protocol, either because they were transferred to a residential drug treatment programme or were released early.

Cost-effectiveness

No studies were found on the cost-effectiveness of interventions to increase linkage to care post-release.

Guidelines

Seven guidelines that reported on throughcare were included, five of which were specific to the prison setting (two supranational and three national guidelines). One was a supranational document not specific to prison settings, and one was a national document not specific to prison settings (Table 15). See Annex 12 for a more detailed summary of relevant information. In short, these guidelines set out the following recommendations which are of interest for this project.

Table 15. Guidelines providing recommendations on throughcare at release (linkage to care)

Guidelines	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	For both HIV and hepatitis C, continuity of treatment is essential to ensure the best outcomes and prevent the development of resistance. Health programmes in prisons should therefore work in close collaboration with the HIV programme in the community to ensure that treatment is not interrupted when people enter and leave prison.
WHO, 2007 [53]	Ensuring continuity of care from the community to the prison and back to the community, as well as continuity of care within the prison system is a fundamental component of successful efforts to scale up treatment.
<i>Specific to prison setting – national guidelines</i>	
SIMIT/ Ministero della Salute (Italy), 2016 [57]	Assure the linkage of HIV infected prisoners to the local Infectious Diseases (ID) division and arrange a calendar of weekly visits. In order to assure continuity of care, at least seven days of ART treatment should be given to the prisoner upon release. In order to guarantee continuity of care (50% of prisoners do not show up at the specialist visit after release), the referral ID specialist must be involved in outpatients' networks present in the community.
SAMHSA, 2017 [142]	Guideline 5: Anticipate that the periods following release (the first hours, days, and weeks) are critical and identify appropriate interventions as part of transition planning practices for individuals with mental health and co-occurring substance use disorders leaving correctional settings.
<u>National prison services (Czech Republic), 2012 [143]</u>	Introduce standardised systems to inform prisoners about drug services provided in the prison by specialised providers, including NGOs; and to set up the system to ensure access to service <ul style="list-style-type: none"> - Implement a referral system within the prison system for drug services. - Set up a catalogue of services outside the prison system, that is also taking care of prisoners post-release. - Intensify cooperation of the prison HCW providing drug services with regional antidrug coordinators and ensure linkage to care after release. - Implement interventions in overdose prevention and other risks in the post-release period. - Implement on obligatory bases referral to specialised drug dependency care units and drug free zones programmes for individuals after release. - Include prevention of relapse in therapeutic programmes. - The prison needs to provide medical records/treatment report to the individual's request upon release. - In case of treatment ordered by court (coercive treatment), there should be a specialised methodology for wards that are implementing this. - Notification of drug test results, including negative results, performed on people in detention should be recorded. - Prisoners can be required to be included in a regime of intensive random testing for drug use. - Drug counselling should be available in every prison. - OST should be implemented in prison by specialised wards according to national standards. OST can be coercive (ordered by court) or voluntary. Patient should be informed about OST regimen and about continuation of treatment in the community. Patient can choose from a set of specialised institutions the preferred one/the one closed to his/her place of residence. Standard referral process is then initiated by the prison
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	If and when transferred, people in prisons and other closed settings should be given a supply of ART to last until healthcare can be established at the new prison location or, if they are being released, until linkage can be made to community-based HIV care.
<i>Other guidelines – national guidelines</i>	
Department of Health (UK), 2017 [41]	It is the responsibility of the prison healthcare/drug team to ensure that the community service/prescriber is notified of a patient's release from prison. The patient should be reviewed in the community drug service on Day One whenever feasible, or otherwise within days of discharge. For unplanned weekend release (including short-term release on temporary licence), a community pharmacist should be located to provide an interim dispensing service and a prescription should be provided to the patient on release requesting supervised daily dispensing as preferable.

4. Discussion

4.1 Main findings

This systematic review provides an overview of the best available evidence in the peer-reviewed and grey literature on prevention and control of BBVs in prison settings. Below, the main findings from the peer-reviewed literature and grey literature are summarised.

4.1.1 Prevention of transmission of blood-borne viruses

Five peer-reviewed articles and one conference abstract were included reporting on a few prevention interventions such as condom provisions, health promotions initiatives and safe tattooing. Additional prevention measures such as active case finding and HBV vaccination were covered elsewhere [24] [ECDC unpublished].

According to the literature, condom distribution was implemented either via vending machines located in various places within prison premises or handed out regularly by staff. Overall, regardless of condom provision modalities, 11–28% of inmates reportedly used condoms through these programmes, but not necessarily for sex [45]. Condom use was estimated to reduce HIV transmission by 25% and be cost-saving in one cost-effectiveness study [48]. Overall, condom distribution was supported by 55–84% of inmates. Although no major incidents were reported during the programmes, concerns were raised over possible increase in sexual activity and the inconsistent message of condom availability with the prohibition of sex in prison.

Safe tattooing in prison was shown to be acceptable for people in detention in one study, however no infection-related outcomes were reported to assess the effectiveness on the measure in reducing infection transmission [46].

Two RCTs investigated a combination of health promotion and skills-building interventions and their impact on HIV knowledge and behaviour outcomes. While one study comparing six weekly group behaviour sessions to usual care (didactic lectures) revealed greater improvements in all measured HIV knowledge and behaviour outcomes [47], another older study comparing six weekly skills building group sessions to unstructured discussion group sessions showed conflicting results [50].

Comparing the results of individual studies is challenging, since the included studies investigated different prevention strategies (i.e. condoms, safe tattooing, a group behaviour intervention and a group skills-building intervention), using different outcomes, follow-up durations and comparison groups (if any), and among different study population sizes and study settings. Due to this heterogeneity, it is hard to draw conclusions based on the studies included on which prevention intervention should best be implemented in prison settings.

On the other hand, a number of supranational and national guidelines were identified providing recommendations on prevention for BBVs in prison settings. Based on the existing evidence in prison settings and, by analogy, in community settings, these documents promoted a comprehensive basket of prevention measures, including, over and above the interventions listed above, prevention of mother-to-child transmission for pregnant women, pre- and post-exposure prophylaxis as well as infection control measures to prevent iatrogenic transmission (safe health care services).

Prevention of injecting-related infections among people who inject drugs

Six studies were included, reporting on the prevention of injecting-related infections in prison settings and covering NSP and provision of OST in prison settings. No studies were retrieved reporting on prevention of injecting-related infections other than BBVs.

Two comparative studies on OST found no difference in HIV and HCV seroconversions between the OST and the control groups [59,60], possibly due to the study sample size not being powered to detect meaningful changes in HIV or HCV incidence. However, periods of imprisonment of less than two months and being on OST for less than five months were both significantly associated with increased risk of HCV seroconversion [60]. Moreover, compared to community settings, OST dropout risk was higher in prison during short sentences (≤ 1 month), and lower during longer (> 4 months) sentences. Finally, according to a cost-effectiveness study OST programmes in prison are no more costly than community-based programmes [64].

The studies reporting on NSP were heterogeneous with two assessing NSP programmes implemented in single prison institutions [61,62], and one reporting on a country-wide prison NSP programme [63]. Clean injecting equipment was either distributed through vending machines located within prison premises, or by healthcare staff, and based on one-to-one exchange. HCV seroconversions were reported in one of the two single-institution studies and attributed to sharing of injection paraphernalia; no HIV or HBV seroconversions were reported. In the country-wide study, a reduction in HCV and HIV prevalence in the prison population over a period of more than 15 years was reported, however such reduction is likely to be the result of a comprehensive basket of prevention measures targeting PWID, including OST, in community and prison settings. It is noteworthy that prison staff and, to a less

extent, people in detention, reported concerns about prison security following the distribution of needles and syringes and were not persuaded of the need for such a measure.

Overall, the evidence on the effectiveness of NSP and OST measures to control BBVs transmission in prison settings is limited, mostly due to study designs largely aiming to assess the impact of prevention interventions on drug use and injecting behaviour rather than on communicable disease transmission. However, a substantial body of evidence regarding these interventions exists from community settings⁵ showing the effectiveness of combined and up-to-scale NSP and OST programmes on disease incidence, which may be considered valid, by analogy, in prison settings, given the necessary implementation considerations.

Along these lines, existing UN-system guidelines recommend the implementation of OST programmes in prison settings and the provision of clean and sterile injecting equipment via NSP [7,25,52,58].

4.1.2 HIV treatment

Sixteen studies from the peer-reviewed literature, six of which were from the EU/EEA, and five conference abstracts were included reporting on HIV treatment in prison settings. No cost-effectiveness studies were found.

The studies reported largely on two models of care, SAT and DOT, for the provision of ART in prison settings, implemented either separately or in combination, based on patients' needs. Two non-EU/EEA comparative studies found no significant difference in the two main treatment endpoints, adherence and viral suppression, between the two treatment provision modalities [79,80], while another study from Italy reported a significantly higher proportion of individuals achieving viral suppression among those receiving ART via DOT [81]. It is worth noting that two studies reported on patients voluntarily transitioning from SAT to DOT modality of ART provision and vice versa, which may be suggestive of changing preference over time [74,75].

Another comparative study assessed the introduction of a telemedicine approach to improve HIV quality of care in prison settings [82]. A significant increase in the likelihood of achieving viral suppression was found in the telemedicine group compared to the usual care group, which may indicate this to be a potentially effective approach in the absence of direct access to HIV specialised care in prison settings.

Overall, all studies reported sufficiently high ranges of treatment adherence and levels of viral suppression when ART was provided in prison settings, indicating a good feasibility of HIV treatment implementation in correctional facilities. The proportion of HIV treatment acceptance among those eligible was reasonably high (73–80%) [72,76,77]. Significant personal predictors of treatment adherence were good general or medication management, perception of the benefits of ART and acceptance of treatment, no depression or fatigue, higher academic background, and no IDU as risk factor for HIV transmission. Significant environmental predictors were active occupation inside prison, having supportive prison officers (i.e. willing to open cell to let prisoners take pills), having a social network inside and outside prison and trust in healthcare staff.

In conclusion, while there is sufficient evidence to support HIV treatment implementation in prison settings, no definitive conclusions can be drawn based on the available evidence on treatment models of care to be best implemented in prison settings.

A number of supranational and national guidelines have been retrieved recommending the provision of ART to detained HIV-positive individuals by the same standards as in the community. This includes the initiation of ART irrespective of CD4 count at diagnosis [30].

4.1.3 Viral hepatitis treatment

Twenty-one studies (seven from the EU/EEA), eleven conference abstracts and two unpublished research reports were included reporting on HCV treatment implementation in prison settings, while no study was retrieved on HBV treatment.

The majority of the included studies described provision of IFN-based regimens for the treatment of HCV, using SAT, DOT, or combination of the two as main models of care delivery. One study reported on the introduction of a telemedicine approach to provide specialised care in one prison [98]. Two comparative studies found no significant difference in the two main treatment endpoints, treatment completion and SVR, between SAT and DOT models of care provision [108,109]. Alternative clinical protocols were assessed in two similar economic evaluation studies. The studies concurred that performing a liver biopsy before starting IFN-based treatment is likely to be a cost-effective approach compared to treating all patients [119,120], however this approach may be superseded with the advent of new non-invasive diagnostic technologies to assess liver disease stage (i.e. transient elastography). When assessing the impact of the setting (community vs prison) on treatment initiation, completion and outcome, two comparative studies found no significant difference between the two groups, unless patients were released or

⁵ Refer to EMCDDA Best Practice portal for an overview of the most recent available evidence: <http://www.emcdda.europa.eu/best-practice/harm-reduction/opioid-injectors>

transferred from prison while on treatment [88,107]. Similarly, release or transfer was reported as a major predictor of treatment discontinuation in a number of studies, alongside IDU in and out of prison and having cirrhosis. Furthermore, the acceptance of IFN-based regimens varied widely (26–69%), as reported in nine studies [87,90,92,94,96,103,110-112].

The recent advent of DAAs has opened up new opportunities for the treatment and cure of HCV, in the community as well as in prison. Due to the recent developments in the field, only grey literature sources were retrieved reporting on DAA provision in prison. According to those, and as observed in the community, the proportion of detained patients achieving SVR was much higher (85–98%) compared with IFN-based regimens (42.8-73.6%). These studies indicate a good feasibility for DAA provision in prison settings, while a US cost-effectiveness study suggests that HCV treatment with DAAs is cost-effective for incarcerated persons compared to no treatment or treatment with older regimens [118].

The studies included investigated diverse sets of factors associated with treatment adherence, completion and SVR (e.g. different treatment regimens, adherence interventions). It is challenging to determine the relative effect of each single factor, as they were often investigated in combination, used among different populations, and applied in different settings. However, the available evidence shows that HCV treatment in prison settings is feasible and the introduction of DAAs will result in better treatment outcomes for the prison populations, given the caveat of affordability.

A number of national and supranational guidelines recommend treatment for HCV in the prison settings, with at least one document listing detained individuals as one of the priority groups for treatment initiation on the basis of the risk of further transmission [34].

4.1.4 Throughcare

Nineteen studies, all from outside the EU/EEA, were included reporting on throughcare, and no economic evaluation was retrieved. While throughcare encompasses the two transition periods of admission to and release from prison, all retrieved studies only reported on the latter.

A number of comparative studies described and reported on the impact of behavioural and skills-building interventions aimed at improving BBV prevention post-release [124-130]. In most cases the interventions resulted in significant improvements in several behavioural outcomes, such as occurrence of unprotected sexual intercourse, compared to usual care. However, this was not the case for all measured outcomes, including some specifically relevant ones such as IDU and sharing needles. In general, interventions were well accepted with low rates of refusal. Attendance at intervention sessions varied widely and different measures were used, however it was reported to be higher for pre-release sessions [130].

Linkage to HIV care post-release was investigated in five comparative studies assessing the impact of a range of interventions, from individual education and skills-building programmes to active referral, intensified case management and retention on OST [132-134,136,138]. A study describing an intensified post-release case management approach (being met at the gate by a case manager) showed a significantly higher likelihood of participation in drug/alcohol treatment and significantly less engagement in sex exchange and street drug use in the intervention group compared with the control group [132]. A study reported that retention on OST post release was associated with better treatment outcome, such as viral suppression [138]. No significant difference was reported in access to HIV care or substance abuse services, and adherence to HIV treatment post-release between intervention and control groups in the other studies. Other studies described usual care approaches such as active referral to community healthcare services, including provision of drug prescription to the patient upon release [131,135].

Linkage to and retention on drug dependency treatment post-release was investigated in three RCTs assessing the impact of induction on OST pre-release [139-141]. All studies showed increased likelihood of enrolment and retention in OST programmes among those receiving OST pre-release.

Based on the available evidence, it is hard to draw conclusions on the intervention to be best implemented in prison settings, since all studies investigated different intervention and prevention strategies and comparison groups (or none at all), among different populations and applied in different settings, using diverse outcomes over variable follow-up periods.

Linkage to care post-release is identified as a key step in providing continuity of care in several national and supranational guidelines. In particular, these documents stress the responsibility of the prison healthcare system for designing and implementing effective referral pathways to guarantee linkage and promote access to adequate care after release to avoid treatment discontinuation, including HIV, OST and viral hepatitis.

4.2 Knowledge gaps

4.2.1 General gaps

Overall, this review highlighted a large heterogeneity among studies in both the peer-reviewed and grey literature, making comparisons and conclusions difficult. Moreover, a substantial part of the research was carried out in the USA, which raises concerns on the applicability of the findings to the EU/EEA situation. More well-designed comparative studies are needed on the effectiveness and impact of the different prevention and control strategies for BBVs in the EU/EEA. Moreover, implementation research is needed to report on the operational aspects of intervention set-up, implementation and impact in EU/EEA prison settings.

Topic-specific knowledge gaps are outlined below.

4.2.2 Topic-specific gaps

Prevention of blood-borne viruses

Hardly any data were available on the effectiveness, acceptability and cost-effectiveness of prevention of BBVs in prison settings, especially in the EU/EEA. No studies were found reporting on the outcome seroconversion after the introduction of a BBV prevention intervention. The evidence was largely focused on HIV, and the included studies covered very few of the available prevention interventions (e.g. pre- or post-exposure prophylaxis, safe piercing, sharing everyday items, etc. were not covered).

Prevention of injecting-related infections among people who inject drugs

Very few studies were found that reported on direct infection outcomes of prevention interventions among PWID in prison settings. Only one cost-effectiveness study was found. The studies included covered no alternative prevention interventions other than NSPs or OST. Finally, no evidence was found on prevention of other injecting-related infections, such as bacterial infections at the site of injections.

HIV treatment

Literature on HIV treatment in prison settings was sizeable, although largely using a descriptive design and from non-EU/EEA countries. No cost-effectiveness studies were found.

Viral hepatitis treatment

No evidence was identified on treatment for HBV in prison settings. In the peer-reviewed literature, no evidence was found on provision of DAAs in prison settings, with the exception of one cost-effectiveness study. Hardly any comparative studies were retrieved that could support decision-making on models of care to deliver HCV treatment in prison settings to achieve treatment completion and a sustained viral response.

Throughcare

No studies were found on throughcare when transitioning from community to prison. No studies were found reporting on the outcome seroconversion after the introduction of a BBV prevention intervention in preparation for release from prison. The evidence on linkage to care post-release was mainly focused on HIV treatment, while no studies were found on treatment for hepatitis or OST after release. No cost-effectiveness studies were found. None of the included studies was conducted in the EU/EEA region.

4.3 Strengths and limitations

4.3.1 General strengths and limitations

The strengths of this systematic review include the use of three peer-reviewed literature databases. A broad search over a long period of time was conducted, not limited by outcomes of interest or language. Additional searches for grey literature, such as guidelines, protocols, conference abstracts and unpublished research reports were conducted to counterbalance the fact that research on the topic of prisons and health is generally underrepresented in peer-reviewed literature databases. Multiple grey literature sources were searched. Supplemental documents were retrieved by experts (including documents in languages other than English). Four field researchers performed extensive literature searches in their countries.

A rigorous methodology was applied to identify, critically appraise, analyse and summarise the relevant evidence in order to minimise selection and confirmation bias due to preconceived notions. Researchers adhered to international methodological standards such as Cochrane [43] and PRISMA [44]. The same methodology was also employed by ECDC during the scoping phase of the project. A multi-sectorial expert panel in the field of prison health, prevention and control of communicable diseases and guidance development was closely involved during all stages of the review process.

This systematic review is mainly limited by the scarcity of the literature found. A large number of studies had a descriptive and observational design, which cannot be used to assess effectiveness or causality because of the lack of control groups. Moreover, descriptive studies are subject to certain biases - e.g. a risk of confounding, poor sampling procedures, and loss to follow-up. Drawing conclusions based on indirect comparisons between studies has serious limitations, as differences in population characteristics, settings, countries, treatment regimens, follow-up periods etc. can influence study outcomes. In addition, study characteristics, interventions and outcomes were often poorly described, hampering comparisons. Most studies did not compare the characteristics of participants with those who did not participate in the study. Moreover, most studies did not take confounding or modifying factors into account, and making corrections for such factors can substantially influence the results of a study. Many studies were also conducted in only one institution and had relatively small sample sizes (several below 100 persons), which limits their generalisability. These limitations resulted in the inclusion of studies of mostly low or very low quality. Although for topics other than treatment, some direct comparative studies were found, these were often of lower quality due to methodological flaws (e.g. no or limited description of the randomisation method and allocation concealment, small follow-up periods, and the possibility of contamination between intervention groups due to the confined setting). Limitations of each study were added to the evidence tables (see annexes).

The focus of this report was on EU/EEA countries. Unfortunately, few studies were retrieved from these countries, while the majority of studies came from the USA. While studies from non-EU/EEA countries may be a valuable source of data on the topics of interest, their findings cannot simply be extrapolated to the EU/EEA context due to differences in population structure, healthcare delivery, and correctional systems.

Although this review was focused on adults, the researchers did not reject studies that included people below 18 years of age. Studies focusing solely on young populations were not included.

It was difficult to determine the factors responsible for the observed outcomes in many studies because interventions were often part of a bundle of measures which were not examined separately (i.e. different drugs, regimens, use of DOT, use of and place of adherence interventions for treatment studies; or different intervention contents, duration/intensity, formats, comparison groups, outcomes for prevention studies).

Study settings varied widely among the studies included. In detention centres where people are generally incarcerated for shorter periods, treatment completion is often hampered by the fact that inmates are released or transferred soon after entry. This is less of a problem in prisons, where inmates are incarcerated for longer periods of time. Moreover, detention centres or prisons tend to be different in different countries (e.g. prison setting, composition of the population). Similar settings are therefore not directly comparable between countries. This also applies to healthcare settings, which can differ considerably among countries, even within the EU/EEA.

Outcome definitions varied between studies, and were lacking in some studies. This mostly related to the denominators used for various rates, such as the treatment adherence rate or treatment completion rate. Where possible, outcome values were recalculated to prevent incorrect comparisons. Additionally, many outcomes in the studies included were based on self-reported data, mostly collected during interviews and therefore creating additional bias.

5. Conclusions

The overall objective of this project was to develop a series of evidence-based guidance documents on prevention and control of communicable diseases in prisons. This specific systematic review focused on HIV, viral hepatitis and PWID-targeted interventions and is designed to inform guidance on prevention and control of BBVs in prison settings. In this systematic review we have retrieved evidence on prevention, treatment and care for BBVs, namely HIV, HBV and HCV, including interventions specifically targeting PWID. While the number of studies was sizable for some of these topics (e.g. HIV treatment), we have found an overall weak evidence base, with few comparative studies and a wide variation among studies. In addition, a sizeable fraction of the identified evidence comes from non-EU/EEA countries, posing concerns regarding the generalisability of the findings to the region. Thus, collating and comparing the studies is extremely challenging and it is impossible to provide clear conclusions on which interventions are most effective in prison settings in the EU/EEA. However, through this systematic review we identified a wide variety of interventions that use a range of prevention measures, treatment service models and linkage to care interventions directed at different sub-populations within the prison setting. We also identified predictors of intervention uptake, as well as barriers to their implementation. Most notably, release or transfer from prison was identified as the main factor hampering adherence to and/or completion of treatment for HIV, HCV and OST. These findings are relevant for informing and devising public health interventions to increase coverage and uptake of BBV prevention measures and to scale up treatment in the EU/EEA.

This systematic review highlighted important knowledge gaps. More operational research is needed to assess the effectiveness and cost-effectiveness of BBV prevention and control intervention in prison settings. At the same time this review revealed the value of grey literature as a source of evidence on prevention and control of HIV and viral hepatitis in prison settings in the EU/EEA. Sharing of knowledge and experiences among EU/EEA countries may be a useful approach to stimulate research on this specific topic and to promote spreading of good practices in the region.

Against this perspective, the findings from the systematic review will inform the development of a public health guidance on prevention and control of BBVs in prison setting.

6. Next steps

The findings of this systematic review will serve as the evidence base for the development of an ECDC public health guidance document on prevention and control of BBVs in prison settings. This guidance will be part of a broader set of guidance documents on the prevention and control of communicable diseases in prison settings, which will also encompass other specific interventions, such as active case finding, vaccination, and diagnosis, treatment, care and prevention of TB.

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Annex 1. Search and selection strategy for MA1, MA2 and MA3

This Annex covers the general methodology used for all three macro areas (MA). This annex is attached to give a more extensive overview of the methodology used, while in the methods section of this systematic review report only a summary of the process is presented.

1. Review objectives and questions

The following three review objectives were defined:

Macro area 4: HIV prevention and care

To gain insight in the evidence base (peer-reviewed as well as grey literature) for prevention, care and treatment of HIV in prison settings, including throughcare.

Macro area 5: Viral hepatitis prevention and care

To gain insight in the evidence base (peer-reviewed as well as grey literature) for prevention, care and treatment of viral hepatitis in prison settings, with a focus on treatment of hepatitis C, including throughcare.

Macro area 6: injecting-related infections prevention and control

To gain insight in the evidence base (peer-reviewed as well as grey literature) for prevention and control of injecting-related infections among current and former drug users, including throughcare.

The PICO method was used to develop specific research questions from these review objectives

4 Prevention, care and treatment of HIV	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention, care and treatment of HIV
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in HIV incidence or prevalence, number of people who adhered to treatment, number of people who are linked to care – including community care after release) • Cost-effectiveness
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)
5 Prevention, care and treatment of viral hepatitis	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention, care and treatment of viral hepatitis
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in hepatitis incidence or prevalence, number of people who have completed treatment, number of people who are linked to care – including community care after release) • Cost-effectiveness
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)
6 Prevention and control of injecting-related infections among PWID	
P	Adult individuals (≥ 18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))
I	Prevention and control of injecting-related infections among former/current PWID
C	<ul style="list-style-type: none"> • Comparison with no intervention • Comparison with alternative intervention • No comparison • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.) • Comparison with community setting
O	<p>Qualitative outcomes:</p> <ul style="list-style-type: none"> • Accessibility • Suitability, feasibility and acceptability of interventions • Qualitative description of interventions/modes of service delivery <p>Quantitative outcomes:</p> <ul style="list-style-type: none"> • Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention) • Measures of effectiveness (e.g. change in BBVs incidence or prevalence) • Cost-effectiveness
S	Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms)

For each of these macro areas specific review questions were defined and formulated:

Macro area 4: HIV prevention and care

1. Which prevention interventions for HIV are effective in prison settings?
2. Which care and/or treatment interventions aimed at control of HIV are effective in prison settings?
3. Which service models for prevention, care and/or treatment of HIV are effective in prison settings?
4. Which prevention interventions for HIV are cost-effective in prison settings?
5. Which care and/or treatment interventions aimed at control of HIV are cost-effective in prison settings?
6. Which service models for prevention, care and/or treatment of HIV are cost-effective in prison settings?
7. What is the acceptance/uptake/coverage of prevention, care and/or treatment of HIV in prison settings?
8. How to improve the acceptance/uptake/coverage of prevention, care and/or treatment of HIV in prison settings?
9. Who should be targeted for prevention, care and/or treatment of HIV in prison settings?

Macro area 5: Viral hepatitis prevention and care

10. Which prevention interventions for viral hepatitis are effective in prison settings?
11. Which care and/or treatment interventions aimed at control of viral hepatitis are effective in prison settings?
12. Which service models for prevention, care and/or treatment of viral hepatitis are effective in prison settings?
13. Which prevention interventions for viral hepatitis are cost-effective in prison settings?
14. Which care and/or treatment interventions aimed at control of viral hepatitis are cost-effective in prison settings?
15. Which service models for prevention, care and/or treatment of viral hepatitis are cost-effective in prison settings?
16. What is the acceptance/uptake/coverage of prevention, care and/or treatment of viral hepatitis in prison settings?
17. How to improve the acceptance/uptake/coverage of prevention, care and/or treatment of viral hepatitis in prison settings?
18. Who should be targeted for prevention, care and/or treatment of viral hepatitis in prison settings?

Macro area 6: injecting-related infections prevention and control

19. Which prevention interventions for injecting-related infections among current drug users are effective in prison settings?
20. Which interventions aimed at control of injecting-related infections among current or former drug users are effective in prison settings?
21. Which service models for prevention and control of injecting-related infections among current or former drug users are effective in prison settings?
22. Which prevention interventions for injecting-related infections among current or drug users are cost-effective in prison settings?
23. Which interventions aimed at control of injecting-related infections among current or former drug users are cost-effective in prison settings?
24. Which service models for prevention and control of injecting-related infections among current or former drug users are cost-effective in prison settings?
25. What is the acceptance/uptake/coverage of prevention and control of injecting-related infections among current or former drug users in prison settings?
26. How to improve the acceptance/uptake/coverage of prevention and control of injecting-related infections among current or former drug users in prison settings?

2. Peer reviewed literature search

The search strategy was developed building on the scoping phase by ECDC with respect to using PubMed and Embase as peer-reviewed data sources. Additionally, the Cochrane Library database was searched for systematic reviews and economic evaluations.

Search strings

In order to find relevant articles for the macro areas in PubMed and Embase.com, search strings were developed for each of the following concepts:

1. Prisons, jails and other custodial settings
2. HIV
3. Viral hepatitis
4. Injecting-related infections

It was decided not to add a search string on outcomes, to prevent missing relevant articles. In PubMed and Embase search string #1 was combined using 'AND' with each of the macro area specific search strings (i.e. #1 AND (#2 OR #3 OR #4)).

For Cochrane Library one generic search using the terms for prisons was used to search for all relevant systematic reviews and economic evaluations.

PUBMED

#1 Prisons and other custodial settings

"Prisons"[Mesh] OR "Prisoners"[Mesh] OR prison*[tw] OR penal[tw] OR jail*[tw] OR reformatory*[tw] OR custodial[tw] OR custody[tw] OR gaol*[tw] OR remand*[tw] OR penitentiary*[tw] OR detention*[tw] OR correctional[tw] OR detainee*[tw] OR inmate*[tw] OR imprison*[tw] OR confinement[tw] OR incarcerate*[tw] OR cellmate*[tw]

#2 HIV

"HIV"[Mesh] OR HIV[tw] OR "human immunodeficiency virus"[tw] OR "human immuno-deficiency virus"[tw] OR "human immune-deficiency virus"[tw] OR "human immune deficiency virus"[tw] OR "human immunodeficiency viruses"[tw] OR "human immuno-deficiency viruses"[tw] OR "human immune-deficiency viruses"[tw] OR "human immune deficiency viruses"[tw] OR "Acquired Immunodeficiency Syndrome"[Mesh] OR "acquired immunodeficiency syndrome"[tw] OR "acquired immuno-deficiency syndrome"[tw] OR "acquired immune deficiency syndrome"[tw] OR "acquired immunodeficiency syndromes"[tw] OR "acquired immuno-deficiency syndromes"[tw] OR "acquired immune deficiency syndromes"[tw] OR AIDS[tw]

#3 Viral hepatitis

"Hepatitis"[Mesh] OR "Hepatitis, Viral, Human"[Mesh] OR "Hepatitis Viruses"[Mesh] OR hepatitis[tw] OR HAV[tw] OR HBV[tw] OR HCV[tw] OR HDV[tw] OR HEV[tw] OR "hep a"[tw] OR "hep b"[tw] OR "hep c"[tw] OR "hep d"[tw] OR "hep e"[tw] OR hepacivirus*[tw] OR hepatovirus*[tw]

#4 Injecting-related infections

("Communicable Diseases"[Mesh] OR "Infection"[Mesh] OR infection*[tw] OR virus*[tw] OR pathogen*[tw] OR ((communicable[tw] OR infectious[tw]) AND disease*[tw])) AND ("Drug Users"[Mesh] OR "Needle Sharing"[Mesh] OR "Syringes"[Mesh] OR inject*[tw] OR needle*[tw] OR syringe*[tw] OR paraphernalia*[tw] OR IDU[tw] OR PWID[tw] OR intravenous*[tw] OR intramuscular*[tw] OR subcutaneous*[tw] OR "Cocaine"[Mesh] OR cocaine[tw] OR coke[tw] OR crack[tw] OR "Heroin"[Mesh] OR heroin[tw] OR dope[tw] OR "Methamphetamine"[Mesh] OR methamphetamine*[tw] OR meth[tw] OR "Amphetamine"[Mesh] OR amphetamine*[tw] OR speed[tw] OR crystal[tw] OR speedball[tw] OR "cathinone" [Supplementary Concept] OR cathinone*[tw] OR "Cannabinoids"[Mesh] OR cannabinoid*[tw] OR cannabis[tw] OR "Methadone"[Mesh] OR methadone*[tw] OR "Buprenorphine"[Mesh] OR buprenorphine*[tw] OR "Steroids"[Mesh] OR steroid*[tw] OR "Central Nervous System Stimulants"[Mesh] OR stimulant*[tw] OR "Analgesics, Opioid"[Mesh] OR opioid*[tw] OR "Tattooing"[Mesh] OR "Body Piercing"[Mesh] OR tattoo*[tw] OR pierc*[tw])

Embase

#1 Prisons and other custodial settings

'prison'/exp OR 'prisoner'/exp OR prison*:ti,ab OR penal:ti,ab OR jail*:ti,ab OR reformatory*:ti,ab OR custodial:ti,ab OR custody:ti,ab OR gaol*:ti,ab OR remand*:ti,ab OR penitentiary*:ti,ab OR detention*:ti,ab OR correctional:ti,ab OR detainee*:ti,ab OR inmate*:ti,ab OR imprison*:ti,ab OR confinement:ti,ab OR incarcerate*:ti,ab OR cellmate*:ti,ab

#2 HIV

'Human immunodeficiency virus'/exp OR HIV:ti,ab OR "human immunodeficiency virus":ti,ab OR "human immuno-deficiency virus":ti,ab OR "human immune-deficiency virus":ti,ab OR "human immune deficiency virus":ti,ab OR "human immunodeficiency viruses":ti,ab OR "human immuno-deficiency viruses":ti,ab OR "human immune-deficiency viruses":ti,ab OR "human immune deficiency viruses":ti,ab OR 'acquired immune deficiency syndrome'/exp OR "acquired immunodeficiency syndrome":ti,ab OR "acquired immuno-deficiency syndrome":ti,ab OR "acquired immune deficiency syndrome":ti,ab OR "acquired immunodeficiency syndromes":ti,ab OR "acquired immuno-deficiency syndromes":ti,ab OR "acquired immune deficiency syndromes":ti,ab OR AIDS:ti,ab

#3 Viral hepatitis

'hepatitis'/exp OR hepatitis:ti,ab OR HAV:ti,ab OR HBV:ti,ab OR HCV:ti,ab OR HDV:ti,ab OR HEV:ti,ab OR "hep a":ti,ab OR "hep b":ti,ab OR "hep c":ti,ab OR "hep d":ti,ab OR "hep e":ti,ab OR hepacivirus*:ti,ab OR hepatovirus*:ti,ab

#4 Injecting-related infections

('communicable disease'/exp OR 'infection'/exp OR infection*:ti,ab OR virus*:ti,ab OR pathogen*:ti,ab OR ((communicable:ti,ab OR infectious:ti,ab) AND disease*:ti,ab)) AND ('intravenous drug abuse'/exp OR 'drug abuse'/exp OR 'drug use'/exp OR 'syringe'/exp OR inject*:ti,ab OR needle*:ti,ab OR syringe*:ti,ab OR paraphernalia*:ti,ab OR IDU:ti,ab OR PWID:ti,ab OR intravenous*:ti,ab OR intramuscular*:ti,ab OR subcutaneous*:ti,ab OR 'cocaine'/exp OR cocaine:ti,ab OR coke:ti,ab OR crack:ti,ab OR 'diamorphine'/exp OR heroin:ti,ab OR dope:ti,ab OR 'methamphetamine'/exp OR methamphetamine*:ti,ab OR meth:ti,ab OR 'amphetamine'/exp OR amphetamine*:ti,ab OR speed:ti,ab OR crystal:ti,ab OR speedball:ti,ab OR 'cathinone'/exp OR cathinone*:ti,ab OR 'cannabinoid'/exp OR cannabinoid*:ti,ab OR cannabis:ti,ab OR 'methadone'/exp OR methadone*:ti,ab OR 'buprenorphine'/exp OR buprenorphine*:ti,ab OR 'steroid'/exp OR steroid*:ti,ab OR 'central stimulant agent'/exp OR stimulant*:ti,ab OR 'narcotic analgesic agent'/exp OR opioid*:ti,ab OR 'tattooing'/exp OR 'body piercing'/exp OR tattoo*:ti,ab OR pierc*:ti,ab)

Cochrane Library

#1 Prisons and other custodial settings

MeSH descriptor: [prisons] explode all trees OR MeSH descriptor: [prisoners] explode all trees OR prison*:ti,ab,kw OR penal:ti,ab,kw OR jail*:ti,ab,kw OR reformatory*:ti,ab,kw OR custodial:ti,ab,kw OR custody:ti,ab,kw OR gaol*:ti,ab,kw OR remand*:ti,ab,kw OR penitentiary*:ti,ab,kw OR detention*:ti,ab,kw OR correctional:ti,ab,kw OR detainee*:ti,ab,kw OR inmate*:ti,ab,kw OR imprison*:ti,ab,kw OR confinement:ti,ab,kw OR incarcerat*:ti,ab,kw OR cellmate*:ti,ab,kw

Search limits

The only search limits that were applied for this systematic review are a time limit and a geographical limit. Literature was searched in PubMed and Embase from 1990 onwards and in Cochrane Library, systematic reviews and economic evaluations were searched from 1980 onwards. The literature search was further limited to include only literature from EU/EEA/EFTA countries or their candidate countries and other Western countries (i.e. USA, Canada, Australia and New Zealand). Articles from these non-EU/EEA/EFTA high-income countries were included to broaden the evidence base. A geographical search string was used to limit the searches in PubMed and Embase (see Annex 2).

Language limits were not applied. Additionally, an age limit was not applied in the search phase. Rather, during title and abstract screening phase, articles focusing only on those <18 years were not included.

Running the literature search

The final searches in PubMed, Embase and Cochrane Library were run on the 12th of January 2017. Due to overlap between the three macro areas, the search strings were combined in a single search. The relevant full text publications were subdivided into the three separate macro areas during the screening of full article phase.

PubMed, Embase, and Cochrane Library output, including all indexed fields per hit (e.g. title, authors, abstract), were exported to Endnote version X7.4 and saved in separate folders per database. Duplicate articles were removed through automatic and manual duplicate removal.

Hand search

Reference lists of good quality systematic review articles were checked for further potentially relevant articles.

3. Peer reviewed literature selection

From the articles retrieved from PubMed, Embase, and Cochrane Library the relevant references were selected by a three-phase selection procedure, based on:

- Screening of title and abstract (first selection phase): in this phase, titles of publications were screened based on the inclusion and exclusion criteria (see below). If the title was inconclusive, the abstract was read. Articles with titles and abstracts that suggest that they did not contain information relevant to the review objectives were not selected for full-text assessment (no reason for exclusion documented per article). In case of doubt, the article was checked full-text in the second selection step. Articles that were excluded during screening of title and abstract were stored in an indexed folder in Endnote.
- Screening of full article (second selection phase): the articles selected during the first phase were assessed in full text. PDF-files of the original articles were downloaded and stored. Articles were included if the reported information was relevant (based on the inclusion and exclusion criteria, see below) and of sufficient quality (see section 2.3). The reasons for exclusion of full-text papers were documented per article and summarised in an exclusion table.

- Screening during data-extraction phase: further scrutiny of the article during the data-extraction phase could have led to exclusion. For example, when articles make use of the same dataset and present identical outcome measures, the most recent or the most extensive article was included.

The process of selection and inclusion and exclusion of articles was registered in an Excel file and an Endnote library.

Inclusion and exclusion criteria

The inclusion and exclusion criteria are listed in Table 1 below.

Table 1. Inclusion and exclusion criteria peer-reviewed literature

	Inclusion	Exclusion
Study design/type	<ul style="list-style-type: none"> • Randomised controlled trials (RCTs) • Non-randomised, prospective comparative studies • Prospective observational studies (e.g. cohort studies) • Retrospective observational studies (e.g. case-control studies) • Cross-sectional studies 	<ul style="list-style-type: none"> • Meta-analysis or systematic review¹ • Narrative review • Case reports/small case series • Non-pertinent publication types (e.g. expert opinions, letters to the editor, editorials, comments, conference abstract/poster, news, consensus document, chapter) • Animal studies • Genetic studies, biochemistry or molecular studies • Modelling studies (i.e. this did not apply to economic evaluation studies)
Study quality	<ul style="list-style-type: none"> • Study duration (no minimum) • Number of subjects (no minimum) 	<ul style="list-style-type: none"> • Insufficient methodological quality (both inherent methodology as well as insufficient description of inherent methodology provided; based on quality checklists)
Study population	Adults in prisons, jails and other custodial settings that function as a prison <ul style="list-style-type: none"> • Detained persons, including persons in remand • Persons 'going through the gate' (e.g. prison guards, healthcare workers, etc.) 	<ul style="list-style-type: none"> • Children (<18 years) • Persons in police custody • Persons in migrant detention centres
Study comparison	<ul style="list-style-type: none"> • Comparison appropriate for a specific outcome 	
Specific outcomes of interest	<ul style="list-style-type: none"> • Quantitative outcomes • Qualitative outcomes 	<ul style="list-style-type: none"> • No exclusion based on outcomes

¹ Relevant meta-analyses and systematic reviews will be selected during the screening of title and abstract phase. During the full text phase, reference lists of these meta-analyses and systematic reviews will be checked for possibly missed relevant individual articles. No data extraction will be performed for meta-analyses or systematic reviews, only for relevant individual articles.

4. Grey literature search

A grey literature search with a focus on EU/EEA countries was performed to complement the evidence from the peer-reviewed literature. Reports and documents focusing on prisons and people in prisons were searched for.

The following types of documents were searched for:

- Articles, abstracts, research reports
- Guidelines and protocols
- Case studies, service models

This grey literature search comprised the following sources:

- A pre-defined list of websites
- Call for papers/experts input

Search on websites of conference abstracts

In order to capture studies not published yet in peer-reviewed literature, conference abstracts published from 2010 onwards were searched for on all the following websites of relevant congresses:

- International Corrections and Prisons Association (ICPA, <http://icpa.ca/>)
- American Correctional Association (http://www.aca.org/aca_prod_imis/aca_member)
- Experiencing Prison 7th Global Conference (<http://www.inter-disciplinary.net/probing-the-boundaries/persons/experiencing-prison/>)
- National Conference on Correctional Health Care (<http://www.ncchc.org/national-conference>)

Search on other websites

The following sources were searched for other grey literature documents published from 2005 onwards:

Guidelines:

- Guidelines International Network (<http://www.g-i-n.net/>)
- NICE guidelines (<https://www.evidence.nhs.uk/>)

Organisations and institutes:

- WHO – Health in prisons programme (HIPP) (<http://www.euro.who.int/prisons>)
- WHO – EU (<http://www.euro.who.int/en/home>)
- WHO – IRIS (<http://apps.who.int/iris/>)
- Council of Europe/POMPIDOU Group (http://www.coe.int/T/DG3/Pompidou/AboutUs/default_en.asp), and other Council of Europe documents
- UNODC (<http://www.unodc.org/>)
- ECDC (<http://ecdc.europa.eu/en/Pages/home.aspx>)
- Public Health England (PHE) – (<http://www.gov.uk>)
- European Monitoring Centre for Drugs and Drug Addition (EMCDDA) (<http://www.emcdda.europa.eu/>)
- International Corrections and Prisons Association (ICPA, <http://icpa.ca/>)

Bibliographies:

- Campbell Collaboration (<http://www.campbellcollaboration.org/>)
- Bibliography on HIV/AIDS and Hepatitis C in prisons (<http://www.aidslaw.ca/>)
- IDEAS (<https://ideas.repec.org/>)
- Evidence in Health and Social Care (NHS Evidence, <https://www.evidence.nhs.uk/>)
- Open grey (<http://www.opengrey.eu>)

Conduct of the main search on pre-defined websites and corresponding search terms

The main search for grey literature on the pre-defined websites was performed by two senior researchers. The main search was performed in English. On each website, a more general search was conducted at first using only terms for prisons (i.e. prison, jail, correctional, incarcerated). If this resulted in many hits, a more specific search was performed by combining the prison terms with e.g. 'HIV', 'hepatitis', 'vaccination' and 'injecting drug users'. In case a website was only focused on prison populations, only this latter search was performed.

Expert input

In addition to the search on pre-defined websites, expert input was used in the form of:

- A search for documents conducted by field researchers of the HWBs Federation Network
- A 'call for paper' issued to experts contacted via the HWBs Federation Network and members of the ECDC expert panel

See Annex 7 for more details.

Activities of field researchers

Five national field researchers and infectious diseases specialists were identified within the HWBs network, one for each of the EU/EEA countries represented in the Federation, namely France, Germany, Italy, the Netherlands and Spain. The field researchers conducted a search for national guidelines, protocols (clinical/intervention), and unpublished research reports relevant to the objectives (based on the inclusion and exclusion criteria, see below); documents written in English or in other EU/EEA languages were searched. This was done by searching the national websites of HWBs member organisations:

- SIMSPe-Onlus: Italian Society for Prison Health and Medicine (<http://www.sanitapenitenziaria.org/>)
- APSEP: Association des Professionnels de Santé Exerçant en Prison (<http://www.sante-prison.com/fr/>)
- NAPDUK: National Association of Prison Dentistry UK (<http://www.napduk.org/>)
- SESP: Sociedad Espanola de Sanidad Penitenciaria (<http://www.sesp.es/>)
- DJI: Netherlands National Agency for Correctional Institutions (<https://www.dji.nl/>).

Call for paper

A 'call for paper' was issued to stakeholders in the field by the selected national field researchers, via e-mail. The grey literature search officially started on 18 April 2016, with an official letter and call to the researchers sent by HWBs' Secretariat. After two weeks, an e-mail reminder was sent. If clarifications or additional details were needed, the respective national contact point was contacted. The call was also shared with the ECDC expert panel members.

The initial deadline was set on 2 May 2016. However, due to the low number of contributions received in particular on MA 6, the replacement of some field researchers and the possibility to collect further documents by the panel members, the definitive deadline for the collection of documents was extended to 31 July 2016.

A further call for papers was issued on 7th July 2017 and to the expert panel members during the Lisbon meeting on 21-23 June 2017 on specific topics of interest that were raised during the extensive discussion. The additional grey literature documents from the expert panel were received on June 28th and those from the field researchers were sent by HWB on July 14th, 2017.

The call targeted stakeholders, service providers or technical experts working in the field to submit additional documents including abstracts, national guidelines, protocols, unpublished research reports and/or intervention case studies/service models regarding the three macro areas. For the latter, a short pre-defined format was provided to collect clearly described accounts of their intervention/service model related to the relevant macro areas.

5. Grey literature selection

All retrieved documents were reviewed by two researchers. Documents were included if the reported information was relevant and of sufficient quality (see inclusion and exclusion criteria below). A record was kept of the reasons for exclusion of documents screened in full text.

Inclusion and exclusion criteria

Table 2. Inclusion and exclusion criteria grey literature

	Inclusion	Exclusion
Period of publication	Conference abstracts: from 2010 onwards Other documents: from 2005 onwards	
Type of document	<ul style="list-style-type: none"> • Conference abstracts • Guidelines • Intervention or clinical protocols • Unpublished research results • Case studies/service models, including measures of effectiveness 	<ul style="list-style-type: none"> • Published article
Document quality	Only grey literature documents with a methods section or an overview of sources	Document without a clear source/reference for the relevant information
Document population	Adults in prisons, jails and other custodial settings that function as a prison <ul style="list-style-type: none"> • Detained persons, including persons in remand • Persons 'going through the gate' (e.g. prison guards, healthcare workers, etc.) 	<ul style="list-style-type: none"> • Children (<18 years) • Persons in police custody • Persons in migrant centres
Subject of the document	<ul style="list-style-type: none"> • Prevention, care and treatment of HIV • Prevention, care and treatment of viral hepatitis • Prevention and control of injecting-related infections among current or former drug users 	
Geographical area	<ul style="list-style-type: none"> • EU/EEA 	
Specific outcomes of interest	<ul style="list-style-type: none"> • Quantitative outcomes • Qualitative outcomes 	<ul style="list-style-type: none"> • No exclusion based on outcomes

Guidelines selection

Guidelines were selected in a three-step approach. First, only prison-focused guidelines were searched for relevant information. However, when there was not sufficient information on certain review objectives coming from these prison-focused guidelines, guidelines that have a relevant section on prisoners were searched for relevant information. To include such guidelines, multiple transparent sources should have been stated for the prisoner group and a recommendation for this specific group should have been made. In case there was still a lack of information on a certain topic, general population guidelines were reviewed for relevant information.

Annex 2. Geographical search string used for PubMed and Embase

PubMed

(((((Europe*[ad] OR Europa*[ad] OR EU[ad] OR EEA[ad] OR EFTA[ad] OR "EU/EEA"[ad] OR "EU/EFTA"[ad] OR ECSC[ad] OR Euratom[ad] OR Eurozone[ad] OR EEC[ad] OR ec[ad] OR (Schengen[ad] AND (area[ad] OR countr*[ad] OR region*[ad] OR state[ad] OR states[ad])) OR Euroregion[ad] OR Euroregions[ad] OR Balkan[ad] OR Balkans[ad] OR Baltic[ad] OR (Mediterranean[ad] AND (area[ad] OR countr*[ad] OR region*[ad] OR state[ad] OR states[ad])) OR (Alpine[ad] AND (area[ad] OR countr*[ad] OR region*[ad] OR state[ad] OR states[ad])) OR Scandinavia[ad] OR Scandinavian[ad] OR "Nordic country"[ad] OR "Nordic countries"[ad] OR "Nordic state"[ad] OR "Nordic states"[ad] OR Danubian[ad] OR "Iberian peninsula"[ad] OR "Peninsula iberica"[ad] OR "Peninsule Iberique"[ad] OR "Iberiar Penintsula"[ad] OR Iberia[ad] OR Anatolia[ad] OR Anadolu[ad] OR Anatole[ad] OR Anatolian[ad] OR Yugoslavia[ad] OR Czechoslovakia[ad] OR "Czecho Slovakia"[ad] OR Ceskoslovensko[ad] OR "Cesko slovensko"[ad] OR Benelux[ad] OR Fennoscandia[ad] OR "Fenno Scandinavia"[ad] OR Fennoskandi*[ad] OR (Visegrad[ad] AND (Group[ad] OR Four[ad] OR Triangle[ad])) OR "Visegradska ctyrka"[ad] OR "Visegradska skupina"[ad] OR "Visegradi Egyuttmukodes"[ad] OR "Visegradi negyek"[ad] OR "Grupa Wyszehradzka"[ad] OR "Vysehradska skupina"[ad] OR "Vysehradska stvorka"[ad])) OR (("Serbia"[Mesh] OR Serbia*[tw] OR Srbija[tw] OR Serb[tw] OR Serbs[tw] OR Srbi[tw] OR Vojvodina[tw] OR Belgrade[tw] OR Beograd[tw] OR Sumadija[tw] OR Kolubara[tw] OR Kolubarski[tw] OR Macva[tw] OR Macvanski[tw] OR Moravica[tw] OR Moravicki[tw] OR Pomoravlje[tw] OR Pomoravski[tw] OR Rasinski[tw] OR Rasina[tw] OR Raska[tw] OR Raski[tw] OR Sumadijski[tw] OR Zlatibor[tw] OR Zlatiborski[tw] OR Bor[tw] OR Borski[tw] OR Branicevo[tw] OR Branicevski[tw] OR Jablanica[tw] OR Jablanicki[tw] OR Nisava[tw] OR Nisavski[tw] OR Pcinja[tw] OR Pcinjski[tw] OR Piroto[tw] OR Pirotski[tw] OR Podunavlje[tw] OR Podunavski[tw] OR Toplica[tw] OR Toplicki[tw] OR Zajecar[tw] OR Zajecarski[tw] OR Banat[tw] OR Srendjebanatski[tw] OR Backa[tw] OR Severnobacki[tw] OR Severnobanatski[tw] OR Juznbacki[tw] OR Juznobanatski[tw] OR Srem[tw] OR Sremski[tw] OR Zapadnbacki[tw] OR "Novi Sad"[tw] OR "Novy Sad"[tw] OR Ujvidek[tw] OR Nis[tw] OR Nish[tw] OR Nissa[tw] OR Kragujevac[tw] OR Subotica[tw] OR Szabadka[tw] OR Zrenjanin[tw] OR Pancevo[tw] OR Cacak[tw] OR Kraljevo[tw] OR "Novi Pazar"[tw] OR "Novy Pazar"[tw] OR ("Albania"[Mesh] OR Albania*[tw] OR Shqiperi*[tw] OR Schqipt*[tw] OR Berat[tw] OR Beratit[tw] OR Diber[tw] OR Dibres[tw] OR Durres[tw] OR Durresit[tw] OR Elbasan[tw] OR Elbasanit[tw] OR Fier[tw] OR Fierit[tw] OR Gjirokaster[tw] OR Gjirokastres[tw] OR Korce[tw] OR Korces[tw] OR Kukes[tw] OR Kukesit[tw] OR Lezhes[tw] OR Lezhe[tw] OR Shkodres[tw] OR Shkoder[tw] OR Tirana[tw] OR Tirane*[tw] OR Vlore[tw] OR Vlores[tw] OR Kamez[tw] OR Beraz[tw] OR Lushnje[tw] OR ("Macedonia (Republic)"[Mesh] OR Makedon*[tw] OR Macedon*[tw] OR Fyrom[tw] OR Istocen[tw] OR Severoistocen[tw] OR Jugoistocen[tw] OR Jugozapaden[tw] OR Pelagonski[tw] OR Pelagonia[tw] OR Poloski[tw] OR Polog[tw] OR Skopski[tw] OR Skopje[tw] OR Kconje[tw] OR Vardar*[tw] OR Bitola[tw] OR Kumanovo[tw] OR Prilep[tw] OR Tetovo[tw] OR Tetova[tw] OR Tetove[tw] OR Veles[tw] OR Stip[tw] OR Shtip[tw] OR Ohrid[tw] OR Gostivar[tw] OR Gostivari[tw] OR Strumica[tw] OR ("Iceland"[Mesh] OR Iceland[tw] OR Icelandic*[tw] OR islenska*[tw] OR Icelander*[tw] OR islendinga*[tw] OR Islendigar[tw] OR Inslenska[tw] OR Reykjavik[tw] OR Reykjavikurborg[tw] OR Hofudborgarsvaedif[tw] OR Sudurnes[tw] OR Vesturland[tw] OR Vestfiridir[tw] OR Nordurland[tw] OR Austurland[tw] OR Sudurland[tw] OR Kopavogur[tw] OR Hafnarfjordur[tw] OR Akureyri[tw] OR Gardabaer[tw] OR Mosfellsbaer[tw] OR Keflavik[tw] OR Akranes[tw] OR Selfoss[tw] OR Seltjarnarnes[tw] OR ("Montenegro"[Mesh] OR Montenegr*[tw] OR "Crna Gora"[tw] OR Crnogorci[tw] OR Andrijevica[tw] OR (Bar[tw] AND (Opstina[tw] OR municipality[tw] OR city[tw] OR town[tw])) OR Berane[tw] OR "Bijelo polje"[tw] OR Budva[tw] OR Cetinje[tw] OR Danilovgrad[tw] OR Gusinje[tw] OR "herceg Novi"[tw] OR Kolasin[tw] OR Kotor[tw] OR Mojkovac[tw] OR Niksic[tw] OR Petnija[tw] OR Plav[tw] OR Pluzine[tw] OR Pljevlja[tw] OR Podgorica[tw] OR Rozaje[tw] OR Savnik[tw] OR Tivat[tw] OR Ulcinj[tw] OR Zabljak[tw] OR ("Turkey"[Mesh] OR Turkey[tw] OR Turkiye[tw] OR Turkish[tw] OR Turk[tw] OR Turck*[tw] OR Adana[tw] OR Adiyaman[tw] OR Ayfon*[tw] OR Agri[tw] OR Aksaray[tw] OR Aksaray[tw] OR Amasya[tw] OR Ankara[tw] OR Antalya[tw] OR Ardahan[tw] OR Artvin[tw] OR Aydin[tw] OR Balikesir[tw] OR Bartin[tw] OR Batman[tw] OR Bayburt[tw] OR Bilecik[tw] OR Bingol[tw] OR Bitlis[tw] OR Bolu[tw] OR Burdur[tw] OR Bursa[tw] OR Canakkale[tw] OR Cannkiri[tw] OR Corum[tw] OR Denizli[tw] OR Diyarbakir[tw] OR Duzce[tw] OR Edirne[tw] OR Elazig[tw] OR Erzincan[tw] OR Erzurum[tw] OR Eskishir[tw] OR Gaziantep[tw] OR Giresun[tw] OR Gumushane[tw] OR Hakkari[tw] OR Hatay[tw] OR Igdirdir[tw] OR Isparta[tw] OR Istanbul[tw] OR Izmir[tw] OR Kahramanmaraş[tw] OR Karabuk[tw] OR Karaman[tw] OR Kars[tw] OR Kastamonu[tw] OR Kayseri[tw] OR Kirikkale[tw] OR Kirlarely[tw] OR Kirlareli[tw] OR Kirsheir[tw] OR Kocaeli[tw] OR Konya[tw] OR Kutahya[tw] OR Malatya[tw] OR Manisa[tw] OR Mardin[tw] OR Mersin[tw] OR Mugla[tw] OR Mus[tw] OR Nevsehir[tw] OR Nigde[tw] OR Ordu[tw] OR Osmaniye[tw] OR Rize[tw] OR Sakarya[tw] OR Samsun[tw] OR Sanliurfa[tw] OR Siirt[tw] OR Sinop[tw] OR Sivas[tw] OR Sirnak[tw] OR Tekirdag[tw] OR Tokat[tw] OR Trabzon[tw] OR Tunceli[tw] OR Usak[tw] OR (Van[tw] AND (province[tw] OR ili[tw])) OR Yalova[tw] OR Yozgat[tw] OR Kilis[tw] OR ("Bosnia-Herzegovina"[Mesh] OR Bosnia*[tw] OR Herzegov*[tw] OR Herzegonine[tw] OR Bosna[tw] OR Bosne[tw] OR Bosanski[tw] OR Bosanac[tw] OR Bosanci[tw] OR Srpska[tw] OR Brcko[tw] OR Posavski[tw] OR Posavina[tw] OR posavska[tw] OR Tuzlanski[tw] OR Tuzla[tw] OR Tuzlanski[tw] OR "Zenicko dobojski"[tw] OR "Zenicko dobojska"[tw] OR Zenica[tw] OR "Bosansko Podrinjski"[tw] OR "Bosansko Podrinjska"[tw] OR Srednjobosanski[tw] OR hercegovacko[tw] OR Zapadnohercegovacki[tw] OR Zapadnohercegovacka[tw] OR Sarajevo[tw] OR Sarajevska[tw] OR "Kanton 10"[tw] OR "10 kanton"[tw] OR Hercegbosanska[tw] OR "Unsko sanski"[tw] OR "Una Sana"[tw] OR "Banja Luka"[tw] OR bijeljina[tw] OR Mostar[tw] OR Prijedor[tw] OR Cazin[tw] OR Dobojski[tw] OR Zupanija[tw] OR ("Kosovo"[Mesh] OR Kosov*[tw] OR Ferizaj*[tw] OR Urosevac*[tw] OR Gjakov*[tw] OR Dakovic*[tw] OR Gjilan*[tw] OR Gnjilan*[tw] OR Mitrovic*[tw] OR Pejes[tw] OR Peja[tw] OR Peje[tw] OR Pecki[tw] OR Pec[tw] OR Pristin*[tw] OR Prishtin*[tw] OR Prishtinski[tw] OR Prizrenit[tw] OR Prizrenski[tw] OR Prizen[tw] OR Prizren[tw] OR Prizreni[tw] OR Produjev*[tw] OR Vucitrn[tw] OR Vushtrri*[tw] OR "Suva reka"[tw] OR Suhareka[tw] OR Besiana[tw] OR Metohija[tw] OR Dukagjini[tw] OR Dukagjinit[tw])))) OR ((Iceland[ad] OR Icelandic*[ad] OR islenska*[ad] OR Icelander*[ad] OR islendinga*[ad] OR Islendigar[ad] OR Inslenska[ad] OR Reykjavik[ad] OR Reykjavikurborg[ad] OR Hofudborgarsvaedi[ad] OR Sudurnes[ad] OR Vesturland[ad] OR Vestfiridir[ad] OR Westfjords[ad] OR Nordurland[ad] OR Austurland[ad] OR Sudurland[ad] OR Kopavogur[ad] OR Hafnarfjordur[ad] OR Akureyri[ad] OR Gardabaer[ad] OR Mosfellsbaer[ad] OR Keflavik[ad] OR Akranes[ad] OR Selfoss[ad] OR Seltjarnarnes[ad] OR (Switzerland[ad]

OR Schweiz[ad] OR Schweizerische[ad] OR Swiss[ad] OR Suisse*[ad] OR Svizzera[ad] OR Svizzeri[ad] OR Svizzers[ad] OR Svizra[ad] OR Helvetica[ad] OR Aargau[ad] OR Argovia[ad] OR Ausserrhoden[ad] OR "Outer Rhodes"[ad] OR Innerrhoden[ad] OR "Inner Rhodes"[ad] OR Basel[ad] OR Bale[ad] OR Basilea[ad] OR Bern[ad] OR Berne[ad] OR Berna[ad] OR Fribourg[ad] OR Freiburg[ad] OR Friburg[ad] OR Geneva[ad] OR Geneve[ad] OR Genf[ad] OR Ginevra[ad] OR Genevra[ad] OR Glarus[ad] OR Graubunden[ad] OR Graubuenden[ad] OR Grisons[ad] OR Grigioni[ad] OR Grischun[ad] OR jura[ad] OR Lucerne[ad] OR Luzern[ad] OR Losanna[ad] OR Neuchatel[ad] OR Nidwalden[ad] OR Nidwald[ad] OR Obwalden[ad] OR Obwald[ad] OR Schaffhausen[ad] OR Schaffhouse[ad] OR Schwyz[ad] OR Solothurn[ad] OR Soleure[ad] OR Thurgau[ad] OR Thurgovia[ad] OR Ticino[ad] OR Tessin[ad] OR Uri[ad] OR Valais[ad] OR Wallis[ad] OR Vaud[ad] OR Zug[ad] OR Zurich[ad] OR Zuerich[ad] OR Zurigo[ad] OR Lausanne[ad] OR Losanna[ad] OR Winterthur[ad] OR 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Turkish[ad] OR Turk[ad] OR Turkc*[ad] OR Adana[ad] OR Adiyaman[ad] OR Ayfon*[ad] OR Agri[ad] OR Aksaray[ad] OR Aksaray[ad] OR Amasya[ad] OR Ankara[ad] OR Antalya[ad] OR Ardahan[ad] OR Artvin[ad] OR Aydin[ad] OR Balikesir[ad] OR Bartin[ad] OR Batman[ad] OR Bayburt[ad] OR Bilecik[ad] OR Bingol[ad] OR Bitlis[ad] OR Bolu[ad] OR Burdur[ad] OR Bursa[ad] OR Canakkale[ad] OR Cannkiri[ad] OR Corum[ad] OR Denizli[ad] OR Diyarbakir[ad] OR Duzce[ad] OR Edirne[ad] OR Elazig[ad] OR Erzincan[ad] OR Erzurum[ad] OR Eskishir[ad] OR Gaziantep[ad] OR Giresun[ad] OR Gumushane[ad] OR Hakkari[ad] OR Hatay[ad] OR Igdirdir[ad] OR Isparta[ad] OR Istanbul[ad] OR Izmir[ad] OR Kahramanmaraş[ad] OR Karabuk[ad] OR Karaman[ad] OR Kars[ad] OR Kastamonu[ad] OR Kayseri[ad] OR Kirikkale[ad] OR Kirklarely[ad] OR Kirklareli[ad] OR Kirsheir[ad] OR Kocaeli[ad] OR Konya[ad] OR Kutahya[ad] OR Malatya[ad] OR Manisa[ad] OR Mardin[ad] OR Mersin[ad] OR Mugla[ad] OR Mus[ad] OR Nevsehir[ad] OR Nigde[ad] OR Ordu[ad] OR Osmaniye[ad] OR Rize[ad] OR Sakarya[ad] OR Samsun[ad] OR Sanliurfa[ad] OR Siirt[ad] OR Sinop[ad] OR Sivas[ad] OR Sirnak[ad] OR Tekirdag[ad] OR Tokat[ad] OR Trabzon[ad] OR Tunceli[ad] OR Usak[ad] OR (Van[ad] AND (province[ad] OR ili[ad])) OR Yalova[ad] OR Yozgat[ad] OR Kilis[ad]) OR (Bosnia*[ad] OR Herzegov*[ad] OR Herzegovine[ad] OR Bosna[ad] OR Bosne[ad] OR Bosanski[ad] OR Bosanac[ad] OR Bosanci[ad] OR Srpska[ad] OR Brcko[ad] OR Posavski[ad] OR Posavina[ad] OR posavska[ad] OR Tuzlanski[ad] OR Tuzla[ad] OR Tuzlanska[ad] OR "Zenicko dobojski"[ad] OR "Zenicko dobojska"[ad] OR Zenica[ad] OR "Bosansko Podrinjski"[ad] OR "Bosansko Podrinjska"[ad] OR Srednjobosanski[ad] OR hercegovacko[ad] OR Zapadnohercegovacki[ad] OR Zapadnohercegovacka[ad] OR Sarajevo[ad] OR Sarajevska[ad] OR "Kanton 10"[ad] OR "10 kanton"[ad] OR Hercegbosanska[ad] OR "Unsko sanski"[ad] OR "Una Sana"[ad] OR "Banja Luka"[ad] OR bijeljina[ad] OR Mostar[ad] OR Prijedor[ad] OR Cazin[ad] OR Dobojski[ad] OR Zupanija[ad]) OR (Kosov*[ad] OR Ferizaj*[ad] OR Urosevac*[ad] OR Gjakov*[ad] OR Dakovic*[ad] OR Gijlan*[ad] OR Gnijlan*[ad] OR Mitrovic*[ad] OR Pejes[ad] OR Peja[ad] OR Peje[ad] OR Pecki[ad] OR Pec[ad] OR Pristin*[ad] OR Prishtin*[ad] OR Pristinski[ad] OR Prizrenit[ad] OR Prizrenski[ad] OR Prizen[ad] OR Prizren[ad] OR Prizreni[ad] OR Produjev*[ad] OR Vucitrn[ad] OR Vushtrri*[ad] OR "Suva reka"[ad] OR Suhareka[ad] OR Besiana[ad] OR Metohija[ad] OR Dukagjini[ad] OR Dukagjinit[ad])) OR (((("Liechtenstein"[Mesh] OR Liechtenstein[tw] OR Lienchtensteiner*[tw] OR Balzers[tw] OR Eschen[tw] OR Gamprin[tw] OR Mauren[tw] OR Planken[tw] OR Ruggell[tw] OR Schaan[tw] OR Schellenberg[tw] OR Triesen[tw] OR Triesenberg[tw] OR Vaduz[tw])) OR ("Norway"[Mesh] OR Norway[tw] OR Norwegian*[tw] OR Norge[tw] OR Noreg[tw] OR Norgga[tw] OR Akershus[tw] OR "Aust Agder"[tw] OR Buskerud[tw] OR Finnmark[tw] OR Hedmark[tw] OR Hordaland[tw] OR "More og Romsdal"[tw] OR "More and Romsdal"[tw] OR "More Romsdal"[tw] OR Nordland[tw] OR Trondelag[tw] OR Oppland[tw] OR Oslo[tw] OR Ostfold[tw] OR Rogaland[tw] OR "Sogn og fjordane"[tw] OR "Sogn and fjordane"[tw] OR "sogn fjordane"[tw] OR Telemark[tw] OR Troms[tw] OR Romsa[tw] OR Romssa[tw] OR "Vest Agder"[tw] OR Vestfold[tw] OR Bergen[tw] OR Stavanger[tw] OR Sandnes[tw] OR Trondheim[tw] OR

Trondhjem[tw] OR Kaupangen[tw] OR Nidaros[tw] OR Drammen[tw] OR Fredrikstad[tw] OR Skien[tw] OR Tromso[tw] OR Sarpborg[tw]) OR ("Switzerland"[Mesh] OR Switzerland[tw] OR Schweiz[tw] OR Schweizerische[tw] OR Swiss[tw] OR Suisse*[tw] OR Svizzera[tw] OR Svizzeri[tw] OR Svizzers[tw] OR Svizra[tw] OR Helvetica[tw] OR Aargau[tw] OR Argovia[tw] OR Ausserrhoden[tw] OR "Outer Rhodes"[tw] OR Innerrhoden[tw] OR "Inner Rhodes"[tw] OR Basel[tw] OR Bale[tw] OR Basilea[tw] OR Bern[tw] OR Berne[tw] OR Berna[tw] OR Fribourg[tw] OR Freiburg[tw] OR Friburg[tw] OR Geneva[tw] OR Geneve[tw] OR Genf[tw] OR Ginevra[tw] OR Genevra[tw] OR Giarus[tw] OR Graubunden[tw] OR Graubuenden[tw] OR Grisons[tw] OR Grigioni[tw] OR Grischun[tw] OR jura[tw] OR Lucerne[tw] OR Luzern[tw] OR Losanna[tw] OR Neuchatel[tw] OR Nidwalden[tw] OR Nidwald[tw] OR Obwalden[tw] OR Obwald[tw] OR Schaffhausen[tw] OR Schaffhouse[tw] OR Schwyz[tw] OR Solothurn[tw] OR Soleure[tw] OR Thurgau[tw] OR Thurgovia[tw] OR Ticino[tw] OR Tessin[tw] OR Uri[tw] OR Valais[tw] OR Wallis[tw] OR Vaud[tw] OR Zug[tw] OR Zurich[tw] OR Zuerich[tw] OR Zurigo[tw] OR Lausanne[tw] OR Losanna[tw] OR Winterthur[tw] OR Winterthour[tw] OR "St Gallen"[tw] OR "Saint Gallen"[tw] OR "Sankt Gallen"[tw] OR "Saint Gall"[tw] OR "San Gallo"[tw] OR "Son Gagl"[tw] OR Turigt[tw]) OR ("Iceland"[Mesh] OR Iceland[tw] OR Icelandic*[tw] OR islenska*[tw] OR Icelander*[tw] OR islendinga*[tw] OR Islendigar[tw] OR Inslenska[tw] OR Reykjavik[tw] OR Reykjavikurborg[tw] OR Hofudborgarsvaedi[tw] OR Sudurnes[tw] OR Vesturland[tw] OR Vestfiridir[tw] OR Westfjords[tw] OR Nordurland[tw] OR Austurland[tw] OR Sudurland[tw] OR Kopavogur[tw] OR Hafnarfjordur[tw] OR Akureyri[tw] OR Gardabaer[tw] OR Mosfellsbaer[tw] OR Keflavik[tw] OR Akranes[tw] OR Selfoss[tw] OR Seltjarnarnes[tw])) OR (("European Union"[Mesh] OR "Europe"[Mesh:noexp] OR Europa*[tw] OR Europa*[tw] OR EU[tw] OR EEA[tw] OR EFTA[tw] OR "EU/EEA"[tw] OR "EU/EFTA"[tw] OR ECSC[tw] OR Euratom[tw] OR Eurozone[tw] OR EEC[tw] OR ec[tw] OR (Schengen[tw] AND (area[tw] OR countr*[tw] OR region*[tw] OR state[tw] OR states[tw])) OR Euroregion[tw] OR Euroregions[tw] OR "Europe, Eastern"[Mesh:noexp] OR "Balkan Peninsula"[Mesh] OR Balkan[tw] OR Balkans[tw] OR "Baltic States"[Mesh] OR Baltic[tw] OR "Mediterranean Region"[Mesh] OR (Mediterranean[tw] AND (area[tw] OR countr*[tw] OR region*[tw] OR state[tw] OR states[tw])) OR (Alpine[tw] AND (area[tw] OR countr*[tw] OR region*[tw] OR state[tw] OR states[tw])) OR "Scandinavian and Nordic Countries"[Mesh] OR Scandinavia[tw] OR Scandinavian[tw] OR "Nordic country"[tw] OR "Nordic countries"[tw] OR "Nordic state"[tw] OR "Nordic states"[tw] OR Danubian[tw] OR "Iberian peninsula"[tw] OR "Peninsula iberica"[tw] OR "Peninsule Iberique"[tw] OR "Iberiar Penintsula"[tw] OR Iberia[tw] OR Anatolia[tw] OR Anadolu[tw] OR Anatole[tw] OR Anatolian[tw] OR "Yugoslavia"[Mesh] OR Yugoslavia[tw] OR "Czechoslovakia"[Mesh] OR Czechoslovakia[tw] OR "Czecho Slovakia"[tw] OR Ceskoslovensko[tw] OR 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"Sankt Polten"[tw] OR "Sankt Poelten"[tw] OR Dornbirn[tw] OR ("Belgium"[Mesh] OR Belgi*[tw] OR Belge*[tw] OR Belg[tw] OR Brussel*[tw] OR Bruxelles[tw] OR Bruxelles[tw] OR Walloon*[tw] OR Wallon*[tw] OR Vlaams[tw] OR Flander*[tw] OR Flandern[tw] OR Flandre[tw] OR Flemish[tw] OR Flamand[tw] OR Flemisch[tw] OR Flamisch*[tw] OR Vlaanderen[tw] OR Flamande[tw] OR Waals[tw] OR Antwerp*[tw] OR Anvers[tw] OR Henegouwen[tw] OR Hennegau[tw] OR Hainault[tw] OR Hainaut[tw] OR Liege[tw] OR Luik[tw] OR Luttich[tw] OR Limbourg[tw] OR Limburg[tw] OR Namur[tw] OR Namen[tw] OR Ostflandern[tw] OR Westflandern[tw] OR Ghent[tw] OR Gent[tw] OR Gand[tw] OR Charleroi[tw] OR Bruges[tw] OR Brugge*[tw] OR Schaarbeek[tw] OR Schaerbeek[tw] OR Anderlecht[tw] OR Leuven[tw] OR Louvain[tw] OR ("Bulgaria"[Mesh] OR Bulgaria*[tw] OR Balgariya[tw] OR Balgarija[tw] OR Blagoevgrad*[tw] OR "Pirin Macedonia"[tw] OR Burgas[tw] OR Dobrich[tw] OR Gabrovo[tw] OR Haskovo[tw] OR Kardzhali[tw] OR Kurdzhali[tw] OR Kustendil[tw] OR Lovech[tw] OR Lovec[tw] OR Montana[tw] OR Pazardzhik[tw] OR Pernik[tw] OR Pleven*[tw] OR Plovdiv[tw] OR Razgrad[tw] OR Rousse[tw] OR Ruse[tw] OR Rusenka[tw] OR Shumen[tw] OR Silistra[tw] OR Sliven[tw] OR Smolyan[tw] OR Sofia[tw] OR Sofyiska[tw] OR Sofiiska[tw] OR "Stara Zagora"[tw] OR Targovishte[tw] OR Varna[tw] OR "Veliko Tarnovo"[tw] OR Vidin[tw] OR Vratsa[tw] OR Vratza[tw] OR Yambol[tw]) OR ("Croatia"[Mesh] OR Croat*[tw] OR Hrvatsk*[tw] OR hrvati[tw] OR Bjelovar[tw] OR "Bjelovarsko bilogorska"[tw] OR "Brod Posavina"[tw] OR "Brodsko posavska"[tw] OR "Dubrovnik Neretva"[tw] OR "dubrovacko neretvanska"[tw] OR Zagreb[tw] OR Zagrebacka[tw] OR Istria[tw] OR Istarska[tw] OR Karlovacka[tw] OR Karlovac[tw] OR "Koprivnicko krizevacka"[tw] OR Koprivnica[tw] OR Krizevci[tw] OR "Krapina Zagorje"[tw] OR "Krapinsko zagorska"[tw] OR "Lika Senj"[tw] OR "Licko senjska"[tw] OR Medimurska[tw] OR Medimurje[tw] OR Osijek[tw] OR Baranja[tw] OR "Osjecko baranjska"[tw] OR "Pozega Slavonia"[tw] OR "Pozesko slavonska"[tw] OR "Primorje Gorski Kotar"[tw] OR "Primorsko goranska"[tw] OR "Sibensko kninska"[tw] OR "Sibensko kninske"[tw] OR Sibenik[tw] OR Knin[tw] OR Sisak[tw] OR "Sisacko moslavacka"[tw] OR Moslavina[tw] OR "Splitsko dalmatinska"[tw] OR Split[tw] OR Dalmatia[tw] OR Varazdin[tw] OR Varazdinska[tw] OR Viroviticko[tw] OR podravska[tw] OR Virovitica[tw] OR Podravina[tw] OR "Vukovarsko srijemska"[tw] OR Vukovar[tw] OR Srijem[tw] OR Zadar[tw] OR Zadska[tw] OR Rijeka[tw] OR "Velika gorica"[tw] OR "Slavonski brod"[tw] OR Pula[tw]) OR ("Cyprus"[Mesh] OR Cyprus[tw] OR Cyriot*[tw] OR Kypros[tw] OR Kibris*[tw] OR kypriaki[tw] OR Kyprioi[tw] OR Nicosia[tw] OR Lefkosa[tw] OR Lefkosia[tw] OR Famagusta[tw] OR Magusa[tw] OR Ammochostos[tw] OR Gazimagusa[tw] OR Kyrenia[tw] OR Girne[tw] OR Keryneia[tw] OR Larnaca[tw] OR Larnaka[tw] OR Iskele[tw] OR Limassol[tw] OR Lemesos[tw] OR Limasol[tw] OR Lemosun[tw] OR Paphos[tw] OR Pafos[tw] OR Baf[tw] OR Strovolos[tw] OR Lakatamia[tw] OR Lakadamyia[tw] OR "Kato Polemidia"[tw] OR "Kato Polemidhia"[tw] OR Aglandjia[tw] OR Eglençe[tw] OR Aglantzia[tw] OR Aradhippou[tw] OR Aradippou[tw] OR Engomi[tw]) OR ("Czech Republic"[Mesh] OR Czech*[tw] OR Cesky[tw] OR Ceska[tw] OR Cech[tw] OR Cestina[tw] OR Prague[tw] OR Praha[tw] OR Prag[tw] OR Stredoces*[tw] OR Jihoces*[tw] OR Bohemia[tw] OR Bohemian[tw] OR Plzen*[tw] OR Pilsen[tw] OR Karlovars*[tw] OR "Karlovy Vary"[tw] OR Usteck*[tw] OR Usti[tw] OR Liberec*[tw] OR "Hradec Kralove"[tw] OR Kralovehradec*[tw] OR Pardubic*[tw] OR Olomouc*[tw] OR Olomoc[tw] OR Holomoc[tw] OR Moravskoslezs*[tw] OR Jihomorav*[tw] OR Moravia[tw] OR Moravian[tw] OR Morava[tw] OR Vysocina[tw] OR Zlin[tw] OR Zlinsk*[tw] OR "Ceske Budejovice"[tw] OR Budeweis[tw] OR Brno[tw] OR Ostrava[tw]) OR ("Denmark"[Mesh] OR Denmark[tw] OR Danish*[tw] OR dane[tw] OR danes[tw] OR Danmark[tw] OR dansk*[tw] OR Hovedstaden[tw] OR Midtjylland[tw] OR Nordjylland[tw] OR Sjælland[tw] OR Sealand[tw] OR "Zealand region"[tw] OR "region Zealand"[tw] OR Syddanmark[tw] OR Jutland[tw] OR Jylland[tw] OR Sonderjyllands[tw] OR Copenhagen[tw] OR Kobenhavn[tw] OR Arhus[tw] OR Aarhus[tw] OR Bornholm[tw] OR Frederiksberg[tw] OR Frederiksborg[tw] OR Ringkjobing[tw] OR Viborg[tw] OR Vejle[tw] OR Roskilde[tw] OR

Storstrom[tw] OR Vestsjaellands[tw] OR "West Zealand"[tw] OR Funen[tw] OR Ribe[tw] OR "Kalaallit Nunaat"[tw] OR Gronland[tw] OR Foroyar[tw] OR Faeroerne[tw] OR "Faroe islands"[tw] OR Aalborg[tw] OR Alborg[tw] OR Odense[tw] OR Esbjerg[tw] OR Gentofte[tw] OR Gladsaxe[tw] OR Randers[tw] OR Kolding[tw] OR ("Estonia"[Mesh] OR Estonia*[tw] OR Eestitw] OR Eestlased[tw] OR Eestlane[tw] OR Harju[tw] OR Harjumaa[tw] OR Hiiu[tw] OR Hiiumaa[tw] OR "Ida Viru"[tw] OR "Ida Virumaa"[tw] OR Jarvamaa[tw] OR Jarva[tw] OR Jogevas[tw] OR Jogevas[tw] OR Laanemaa[tw] OR Laane[tw] OR "Laane Virumaa"[tw] OR Parnu[tw] OR Parnumaa[tw] OR Polva[tw] OR Polvamaa[tw] OR Rapla[tw] OR Raplamaa[tw] OR Saare[tw] OR Saaremaa[tw] OR Tartu[tw] OR Tartumaa[tw] OR Valga[tw] OR Valgamaa[tw] OR Viljandimaa[tw] OR Viljandi[tw] OR Voru[tw] OR Vorumaa[tw] OR Tallinn[tw] OR Narva[tw] OR "Kohtla Jarve"[tw] OR Rakvere[tw] OR Maardu[tw] OR Sillamae[tw] OR Kuressaare[tw] OR ("Finland"[Mesh] OR Finland[tw] OR Finnish*[tw] OR Finn[tw] OR Finns[tw] OR Suomi[tw] AND Suomen[tw] OR Suomalaiset[tw] OR Aland[tw] OR Ahvenanmaa[tw] OR Uusimaa[tw] OR Nyland[tw] OR Karelia[tw] OR Karjala[tw] OR Karelen[tw] OR Ostrobothnia[tw] OR Pohjanmaa[tw] OR Osterbotten[tw] OR Savonia[tw] OR Savo[tw] OR Savolax[tw] OR Kainuu[tw] OR Kajanaland*[tw] OR "Kanta Hame"[tw] OR Tavastia[tw] OR Tavastland[tw] OR Kymenlaakso[tw] OR Kymmenedalen[tw] OR Lapland[tw] OR Lappi[tw] OR Lappland[tw] OR "Paijat Hame"[tw] OR Pirkanmaa[tw] OR Birkaland[tw] OR Satakunta[tw] OR Satakunda[tw] OR Helsinki[tw] OR Helsingfors[tw] OR Espoo[tw] OR Esbo[tw] OR Tampere[tw] OR Tammerfors[tw] OR Vantaa[tw] OR Vanda[tw] OR Oulu[tw] OR Uleaborg[tw] OR Turku[tw] OR Abo[tw] OR Jyvaskyla[tw] OR Kuopio[tw] OR Lahti[tw] OR Lahtis[tw] OR Kouvola[tw] OR ("France"[Mesh] OR France[tw] OR French*[tw] OR Francois*[tw] OR Alsace[tw] OR Elsass[tw] OR Aquitaine[tw] OR Aquitania[tw] OR Akitania[tw] OR Aguiene[tw] OR Auvergne[tw] OR Auvernhe[tw] OR Auverna[tw] OR Normandie[tw] OR Normandy[tw] OR Normaundie[tw] OR Bourgogne[tw] OR Burgundy[tw] OR Bregogne[tw] OR Borgogne[tw] OR Brittany[tw] OR Breizh[tw] OR Bertaeyn[tw] OR Bretagne[tw] OR "Champagne Ardenne"[tw] OR Corse[tw] OR Corsica[tw] OR "Franche Comte"[tw] OR "Frantche Comte"[tw] OR "Franche Comtat"[tw] OR Guadeloupe[tw] OR Guyane[tw] OR Guiana[tw] OR "Languedoc Roussillon"[tw] OR "Lengadoc Rosselhon"[tw] OR "Llenguadoc-Rossello"[tw] OR Limousin[tw] OR Lemosin[tw] OR Lorraine[tw] OR Lothringen[tw] OR Lottringe[tw] OR Martinique[tw] OR "Midi Pyrenees"[tw] OR "Miegjorn Pireneus"[tw] OR "Mieidia Pireneus"[tw] OR "Mediodia Pirineos"[tw] OR "Pays de la Loire"[tw] OR "Broiou al Liger"[tw] OR Picardie[tw] OR Picardy[tw] OR "Poitou Charentes"[tw] OR "Peitau Charantas"[tw] OR "Poitou-Cherentes"[tw] OR Provence[tw] OR Provenca[tw] OR Prouvenco[tw] OR "Cote d Azur"[tw] OR "Cote d'Azur"[tw] OR "Costo d'Azur"[tw] OR "Costo d Azur"[tw] OR "Costa d'Azur"[tw] OR "Costa d Azur"[tw] OR Reunion[tw] OR "Rhone Alpes"[tw] OR "Rono Arpes"[tw] OR "Rose Aups"[tw] OR Ain[tw] OR Aisne[tw] OR Allier[tw] OR "Alpes de Haute Provence"[tw] OR "Haute Alpes"[tw] OR "Alpes Maritimes"[tw] OR Ardeche[tw] OR Ardennes[tw] OR Ariege[tw] OR Aube[tw] OR Aude[tw] OR Aveyron[tw] OR "Bas Rhin"[tw] OR "Bouches du Rhone"[tw] OR Calvados[tw] OR Cantal[tw] OR Charente[tw] OR Cher[tw] OR Correze[tw] OR "Corse du Sud"[tw] OR "Cote d Or"[tw] OR "Cote d'Or"[tw] OR "Cotes d Armor"[tw] OR "Cotes d'Armor"[tw] OR Creuse[tw] OR "Deux Sevres"[tw] OR Dordogne[tw] OR Doubs[tw] OR Drome[tw] OR Essonne[tw] OR Eure[tw] OR Finistere[tw] OR Gard[tw] OR Gers[tw] OR Gironde[tw] OR "Haute Corse"[tw] OR "Haute Garonne"[tw] OR "Haute Marne"[tw] OR "Hautes Alpes"[tw] OR "Haute Saone"[tw] OR "Haute Savoie"[tw] OR "Hautes Pyrenees"[tw] OR "Haute Vienne"[tw] OR "Haut Rhin"[tw] OR "Hauts de Seine"[tw] OR Herault[tw] OR "Ile de France"[tw] OR "Ille et Vilaine"[tw] OR Indre[tw] OR Isere[tw] OR Jura[tw] OR Landes[tw] OR Loire[tw] OR Loiret[tw] OR Lot[tw] AND (departement[tw] OR departement[tw])) OR "Lot et Garonne"[tw] OR "Loir et Cher"[tw] OR Lozere[tw] OR Manche[tw] OR Marne[tw] OR Mayenne[tw] OR Mayotte[tw] OR "Meurthe et Moselle"[tw] OR Meuse[tw] OR Morbihan[tw] OR Moselle[tw] OR (Nord[tw] AND (departement[tw] OR departement[tw])) OR Nièvre[tw] OR Oise[tw] OR Orne[tw] OR "Pas de calais"[tw] OR "Noord-Nauw van Kales"[tw] OR Paris[tw] OR "Puy de dome"[tw] OR "Pyrenees Atlantiques"[tw] OR "Pyrenees Orientales"[tw] OR Rhone[tw] OR Sarthe[tw] OR Savoie[tw] OR "Seine et Marne"[tw] OR "Seine Maritime"[tw] OR Somme[tw] OR Tarn[tw] OR "Territoire de Belfort"[tw] OR "Val de Marne"[tw] OR "Val d Oise"[tw] OR Var[tw] OR Vaucluse[tw] OR Vendee[tw] OR Vienne[tw] OR Vosges[tw] OR Yonne[tw] OR Yvelines[tw] OR Marseille[tw] OR Lyon[tw] OR Nice[tw] OR Nantes[tw] OR Strasbourg[tw] OR Montpellier[tw] OR Bordeaux[tw] OR Lille[tw] OR Toulouse[tw] OR "Outre Mer"[tw] OR "Seine Saint Denis"[tw] OR ("Germany"[Mesh] OR German*[tw] OR Deutsch*[tw] OR Bundesrepublik[tw] OR Westdeutschland[tw] OR Ostdeutschland[tw] OR Baden[tw] OR Wuerttemberg[tw] OR Wurttemberg[tw] OR Bayern[tw] OR Bavaria[tw] OR Berlin[tw] OR Brandenburg[tw] OR Bremen[tw] OR Oldenburg[tw] OR Mitteldeutschland[tw] OR Rhein[tw] OR Rhine[tw] OR Hannover[tw] OR Braunschweig[tw] OR Gottingen[tw] OR Goettingen[tw] OR Nurnberg[tw] OR Nuernberg[tw] OR Ruhr[tw] OR Koln[tw] OR koeln[tw] OR Bonn[tw] OR Hamburg[tw] OR Hessen[tw] OR Hesse[tw] OR Hessia[tw] OR Mecklenburg[tw] OR Vorpommern[tw] OR Pomerania[tw] OR Niedersachsen[tw] OR Neddersassen[tw] OR Saxony[tw] OR Niederbayern[tw] OR "Northern Rhine"[tw] OR "North Rhine"[tw] OR Westphalia[tw] OR Westfalen[tw] OR "Rhineland Palatinate"[tw] OR "Rheinland Pfalz"[tw] OR Saarland[tw] OR Sachsen[tw] OR "Schleswig Holstein"[tw] OR Thuringia[tw] OR Thuringen[tw] OR Thueringen[tw] OR Muenchen[tw] OR Muenchen[tw] OR Munich[tw] OR Frankfurt[tw] OR Stuttgart[tw] OR Dusseldorf[tw] OR Duesseldorf[tw] OR Dortmund[tw] OR Essen[tw] OR ("Greece"[Mesh] OR Greece[tw] OR "Hellenic republic"[tw] OR Greek*[tw] OR Ellada[tw] OR Elladas[tw] OR "Elliniki Dimokratia"[tw] OR Hellas[tw] OR Hellenes[tw] OR Attica[tw] OR Attiki[tw] OR Makedonia*[tw] OR Macedonia[tw] OR Thraki[tw] OR Thrace[tw] OR Crete[tw] OR Kriti[tw] OR "Ionia Nisia"[tw] OR "Ionian neson"[tw] OR "Ionion nIson"[tw] OR "Ionian islands"[tw] OR "Ionian island"[tw] OR Epirus[tw] OR Ipeiros[tw] OR "Perifereia Ipeirou"[tw] OR "North aegean"[tw] OR "Northern Aegean"[tw] OR "Aegean islands"[tw] OR "Aegean island"[tw] OR "Nisoi Agaioi"[tw] OR "Notio Aigaio"[tw] OR Peloponnese[tw] OR Peloponniso*[tw] OR Thessaly[tw] OR Thessalia[tw] OR Thessalian[tw] OR Petthalia[tw] OR "Voreio Aigaio"[tw] OR "Voreio Aigaioi"[tw] OR "South aegean"[tw] OR "Southern Aegean"[tw] OR "Mount athos"[tw] OR "Oros Athos"[tw] OR Cyclades[tw] OR Cycklades[tw] OR Kiklades[tw] OR Dodecanese[tw] OR Dodekanisa[tw] OR Athens[tw] OR Athina[tw] OR Thessaloniki[tw] OR Thessalonica[tw] OR Patras[tw] OR Patra[tw] OR Pireas[tw] OR Piraos[tw] OR Larissa[tw] OR Larisa[tw] OR Heraklion[tw] OR Heraclion[tw] OR Iraklion[tw] OR Irakleion[tw] OR Volos[tw] OR Rhodes[tw] OR Rodos[tw] OR Ioannina[tw] OR Janina[tw] OR Yannena[tw] OR Chania[tw] OR Chalcis[tw] OR Chalkida[tw] OR ("Hungary"[Mesh] OR Hungar*[tw] OR Magyarorszag[tw] OR Magyar*[tw] OR Dunantuli[tw] OR Transdanubia[tw] OR Dunantul[tw] OR "Great Plain"[tw] OR "Eszak Alfold"[tw] OR "Del Alfold"[tw] OR "Alfold es eszak"[tw] OR "Northern Alfold"[tw] OR "North Alfold"[tw] OR "South Alfold"[tw] OR "Southern Alfold"[tw] OR Bacs[tw] OR Kiskun[tw] OR Baranya[tw] OR Bekes[tw] OR Borsod[tw] OR Abauj[tw] OR Zemplen[tw] OR Budapest[tw] OR Csongrad[tw] OR Fejer[tw] OR gyor[tw] OR moson[tw] OR sopron[tw] OR hajdu[tw] OR bihar[tw] OR Heves[tw] OR "jasz nagykun szolnok"[tw] OR komarom[tw] OR esztergom[tw] OR Nograd[tw] OR (Pest[tw] AND (megye[tw] OR county[tw])) OR Somogy[tw] OR szabolcs[tw] OR szatmar[tw] OR bereg[tw] OR Tolna[tw] OR Vas[tw] OR Veszprem[tw] OR Zala[tw] OR Debrecen[tw] OR Miskolc[tw] OR Szeged[tw] OR Pecs[tw] OR Gyor[tw] OR Nyiregyhaza[tw] OR Kecskemet[tw] OR Szekesfehervar[tw] OR Szombathely[tw] OR ("Ireland"[Mesh] OR Ireland[tw] OR

Eire[tw] OR Irish*[tw] OR Fingal[tw] OR "Fine Gall"[tw] OR Dublin[tw] OR "Ath Cliath"[tw] OR "Dun Laoghaire"[tw] OR Wicklow[tw] OR "Cill Mhantain"[tw] OR "Chill Mhantain"[tw] OR Wexford[tw] OR "Loch Garman"[tw] OR Carlow[tw] OR Ceatharlach[tw] OR Kildare[tw] OR "Cill Dara"[tw] OR "Chill Dara"[tw] OR Meath[tw] OR "An Mhi"[tw] OR "Contae na Mi"[tw] OR Louth[tw] OR "Contae Lu"[tw] OR Monaghan[tw] OR Muineachan[tw] OR Mhuineachain[tw] OR Cavan[tw] OR "An Cabhan"[tw] OR "An Cabhain"[tw] OR Longford[tw] OR "An Longfort"[tw] OR "an Longfoirt"[tw] OR Langfurd[tw] OR Westmeath[tw] OR "An Iarmhi"[tw] OR "na Iarmhi"[tw] OR Offaly[tw] OR "Uibh Fhaili"[tw] OR Laois[tw] OR Laoise[tw] OR Kilkenny[tw] OR "Chill Chainnigh"[tw] OR "Cill Chainnigh"[tw] OR Waterford[tw] OR "Port Lairge"[tw] OR Watterford[tw] OR Cork[tw] OR Corcaigh[tw] OR Chorcaí[tw] OR Kerry[tw] OR Ciarrái[tw] OR Chiarraí[tw] OR Limerick[tw] OR Luimneach[tw] OR Luimnigh[tw] OR Tipperary[tw] OR "Tiobraid Arann"[tw] OR "Thiobraid Arann"[tw] OR Clare[tw] OR "An Clar"[tw] OR "an Chlair"[tw] OR Galway[tw] OR Gaillimh[tw] OR "na Gaillimhe"[tw] OR Mayo[tw] OR "Maigh Eo"[tw] OR "Mhaigh Eo"[tw] OR Roscommon[tw] OR "Ros comain"[tw] OR Sligo[tw] OR Sligeach[tw] OR Shligigh[tw] OR Leitrim[tw] OR Liatroim[tw] OR Liatroma[tw] OR Donegal[tw] OR "Dhun na nGall"[tw] OR Dinnygal[tw] OR Dunnyga[tw] OR Leinster[tw] OR Laighin[tw] OR "Cuige Laighean"[tw] OR Munster[tw] OR Mumhain[tw] OR "Cuige Mumhan"[tw] OR Connacht[tw] OR Connachta[tw] OR Drogheda[tw] OR "Droichead Atha"[tw] OR Dundalk[tw] OR "Dun Dealgan"[tw] OR Swords[tw] OR Sord[tw] OR Bray[tw] OR Bre[tw] OR Navan[tw] OR "An Uaimh"[tw] OR ("Italy"[Mesh] OR Italy[tw] OR Italia*[tw] OR Abruzzo[tw] OR Abruzzi[tw] OR Basilicata[tw] OR Lucania[tw] OR Calabria[tw] OR Campania[tw] OR "Emilia Romagna"[tw] OR "friuli venezia giulia"[tw] OR Lazio[tw] OR Latium[tw] OR Liguria*[tw] OR Lombardy[tw] OR Lombardia[tw] OR Marche[tw] OR Marches[tw] OR Molisano[tw] OR Molise[tw] OR Piedmont*[tw] OR Piemonte[tw] OR Bolzano[tw] OR Bozen[tw] OR Trentino[tw] OR Trento[tw] OR Puglia[tw] OR Apulia[tw] OR Sardinia[tw] OR Sardegna[tw] OR Sicily[tw] OR Sicilia[tw] OR Toscana[tw] OR Tuscany[tw] OR Umbria[tw] OR "Valle d Aosta"[tw] OR "Vallee d Aoste"[tw] OR "Valle d'Aosta"[tw] OR "Vallee d'Aoste"[tw] OR "Aosta Valley"[tw] OR Veneto[tw] OR Venetia[tw] OR Triveneto[tw] OR Rome[tw] OR Roma[tw] OR Milan[tw] OR Milano[tw] OR Naples[tw] OR Napoli[tw] OR Turin[tw] OR Torino[tw] OR Palermo[tw] OR Genoa[tw] OR Genova[tw] OR Bologna[tw] OR Florence[tw] OR Firenze[tw] OR Bari[tw] OR Catania[tw] OR ("Latvia"[Mesh] OR Latvi*[tw] OR Riga[tw] OR Courland[tw] OR Kurzeme[tw] OR Kurland[tw] OR Latgale[tw] OR Lettgallia[tw] OR Latgola[tw] OR Latgalia[tw] OR Vidzeme[tw] OR Vidumo[tw] OR Semigallia[tw] OR Semigalia[tw] OR Zemgale[tw] OR Pieriga[tw] OR Daugavpils[tw] OR Dinaburg[tw] OR Jakabpils[tw] OR Jakobstadt[tw] OR Jelgava[tw] OR Jurmala[tw] OR Liepaja[tw] OR Libau[tw] OR Rezekne[tw] OR Rezne[tw] OR Rositten[tw] OR Valmiera[tw] OR Wolmar[tw] OR Ventspils[tw] OR Windau[tw] OR Ogre[tw] OR ("Lithuania"[Mesh] OR Lithuania*[tw] OR "Lietuvos Respublika"[tw] OR Lietuva[tw] OR lietuviu[tw] OR Alytus[tw] OR Alytaus[tw] OR Kaunas[tw] OR Kauno[tw] OR Klaipeda[tw] OR Klaipedos[tw] OR Marijampoles[tw] OR Marijampole[tw] OR Panevezys[tw] OR Panevezio[tw] OR Siauliai[tw] OR Siauliu[tw] OR Taurages[tw] OR Taurage[tw] OR Telsiu[tw] OR Telsiai[tw] OR Utenos[tw] OR Utena[tw] OR Vilnius[tw] OR Vilniaus[tw] OR Mazeikiai[tw] OR Jonava[tw] OR Mazeikiu[tw] OR Jonavos[tw] OR ("Luxembourg"[Mesh] OR Luxembourg*[tw] OR Luxemburg[tw] OR Letzebuerg[tw] OR Diekirch[tw] OR Grevenmacher[tw] OR "Esch sur Alzette"[tw] OR "Esch Uelzecht"[tw] OR "Esch an der Alzette"[tw] OR "Esch an der Alzig"[tw] OR Dudelange[tw] OR Diddeleng[tw] OR Dudelingen[tw] OR Duedelingen[tw] OR Schifflange[tw] OR Scheffleng[tw] OR Schifflingen[tw] OR Bettembourg[tw] OR Beeteberg[tw] OR Bettemburg[tw] OR Petange[tw] OR Peiteng[tw] OR Petingen[tw] OR Ettelbruck[tw] OR Ettelbreck[tw] OR Ettelbrueck[tw] OR Diekirch[tw] OR Dikrech[tw] OR Strassen[tw] OR Stroossen[tw] OR Bertrange[tw] OR Bartreng[tw] OR Bartringen[tw] OR ("Malta"[Mesh] OR Malta[tw] OR Maltese*[tw] OR Maltin[tw] OR Gozo[tw] OR Ghawdex[tw] OR Valletta[tw] OR "III Belt"[tw] OR Birkirkara[tw] OR "B Kara"[tw] OR "B'Kara"[tw] OR Birchircara[tw] OR Mosta[tw] OR Qormi[tw] OR "St Paul s Bay"[tw] OR "St Paul's Bay"[tw] OR "Pawl il Bahar"[tw] OR Zabbar[tw] OR Sliema[tw] OR Naxxar[tw] OR Gwann[tw] OR "St John"[tw] OR Zebbug[tw] OR "Citta rohan"[tw] OR Fgura[tw] OR ("Netherlands"[Mesh] OR Netherlands[tw] OR Nederland*[tw] OR Dutch*[tw] OR Drenthe[tw] OR Flevoland[tw] OR Friesland[tw] OR Fryslan[tw] OR Frisia[tw] OR Gelderland[tw] OR Guelders[tw] OR Groningen[tw] OR Limburg[tw] OR Brabant[tw] OR Holland[tw] OR Overijssel[tw] OR Overisssel[tw] OR Utrecht[tw] OR Zeeland[tw] OR Amsterdam[tw] OR Rotterdam[tw] OR Hague[tw] OR "s-Gravenhage"[tw] OR "Den Haag"[tw] OR Eindhoven[tw] OR Tilburg[tw] OR Almere[tw] OR Breda[tw] OR Nijmegen[tw] OR Nimeguen[tw] OR ("Poland"[Mesh] OR Poland[tw] OR Polska[tw] OR Polish[tw] OR Pole[tw] OR Poles[tw] OR Polski[tw] OR Polak[tw] OR Polka[tw] OR Polacy[tw] OR Dolnoslaskie[tw] OR Silesia*[tw] OR Slask[tw] OR Pomorskie[tw] OR Pomerania*[tw] OR Kujawsko[tw] OR Kuyavian[tw] OR Lodzkie[tw] OR Lodz[tw] OR Lubelskie[tw] OR Lublin[tw] OR Lubuskie[tw] OR Lubusz[tw] OR Lubus[tw] OR Malopolskie[tw] OR Mazowieckie[tw] OR Mazowske[tw] OR Masovia[tw] OR Masovian[tw] OR Opolskie[tw] OR Opole[tw] OR Podkarpackie[tw] OR Subcarpathian*[tw] OR Podlaskie[tw] OR Podlachia[tw] OR Podlasie[tw] OR Slaskie[tw] OR Swietokrzyskie[tw] OR "Warmia Mazuria"[tw] OR "Warmian Mazurian"[tw] OR "Warmia Masuria"[tw] OR "Warmian Masurian"[tw] OR "Warmia Mazury"[tw] OR "Warminsko Mazurskie"[tw] OR "Warmian Masurian"[tw] OR Wielkopolskie[tw] OR Zachodniopomorskie[tw] OR Warszawa[tw] OR Krakow[tw] OR Cracow[tw] OR Wroclaw[tw] OR Poznan[tw] OR Gdansk[tw] OR Szczecin[tw] OR Bydgoszcz[tw] OR Katowice[tw] OR ("Portugal"[Mesh] OR Portugal[tw] OR Portugues*[tw] OR Azores[tw] OR Acores[tw] OR Madeira[tw] OR Alentejo[tw] OR Algarve[tw] OR Lisboa[tw] OR Lisbon[tw] OR "Alto Tras-os-Montes"[tw] OR Ave[tw] AND (community[tw] OR intermunicipal[tw] OR comunidade[tw])) OR Mondego[tw] OR Vouga[tw] OR Beira[tw] OR Cavado[tw] OR Lafoes[tw] OR Douro[tw] OR Porto[tw] OR Oporto[tw] OR Tejo[tw] OR Minho[tw] OR Setubal[tw] OR Pinhal[tw] OR "Serra da Estrela"[tw] OR Tamega[tw] OR Leira[tw] OR Santarem[tw] OR Beja[tw] OR Faro[tw] OR Evora[tw] OR Portalegre[tw] OR "Castelo Branco"[tw] OR Guarda[tw] OR Coimbra[tw] OR Aveiro[tw] OR Viseu[tw] OR Braganca[tw] OR Braganza[tw] OR Braga[tw] OR "Vila real"[tw] OR "Viana do Castelo"[tw] OR Gaia[tw] OR Amadora[tw] OR Funchal[tw] OR Coimbra[tw] OR Almada[tw] OR Aigualva[tw] AND Cacem[tw])) OR ("Romania"[Mesh] OR Romania*[tw] OR Rumania*[tw] OR Roumania*[tw] OR Romani[tw] OR Rumani[tw] OR Alba[tw] OR Arad[tw] OR Arges[tw] OR Bacau[tw] OR Bihor[tw] OR "Bistrita Nasaud"[tw] OR Botosani[tw] OR Braila[tw] OR Brasov[tw] OR Kronstadt[tw] OR Brasso[tw] OR Brassovia[tw] OR Coron[tw] OR Bucharest[tw] OR Bucuresti[tw] OR Buzau[tw] OR Calarasi[tw] OR "Caras-Severin"[tw] OR Cluj[tw] OR Klausenburg[tw] OR Kolozsvar[tw] OR Constanta[tw] OR Tomis[tw] OR Konstantia[tw] OR Kostence[tw] OR Covasna[tw] OR Dambovita[tw] OR Dolj[tw] OR Galati[tw] OR Galatz[tw] OR Galac[tw] OR Kalas[tw] OR Giurgiu[tw] OR Gorj[tw] OR Harghita[tw] OR Hunedoara[tw] OR Ialomita[tw] OR Iasi[tw] OR Jassy[tw] OR Lassy[tw] OR Ilfov[tw] OR Maramures[tw] OR Mehedinti[tw] OR Mures[tw] OR Neamt[tw] OR (Olt[tw] AND (river[tw] OR county[tw] OR region[tw] OR judetul[tw] OR Raul[tw])) OR Prahova[tw] OR Salaj[tw] OR "Satu Mare"[tw] OR Sibiu[tw] OR Suceava[tw] OR Teleorman[tw] OR Timis[tw] OR Tulcea[tw] OR Valcea[tw] OR Vilcea[tw] OR Vaslui[tw] OR Vrancea[tw] OR Timisoara[tw] OR Temeswar[tw] OR Temeschburg[tw] OR Temeschwar[tw] OR Temesvar[tw] OR Temisvar[tw] OR Timisvar[tw] OR Temesva[tw] OR Craiova[tw] OR Ploiesti[tw] OR Ploestii[tw] OR Oradea[tw] OR Varad[tw] OR Varat[tw]) OR ("Slovakia"[Mesh] OR Slovakia[tw] OR Slovensk*[tw] OR Slovak*[tw] OR Slovaci[tw] OR Slovenki[tw] OR Bratislav*[tw] OR Presporok[tw] OR Pressburg[tw] OR

Pressburg[tw] OR Posonium[tw] OR Banskobystri* [tw] OR "Banska Bystrica"[tw] OR Neusohl[tw] OR Besztercebanya[tw] OR Kosic* [tw] OR Kaschau[tw] OR Kassa[tw] OR Nitrian* [tw] OR Nitra[tw] OR Neutra[tw] OR Nyitra[tw] OR Nyitria[tw] OR Trnav* [tw] OR Tyrnau[tw] OR Nagyszombat[tw] OR Tyrnavia[tw] OR Presov* [tw] OR Trencian* [tw] OR Trencin[tw] OR Trentschin[tw] OR Trencsen[tw] OR Zilina[tw] OR Sillein[tw] OR Zsolna[tw] OR Zylina[tw] OR (Martin[tw] AND (city[tw] OR Svaty[tw])) OR Turocszentmarton[tw] OR Poprad[tw] OR Deutschendorf[tw] OR Zvolen[tw] OR ("Slovenia"[Mesh] OR Slovenia* [tw] OR Slovenija[tw] OR slovensk* [tw] OR Slovenci[tw] OR Slovenc* [tw] OR Slovene* [tw] OR Gorenjska[tw] OR Carniola[tw] OR Goriska[tw] OR Gorizia[tw] OR Jugovzhodna[tw] OR Koroska[tw] OR Carinthia[tw] OR "Notranjsko kraska"[tw] OR "Obalno kraska"[tw] OR "Coastal karst"[tw] OR Osrednjeslovenska[tw] OR Podravska[tw] OR Drava[tw] OR Pomurska[tw] OR Mura[tw] OR Savinjska[tw] OR Savinja[tw] OR Spodnjeposavska[tw] OR Zasavska[tw] OR "Central Sava"[tw] OR Posavska[tw] OR "Lower Sava"[tw] OR Ljubljana[tw] OR Laibach[tw] OR Lubiana[tw] OR Maribor[tw] OR "Marburg an der Drau"[tw] OR Kranj[tw] OR Carnium[tw] OR Creina[tw] OR Chreina[tw] OR Krainbur[tw] OR Koper[tw] OR Capodistria[tw] OR Kopar[tw] OR Celje[tw] OR "Novo mesto"[tw] OR Neustadt[tw] OR Domzale[tw] OR Velenje[tw] OR Wollan[tw] OR Woellan[tw] OR "Nova Gorica"[tw] OR Kamnik[tw] OR ("Spain"[Mesh] OR Spain[tw] OR Espana[tw] OR Spanish[tw] OR Espanol* [tw] OR Spaniard* [tw] OR Andalucia[tw] OR Andalusia[tw] OR Aragon[tw] OR Arago[tw] OR Cantabria[tw] OR Canarias[tw] OR "Canary Islands"[tw] OR (Canaries[tw] AND island* [tw]) OR "Castile and leon"[tw] OR "Castilla y Leon"[tw] OR "Castile La Mancha"[tw] OR "Castilla La Mancha"[tw] OR Catalonia[tw] OR Catalonia[tw] OR Ceuta[tw] OR Madrid[tw] OR Melilla[tw] OR Navarra[tw] OR Navarre[tw] OR Valencia* [tw] OR Extremadura[tw] OR Galicia[tw] OR Balears[tw] OR "Balearic Islands"[tw] OR "Balear Islands"[tw] OR Balears[tw] OR "La Rioja"[tw] OR "Pais Vasco"[tw] OR "Basque Country"[tw] OR "Baske region"[tw] OR Euskadi[tw] OR Asturias[tw] OR Murcia[tw] OR Coruna[tw] OR Alava[tw] OR Araba[tw] OR Albacete[tw] OR Alicante[tw] OR Alacant[tw] OR Almeria[tw] OR Avila[tw] OR Badajoz[tw] OR Badajos[tw] OR Barcelona[tw] OR Burgos[tw] OR Caceres[tw] OR Cadiz[tw] OR Castellon[tw] OR Castello[tw] OR "Ciudad Real"[tw] OR Cordoba[tw] OR Cuenca[tw] OR Eivissa[tw] OR Ibiza[tw] OR Formentera[tw] OR "El Hierro"[tw] OR Fuerteventura[tw] OR Galiza[tw] OR Girona[tw] OR Gerona[tw] OR "Gran Canaria"[tw] OR Granada[tw] OR Guadalajara[tw] OR Guipuzcoa[tw] OR Gipuzkoa[tw] OR Huelva[tw] OR Huesca[tw] OR Jaen[tw] OR "La Gomera"[tw] OR "La Palma"[tw] OR Lanzarote[tw] OR Leon[tw] OR Lleida[tw] OR Lerida[tw] OR Lugo[tw] OR Malaga[tw] OR Mallorca[tw] OR Majorca[tw] OR Menorca[tw] OR Minorca[tw] OR Murcia[tw] OR Ourense[tw] OR Orense[tw] OR Palencia[tw] OR Pontevedra[tw] OR Salamanca[tw] OR Segovia[tw] OR Segovia[tw] OR Sevilla[tw] OR Seville[tw] OR Soria[tw] OR Tarragona[tw] OR Tenerife[tw] OR Teruel[tw] OR Toledo[tw] OR Valladolid[tw] OR Vizcaya[tw] OR Biscay[tw] OR Zamora[tw] OR Zaragoza[tw] OR Saragossa[tw] OR "Las Palmas"[tw] OR Bilbao[tw] OR Bilbo[tw] OR ("Sweden"[Mesh] OR Sweden[tw] OR Sverige[tw] OR Swedish[tw] OR Svenska[tw] OR svenskar[tw] OR Swede[tw] OR Swedes[tw] OR Norrland[tw] OR Mellansverige[tw] OR Smaland[tw] OR Stockholm* [tw] OR Sydsverige[tw] OR Vastverige[tw] OR Blekinge[tw] OR Dalarna[tw] OR Gavleborg* [tw] OR Gotland* [tw] OR Halland* [tw] OR Jamtland* [tw] OR Jonkoping* [tw] OR Kalmars* [tw] OR Kronoberg* [tw] OR Norrbotten* [tw] OR Orebro[tw] OR Ostergotland* [tw] OR Skane[tw] OR Sodermanlands[tw] OR Uppsala[tw] OR Varmland* [tw] OR Vasterbotten* [tw] OR Vasternorrland* [tw] OR Vastmanland* [tw] OR vastergotland* [tw] OR Gotaland* [tw] OR Gothenburg[tw] OR Goteborg[tw] OR Malmo[tw] OR Vasteras[tw] OR Linkoping[tw] OR Helsingborg[tw] OR Halsingborg[tw] OR Norrkoping[tw] OR ("Great Britain"[Mesh] OR GB[tw] OR "United kingdom"[tw] OR UK[tw] OR Britain[tw] OR British[tw] OR England[tw] OR English[tw] OR Scotland[tw] OR Scottish[tw] OR Scots[tw] OR Wales[tw] OR Cymru[tw] OR Welsh[tw] OR "North Ireland"[tw] OR "Northern Ireland"[tw] OR Irish[tw] OR Avon[tw] OR Bedfordshire[tw] OR Berkshire[tw] OR Bristol[tw] OR Buckinghamshire[tw] OR Cambridgeshire[tw] OR "Isle of Ely"[tw] OR Cheshire[tw] OR Cleveland[tw] OR Cornwall[tw] OR Cumberland[tw] OR Cumbria[tw] OR Derbyshire[tw] OR Devon[tw] OR Dorset[tw] OR Durham[tw] OR Essex[tw] OR Gloucestershire[tw] OR Hampshire[tw] OR Southampton[tw] OR (Hereford[tw] AND Worcester[tw]) OR Hertfordshire[tw] OR Herefordshire[tw] OR Humberside[tw] OR Huntingdon[tw] OR Huntingdonshire[tw] OR "Isle of Wight"[tw] OR Kent[tw] OR Lancashire[tw] OR Leicestershire[tw] OR Lincolnshire[tw] OR London[tw] OR Manchester[tw] OR Merseyside[tw] OR Middlesex[tw] OR Norfolk[tw] OR Northamptonshire[tw] OR Northumberland[tw] OR Nottinghamshire[tw] OR Oxfordshire[tw] OR Peterborough[tw] OR Rutland[tw] OR Shropshire[tw] OR Salop[tw] OR Somerset[tw] OR Yorkshire[tw] OR Staffordshire[tw] OR Suffolk[tw] OR Surrey[tw] OR Sussex[tw] OR (Tyne[tw] AND Wear[tw]) OR Warwickshire[tw] OR Midlands[tw] OR Westmorland[tw] OR Wiltshire[tw] OR Worcestershire[tw] OR "Isle of Man"[tw] OR Jersey[tw] OR Guernsey[tw] OR "Channel Islands"[tw] OR Aberdeen[tw] OR Aberdeenshire[tw] OR Angus[tw] OR Forfarshire[tw] OR Argyll[tw] OR Ayrshire[tw] OR Banffshire[tw] OR Berwickshire[tw] OR Bute[tw] OR Caithness[tw] OR Clackmannanshire[tw] OR Cromartyshire[tw] OR Dumfriesshire[tw] OR Dunbartonshire[tw] OR Dumbarton[tw] OR Dundee[tw] OR Lothian[tw] OR Haddingtonshire[tw] OR Edinburgh[tw] OR Fife[tw] OR Glasgow[tw] OR Inverness-shire[tw] OR Kincardineshire[tw] OR Kinross-shire[tw] OR Kirkcubrightshire[tw] OR Lanarkshire[tw] OR Midlothian[tw] OR Moray[tw] OR Elginshire[tw] OR Nairnshire[tw] OR Orkney[tw] OR Peeblesshire[tw] OR Perthshire[tw] OR Renfrewshire[tw] OR (Ross[tw] AND Cromarty[tw]) OR Ross-shire[tw] OR Roxburghshire[tw] OR Selkirkshire[tw] OR Shetland[tw] OR Zetland[tw] OR Stirlingshire[tw] OR Sutherland[tw] OR Linlithgowshire[tw] OR Wigtownshire[tw] OR Anglesey[tw] OR Brecknockshire[tw] OR Caernarfonshire[tw] OR Carmarthenshire[tw] OR Cardiganshire[tw] OR Ceredigion[tw] OR Clwyd[tw] OR Denbighshire[tw] OR Dyfed[tw] OR Flintshire[tw] OR Glamorgan[tw] OR Gwent[tw] OR Gwynedd[tw] OR Merionethshire[tw] OR Montgomeryshire[tw] OR Monmouthshire[tw] OR Pembrokeshire[tw] OR Powys[tw] OR Radnorshire[tw] OR Antrim[tw] OR Aontroim[tw] OR "Contae Aontroma"[tw] OR Anthrim[tw] OR Antrim[tw] OR Entrim[tw] OR Armagh[tw] OR "Ard Mhacha"[tw] OR Airmagh[tw] OR Belfast[tw] OR (Down[tw] AND (district[tw] OR council[tw] OR County[tw])) OR "An Dun"[tw] OR "an Duin"[tw] OR Doon[tw] OR Doun[tw] OR Fermanagh[tw] OR "Fear Manach"[tw] OR "Fhear Manach"[tw] OR Fermanay[tw] OR Londonderry[tw] OR Doire[tw] OR Dhoire[tw] OR Lunnonderrie[tw] OR Derry[tw] OR Birmingham[tw] OR Leeds[tw] OR Sheffield[tw] OR Bradford[tw] OR Liverpool[tw])) OR ((GB[ad] OR "United kingdom"[ad] OR UK[ad] OR Britain[ad] OR British[ad] OR England[ad] OR English[ad] OR Scotland[ad] OR Scottish[ad] OR Scots[ad] OR Wales[ad] OR Cymru[ad] OR Welsh[ad] OR "North Ireland"[ad] OR "Northern Ireland"[ad] OR Irish[ad] OR Avon[ad] OR Bedfordshire[ad] OR Berkshire[ad] OR Bristol[ad] OR Buckinghamshire[ad] OR Cambridgeshire[ad] OR "Isle of Ely"[ad] OR Cheshire[ad] OR Cleveland[ad] OR Cornwall[ad] OR Cumberland[ad] OR Cumbria[ad] OR Derbyshire[ad] OR Devon[ad] OR Dorset[ad] OR Durham[ad] OR Essex[ad] OR Gloucestershire[ad] OR Hampshire[ad] OR Southampton[ad] OR (Hereford[ad] AND Worcester[ad]) OR Hertfordshire[ad] OR Herefordshire[ad] OR Humberside[ad] OR Huntingdon[ad] OR Huntingdonshire[ad] OR "Isle of Wight"[ad] OR Kent[ad] OR Lancashire[ad] OR Leicestershire[ad] OR Lincolnshire[ad] OR London[ad] OR Manchester[ad] OR Merseyside[ad] OR Middlesex[ad] OR Norfolk[ad] OR Northamptonshire[ad] OR Northumberland[ad] OR Nottinghamshire[ad] OR Oxfordshire[ad] OR Peterborough[ad] OR Rutland[ad] OR Shropshire[ad] OR Salop[ad] OR Somerset[ad] OR Yorkshire[ad] OR Staffordshire[ad] OR

Suffolk[ad] OR Surrey[ad] OR Sussex[ad] OR (Tyne[ad] AND Wear[ad]) OR Warwickshire[ad] OR midlands[ad] OR Westmorland[ad] OR Wiltshire[ad] OR Worcestershire[ad] OR "Isle of Man"[ad] OR Jersey[ad] OR Guernsey[ad] OR "Channel Islands"[ad] OR Aberdeen[ad] OR Aberdeenshire[ad] OR Angus[ad] OR Forfarshire[ad] OR Argyll[ad] OR Ayrshire[ad] OR Banffshire[ad] OR Berwickshire[ad] OR bute[ad] OR Caithness[ad] OR Clackmannanshire[ad] OR Cromartysire[ad] OR Dumfriesshire[ad] OR Dunbartonshire[ad] OR Dumbarton[ad] OR Dundee[ad] OR Lothian[ad] OR Haddingtonshire[ad] OR Edinburgh[ad] OR Fife[ad] OR Glasgow[ad] OR Inverness-shire[ad] OR Kincardineshire[ad] OR Kinross-shire[ad] OR Kirkcudbrightshire[ad] OR Lanarkshire[ad] OR Midlothian[ad] OR Moray[ad] OR Elginshire[ad] OR Nairnshire[ad] OR Orkney[ad] OR Peeblesshire[ad] OR Perthshire[ad] OR Renfrewshire[ad] OR (Ross[ad] AND Cromarty[ad]) OR Ross-shire[ad] OR Roxburghshire[ad] OR Selkirkshire[ad] OR Shetland[ad] OR Zetland[ad] OR Stirlingshire[ad] OR Sutherland[ad] OR Linlithgowshire[ad] OR Wigtownshire[ad] OR Anglesey[ad] OR Brecknockshire[ad] OR Caernarfonshire[ad] OR Carmarthenshire[ad] OR Cardiganshire[ad] OR Ceredigion[ad] OR Clwyd[ad] OR Denbighshire[ad] OR Dyfed[ad] OR Flintshire[ad] OR Glamorgan[ad] OR Gwent[ad] OR Gwynedd[ad] OR Merionethshire[ad] OR Montgomeryshire[ad] OR Monmouthshire[ad] OR Pembrokeshire[ad] OR Powys[ad] OR Radnorshire[ad] OR Antrim[ad] OR Aontroim[ad] OR "Contae Aontroma"[ad] OR Antrim[ad] OR Antrim[ad] OR Entrim[ad] OR Armagh[ad] OR "Ard Mhacha"[ad] OR Airmagh[ad] OR Belfast[ad] OR (Down[ad] AND (district[ad] OR council[ad] OR County[ad])) OR "An Dun"[ad] OR "an Duin"[ad] OR Doon[ad] OR Doun[ad] OR Fermanagh[ad] OR "Fear Manach"[ad] OR "Fhear Manach"[ad] OR Fermanay[ad] OR Londonderry[ad] OR Doire[ad] OR Dhoire[ad] OR Lunnonderrrie[ad] OR Derry[ad] OR Birmingham[ad] OR Leeds[ad] OR Sheffield[ad] OR Bradford[ad] OR Liverpool[ad] OR (Sweden[ad] OR Sverige[ad] OR Swedish[ad] OR Svenska[ad] OR svenskar[ad] OR Swede[ad] OR Swedes[ad] OR Norrland[ad] OR Mellansverige[ad] OR Smaland[ad] OR Stockholm* [ad] OR Sydsvrige[ad] OR Vastsverige[ad] OR Blekinge[ad] OR Dalarna[ad] OR Gavleborg* [ad] OR Gotland* [ad] OR Halland* [ad] OR Jamtland* [ad] OR Jonkoping* [ad] OR Kalmar[ad] OR Kronoberg* [ad] OR Norrbotten* [ad] OR Orebro[ad] OR Ostergotland* [ad] OR Skane[ad] OR Sodermanlands[ad] OR Uppsala[ad] OR Varmland* [ad] OR Vasterbotten* [ad] OR Vasternorrland* [ad] OR Vastmanland* [ad] OR vastergotland* [ad] OR Gotaland* [ad] OR Gothenburg[ad] OR Goteborg[ad] OR Malmo[ad] OR Vasteras[ad] OR Linkoping[ad] OR Helsingborg[ad] OR Halsingborg[ad] OR Norrkoping[ad] OR (Spain[ad] OR Espana[ad] OR Spanish[ad] OR Espanol* [ad] OR Spaniard* [ad] OR Andalucia[ad] OR Andalusia[ad] OR Aragon[ad] OR Arago[ad] OR Cantabria[ad] OR Canarias[ad] OR "Canary Islands"[ad] OR (Canaries[ad] AND island* [ad]) OR "Castile and leon"[ad] OR "Castilla y Leon"[ad] OR "Castile La Mancha"[ad] OR "Castilla La Mancha"[ad] OR Cataluna[ad] OR Catalonia[ad] OR Ceuta[ad] OR Madrid[ad] OR Melilla[ad] OR Navarra[ad] OR Navarre[ad] OR Valencia* [ad] OR Extremadura[ad] OR Galicia[ad] OR Balears[ad] OR "Balearic Islands"[ad] OR "Balear Islands"[ad] OR Balears[ad] OR "La Rioja"[ad] OR "Pais Vasco"[ad] OR "Basque Country"[ad] OR "Baske region"[ad] OR Euskadi[ad] OR Asturias[ad] OR Murcia[ad] OR Coruna[ad] OR Alava[ad] OR Araba[ad] OR Albacete[ad] OR Alicante[ad] OR Alacant[ad] OR Almeria[ad] OR Avila[ad] OR Badajoz[ad] OR Badajoz[ad] OR Barcelona[ad] OR Burgos[ad] OR Caceres[ad] OR Cadiz[ad] OR Castellon[ad] OR Castello[ad] OR "Ciudad Real"[ad] OR Cordoba[ad] OR Cuenca[ad] OR Eivissa[ad] OR Ibiza[ad] OR Formentera[ad] OR "El Hierro"[ad] OR Fuerteventura[ad] OR Galiza[ad] OR Girona[ad] OR Gerona[ad] OR "Gran Canaria"[ad] OR Granada[ad] OR Guadalajara[ad] OR Guipuzcoa[ad] OR Gipuzkoa[ad] OR Huelva[ad] OR Huesca[ad] OR Jaen[ad] OR "La Gomera"[ad] OR "La Palma"[ad] OR Lanzarote[ad] OR Leon[ad] OR Lleida[ad] OR Lerida[ad] OR Lugo[ad] OR Malaga[ad] OR Mallorca[ad] OR Majorca[ad] OR Menorca[ad] OR Minorca[ad] OR Murcia[ad] OR Ourense[ad] OR Ourense[ad] OR Palencia[ad] OR Pontevedra[ad] OR Salamanca[ad] OR Segovia[ad] OR Sevilla[ad] OR Seville[ad] OR Soria[ad] OR Tarragona[ad] OR Tenerife[ad] OR Teruel[ad] OR Toledo[ad] OR Valladolid[ad] OR Vizcaya[ad] OR Biscay[ad] OR Zamora[ad] OR Zaragoza[ad] OR Saragossa[ad] OR "Las Palmas"[ad] OR Bilbao[ad] OR Bilbo[ad] OR (Slovenia* [ad] OR Slovenija[ad] OR slovensk* [ad] OR Slovenci[ad] OR Slovene* [ad] OR Gorenjska[ad] OR Carniola[ad] OR Goriska[ad] OR Gorizia[ad] OR Jugovzhodna[ad] OR Koroska[ad] OR Carinthia[ad] OR "Notranjsko kraska"[ad] OR "Obalno kraska"[ad] OR "Coastal karst"[ad] OR Osrednjeslovenska[ad] OR Podravska[ad] OR Drava[ad] OR Pomurska[ad] OR Mura[ad] OR Savinjska[ad] OR Savinja[ad] OR Spodnjeposavska[ad] OR Zasavska[ad] OR "Central Sava"[ad] OR Posavska[ad] OR "Lower Sava"[ad] OR Ljubljana[ad] OR Laibach[ad] OR Lubiana[ad] OR Maribor[ad] OR "Marburg an der Drau"[ad] OR Kranj[ad] OR Carnium[ad] OR Creina[ad] OR Chreina[ad] OR Krainbur[ad] OR Koper[ad] OR Capodistria[ad] OR Kopar[ad] OR Celje[ad] OR "Novo mesto"[ad] OR Neustadt[ad] OR Domzale[ad] OR Velenje[ad] OR Wollan[ad] OR Woellan[ad] OR "Nova Gorica"[ad] OR Kamnik[ad] OR (Slovakia[ad] OR Slovensk* [ad] OR Slovak* [ad] OR Slovaci[ad] OR Slovenki[ad] OR Bratislav* [ad] OR Presporok[ad] OR Pressburg[ad] OR Pressburg[ad] OR Ponium[ad] OR Banskobystri* [ad] OR "Banska Bystrica"[ad] OR Neusohl[ad] OR Besztercebanya[ad] OR Kosic* [ad] OR Kaschau[ad] OR Kassa[ad] OR Nitrian* [ad] OR Nitra[ad] OR Neutra[ad] OR Nyitra[ad] OR Nyitra[ad] OR Trnav* [ad] OR Tyrnau[ad] OR Nagyszombat[ad] OR Tyrnavia[ad] OR Presov* [ad] OR Trencian* [ad] OR Trencin[ad] OR Trencschin[ad] OR Zilina[ad] OR Sillesin[ad] OR Zsolna[ad] OR Zylina[ad] OR (Martin[ad] AND (city[ad] OR Svaty[ad])) OR Turocszentmarton[ad] OR Poprad[ad] OR Deutschendorf[ad] OR Zvolen[ad] OR (Romania* [ad] OR Rumania* [ad] OR Roumania* [ad] OR Romani[ad] OR Ruman[ad] OR Alba[ad] OR Arad[ad] OR Arges[ad] OR Bacau[ad] OR Bihor[ad] OR "Bistrita Nasaud"[ad] OR Botosani[ad] OR Braila[ad] OR Brasov[ad] OR Kronstadt[ad] OR Brasso[ad] OR Brassovia[ad] OR Coron[ad] OR Bucharest[ad] OR Bucuresti[ad] OR Buzau[ad] OR Calarasi[ad] OR "Caras-Severin"[ad] OR Cluj[ad] OR Klausenburg[ad] OR Kolozsvar[ad] OR Constanta[ad] OR Tomis[ad] OR Konstantia[ad] OR Kostence[ad] OR Covasna[ad] OR Dambovita[ad] OR Dolj[ad] OR Galati[ad] OR Galatz[ad] OR Galac[ad] OR Kalas[ad] OR Giurgiu[ad] OR Gorj[ad] OR Harghita[ad] OR Hunedoara[ad] OR Ialomita[ad] OR Iasi[ad] OR Jassy[ad] OR Lassy[ad] OR Ilfov[ad] OR Maramures[ad] OR Mehedinti[ad] OR Mures[ad] OR Neamt[ad] OR Olt[ad] AND (river[ad] OR county[ad] OR region[ad] OR judetul[ad] OR Raul[ad]) OR Prahova[ad] OR Salaj[ad] OR "Satu Mare"[ad] OR Sibiu[ad] OR Suceava[ad] OR Teleorman[ad] OR Timis[ad] OR Tulcea[ad] OR Valcea[ad] OR Vilcea[ad] OR Vaslui[ad] OR Vrancea[ad] OR Timisoara[ad] OR Temeswar[ad] OR Temeschburg[ad] OR Temeschwar[ad] OR Temesvar[ad] OR Temisvar[ad] OR Temisvar[ad] OR Temesva[ad] OR Craiova[ad] OR Ploiesti[ad] OR Ploesti[ad] OR Oradea[ad] OR Varad[ad] OR Varat[ad] OR (Portugal[ad] OR Portugues* [ad] OR Azores[ad] OR Acores[ad] OR Madeira[ad] OR Alentejo[ad] OR Algarve[ad] OR Lisboa[ad] OR Lisbon[ad] OR "Alto Tras-os-Montes"[ad] OR (Ave[ad] AND (community[ad] OR intermunicipal[ad] OR comunidade[ad])) OR Mondego[ad] OR Vouga[ad] OR Beira[ad] OR Cavado[ad] OR Lafoes[ad] OR Douro[ad] OR Porto[ad] OR Oporto[ad] OR Tejo[ad] OR Minho[ad] OR Setubal[ad] OR Pinhal[ad] OR "Serra da Estrela"[ad] OR Tamega[ad] OR Leira[ad] OR Santarem[ad] OR Beja[ad] OR Faro[ad] OR Evora[ad] OR Portalegre[ad] OR "Castelo Branco"[ad] OR Guarda[ad] OR Coimbra[ad] OR Aveiro[ad] OR Viseu[ad] OR Braganca[ad] OR Braganza[ad] OR Braga[ad] OR "Vila real"[ad] OR "Viana do Castelo"[ad] OR Gaia[ad] OR Amadora[ad] OR Funchal[ad] OR Coimbra[ad] OR Almada[ad] OR (Aguilva[ad] AND Cacem[ad]) OR (Poland[ad] OR Polska[ad] OR Polish[ad] OR Pole[ad] OR Poles[ad] OR Polski[ad] OR Polak[ad] OR Polka[ad] OR Polacy[ad] OR Dolnoslaskie[ad] OR Silesia* [ad] OR Slask[ad] OR

Pomorskie[ad] OR Pomerania*[ad] OR Kujawsko[ad] OR Kuyavian[ad] OR Lodzkie[ad] OR Lodz[ad] OR Lubelskie[ad] OR Lublin[ad] OR Lubuskie[ad] OR Lubusz[ad] OR Lubus[ad] OR Malopolskie[ad] OR Mazowieckie[ad] OR Mazowske[ad] OR Masovia[ad] OR Masovian[ad] OR Opolskie[ad] OR Opole[ad] OR Podkarpackie[ad] OR Subcarpathian*[ad] OR Podlaskie[ad] OR Podlachia[ad] OR Podlasie[ad] OR Slaskie[ad] OR Swietokrzyskie[ad] OR "Warmia Mazuria"[ad] OR "Warmian Mazurian"[ad] OR "Warmia Masuria"[ad] OR "Warmian Masurian"[ad] OR "Warmia Mazury"[ad] OR "Warminsko Mazurskie"[ad] OR "Warmian Masurian"[ad] OR Wielkopolskie[ad] OR Zachodniopomorskie[ad] OR Warsaw[ad] OR Warszawa[ad] OR Krakow[ad] OR Cracow[ad] OR Wroclaw[ad] OR Poznan[ad] OR Gdansk[ad] OR Szczecin[ad] OR Bydgoszcz[ad] OR Katowice[ad] OR (Netherlands[ad] OR Nederland*[ad] OR Dutch*[ad] OR Drenthe[ad] OR Flevoland[ad] OR Friesland[ad] OR Fryslan[ad] OR Frisia[ad] OR Gelderland[ad] OR Guelders[ad] OR Groningen[ad] OR Limburg[ad] OR Brabant[ad] OR Holland[ad] OR Overijssel[ad] OR Overissel[ad] OR Utrecht[ad] OR Zeeland[ad] OR Amsterdam[ad] OR Rotterdam[ad] OR Hague[ad] OR "s-Gravenhage"[ad] OR "Den Haag"[ad] OR Eindhoven[ad] OR Tilburg[ad] OR Almere[ad] OR Breda[ad] OR Nijmegen[ad] OR Nimeguen[ad] OR (Malta[ad] OR Maltese*[ad] OR Maltin[ad] OR Gozo[ad] OR Ghawdex[ad] OR Valletta[ad] OR "III Belt"[ad] OR Birkirkara[ad] OR "B Kara"[ad] OR "B'Kara"[ad] OR Birchircara[ad] OR Mosta[ad] OR Qormi[ad] OR "St Paul s Bay"[ad] OR "St Paul's Bay"[ad] OR "Pawl il Bahar"[ad] OR Zabbar[ad] OR Sliema[ad] OR Naxxar[ad] OR Gwann[ad] OR "St John"[ad] OR Zebbug[ad] OR "Citta rohan"[ad] OR Fgura[ad] OR (Luxembourg*[ad] OR Luxemburg[ad] OR Letzebuerg[ad] OR Diekirch[ad] OR Grevenmacher[ad] OR "Esch sur Alzette"[ad] OR "Esch Uelzecht"[ad] OR "Esch an der Alzette"[ad] OR "Esch an der Alzig"[ad] OR Dudelange[ad] OR Diddeleng[ad] OR Dudelingen[ad] OR Duedelingen[ad] OR Schifflange[ad] OR Scheffleng[ad] OR Schifflingen[ad] OR Bettembourg[ad] OR Beetebuerg[ad] OR Bettemburg[ad] OR Petange[ad] OR Peiteng[ad] OR Petingen[ad] OR Ettelbruck[ad] OR Ettelbreck[ad] OR Ettelbrueck[ad] OR Diekirch[ad] OR Dikrech[ad] OR Strassen[ad] OR Stroossen[ad] OR Bertrange[ad] OR Bartreng[ad] OR Bartringen[ad] OR (Lithuania*[ad] OR "Lietuvos Respublika"[ad] OR Lietuva[ad] OR lietuviu[ad] OR Alytus[ad] OR Alytaus[ad] OR Kaunas[ad] OR Kauno[ad] OR Klaipeda[ad] OR Klaipedos[ad] OR Marijampoles[ad] OR Marijampole[ad] OR Panevezys[ad] OR Panevezio[ad] OR Siauliai[ad] OR Siauliu[ad] OR Taurages[ad] OR Taurage[ad] OR Telsiu[ad] OR Telsiai[ad] OR Utenos[ad] OR Utena[ad] OR Vilnius[ad] OR Vilniaus[ad] OR Mazeikiai[ad] OR Jonava[ad] OR Mazeikiu[ad] OR Jonavos[ad] OR (Latvi*[ad] OR Riga[ad] OR Courland[ad] OR Kurzeme[ad] OR Kurland[ad] OR Latgale[ad] OR Lettgallia[ad] OR Latgola[ad] OR Latgalia[ad] OR Vidzeme[ad] OR Vidumo[ad] OR Semigallia[ad] OR Semigalia[ad] OR Zemgale[ad] OR Pieriga[ad] OR Daugavpils[ad] OR Dinaburg[ad] OR Jekabpils[ad] OR Jakobstadt[ad] OR Jalgava[ad] OR Jurmala[ad] OR Liepaja[ad] OR Libau[ad] OR Rezekne[ad] OR Rezne[ad] OR Rositten[ad] OR Valmiera[ad] OR Wolmar[ad] OR Ventspils[ad] OR Windau[ad] OR Ogre[ad] OR (Italy[ad] OR Italia*[ad] OR Abruzzo[ad] OR Abruzzi[ad] OR Basilicata[ad] OR Lucania[ad] OR Calabria[ad] OR Campania[ad] OR "Emilia Romagna"[ad] OR "friuli venezia giulia"[ad] OR Lazio[ad] OR Latium[ad] OR Liguria*[ad] OR Lombardy[ad] OR Lombardia[ad] OR Marche[ad] OR Marches[ad] OR Molisano[ad] OR Molise[ad] OR Piedmont*[ad] OR Piemonte[ad] OR Bolzano[ad] OR Bozen[ad] OR Trentino[ad] OR Trento[ad] OR Puglia[ad] OR Apulia[ad] OR Sardinia[ad] OR Sardegna[ad] OR Sicily[ad] OR Sicilia[ad] OR Toscana[ad] OR Tuscany[ad] OR Umbria[ad] OR "Valle d Aosta"[ad] OR "Vallee d Aoste"[ad] OR "Valle d'Aosta"[ad] OR "Vallee d'Aoste"[ad] OR "Aosta Valley"[ad] OR Veneto[ad] OR Venetia[ad] OR Triveneto[ad] OR Rome[ad] OR Roma[ad] OR Milan[ad] OR Milano[ad] OR Naples[ad] OR Napoli[ad] OR Turin[ad] OR Torino[ad] OR Palermo[ad] OR Genoa[ad] OR Genova[ad] OR Bologna[ad] OR Florence[ad] OR Firenze[ad] OR Bari[ad] OR Catania[ad] OR (Ireland[ad] OR Eire[ad] OR Irish*[ad] OR Fingal[ad] OR "Fine Gall"[ad] OR Dublin[ad] OR "Ath Cliath"[ad] OR "Dun Laoghaire"[ad] OR Wicklow[ad] OR "Cill Mhantain"[ad] OR "Chill Mhantain"[ad] OR Wexford[ad] OR "Loch Garman"[ad] OR Carlow[ad] OR Ceatharlach[ad] OR Kildare[ad] OR "Cill Dara"[ad] OR "Chill Dara"[ad] OR Meath[ad] OR "An Mhi"[ad] OR "Contae na Mí"[ad] OR Louth[ad] OR "Contae Lu"[ad] OR Monaghan[ad] OR Muineachan[ad] OR Mhuineachain[ad] OR Cavan[ad] OR "An Cabhan"[ad] OR "An Cabhain"[ad] OR Longford[ad] OR "An Longfort"[ad] OR "an Longfoirt"[ad] OR Langfurd[ad] OR Westmeath[ad] OR "An Iarmhí"[ad] OR "na Iarmhí"[ad] OR Offaly[ad] OR "Uibh Fhailí"[ad] OR Laois[ad] OR Laoise[ad] OR Kilkenny[ad] OR "Chill Chainnigh"[ad] OR "Cill Chainnigh"[ad] OR Waterford[ad] OR "Port Lairge"[ad] OR Watterford[ad] OR Cork[ad] OR Corcaigh[ad] OR Chorcai[ad] OR Kerry[ad] OR Ciarrai[ad] OR Chiarrai[ad] OR Limerick[ad] OR Luimneach[ad] OR Luimnigh[ad] OR Tipperary[ad] OR "Tiobraid Arann"[ad] OR "Thiobraid Arann"[ad] OR Clare[ad] OR "An Clar"[ad] OR "an Chlair"[ad] OR Galway[ad] OR Gaillimh[ad] OR "na Gaillimhe"[ad] OR Mayo[ad] OR "Maigh Eo"[ad] OR "Mhaigh Eo"[ad] OR Roscommon[ad] OR "Ros comain"[ad] OR Sligo[ad] OR Sligeach[ad] OR Shligigh[ad] OR Leitrim[ad] OR Liatroim[ad] OR Liatroma[ad] OR Donegal[ad] OR "Dhun na nGall"[ad] OR Dinnygal[ad] OR Dunnya[ad] OR Leinster[ad] OR Laignin[ad] OR "Cuige Laighean"[ad] OR Munster[ad] OR Mumhain[ad] OR "Cuige Mumhan"[ad] OR Connacht[ad] OR Connachta[ad] OR Drogheda[ad] OR "Droichead Atha"[ad] OR Dundalk[ad] OR "Dun Dealgan"[ad] OR Swords[ad] OR Sord[ad] OR Bray[ad] OR Bre[ad] OR Navan[ad] OR "An Uaimh"[ad] OR (Hungar*[ad] OR Magyarorszag[ad] OR Magyar*[ad] OR Dunantuli[ad] OR Transdanubia[ad] OR Dunantul[ad] OR "Great Plain"[ad] OR "Eszak Alfold"[ad] OR "Del Alfold"[ad] OR "Alfud es eszak"[ad] OR "Northern Alföld"[ad] OR "North Alföld"[ad] OR "South Alföld"[ad] OR "Southern Alföld"[ad] OR Bacs[ad] OR Kiskun[ad] OR Baranya[ad] OR Bekes[ad] OR Borsod[ad] OR Abauj[ad] OR Zemplen[ad] OR Budapest[ad] OR Csongrad[ad] OR Fejer[ad] OR gyor[ad] OR moson[ad] OR sopron[ad] OR hajdu[ad] OR bihar[ad] OR Heves[ad] OR "jasz nagykun szolnok"[ad] OR komarom[ad] OR esztergom[ad] OR Nograd[ad] OR (Pest[ad] AND (megye[ad] OR county[ad])) OR Somogy[ad] OR szabolcs[ad] OR szatmar[ad] OR bereg[ad] OR Tolna[ad] OR Vas[ad] OR Veszprem[ad] OR Zala[ad] OR Debrecen[ad] OR Miskolc[ad] OR Szeged[ad] OR Pecs[ad] OR Gyor[ad] OR Nyiregyhaza[ad] OR Kecskemet[ad] OR Szekesfehervar[ad] OR Szombathely[ad] OR (Greece[ad] OR "Hellenic republic"[ad] OR Greek*[ad] OR Ellada[ad] OR Elladas[ad] OR "Elliniki Dimokratia"[ad] OR Hellas[ad] OR Hellenes[ad] OR Attica[ad] OR Attiki[ad] OR Makedonia*[ad] OR Macedonia[ad] OR Thraki[ad] OR Thrace[ad] OR Crete[ad] OR Kriti[ad] OR "Ionia Nisia"[ad] OR "Ionion neson"[ad] OR "Ionion nIson"[ad] OR "Ionian islands"[ad] OR "Ionian island"[ad] OR Epirus[ad] OR Ipeiros[ad] OR "Perifereia Ipeirou"[ad] OR "North aegean"[ad] OR "Northern Aegean"[ad] OR "Aegean islands"[ad] OR "Aegean island"[ad] OR "Nisoi Agaiou"[ad] OR "Notio Aigaiou"[ad] OR Peloponnese[ad] OR Peloponniso*[ad] OR Thessaly[ad] OR Thessalia[ad] OR Thessalian[ad] OR Petthalia[ad] OR "Voreio Aigaiou"[ad] OR "Voreio Aigaiou"[ad] OR "South aegean"[ad] OR "Southern Aegean"[ad] OR "Mount athos"[ad] OR "Oros Athos"[ad] OR Cyclades[ad] OR Cycklades[ad] OR Kiklades[ad] OR Dodecanese[ad] OR Dodekanisa[ad] OR Athens[ad] OR Athina[ad] OR Thessaloniki[ad] OR Thessalonica[ad] OR Patras[ad] OR Patra[ad] OR Pireas[ad] OR Piraeus[ad] OR Larissa[ad] OR Larisa[ad] OR Heraklion[ad] OR Heraclion[ad] OR Iraklion[ad] OR Irakleion[ad] OR Iraklio[ad] OR Volos[ad] OR Rhodes[ad] OR Rodos[ad] OR Ioannina[ad] OR Janina[ad] OR Yannena[ad] OR Chania[ad] OR Chalcis[ad] OR Chalkida[ad] OR (German*[ad] OR Deutsch*[ad] OR Bundesrepublik[ad] OR Westdeutschland[ad] OR Ostdeutschland[ad] OR Baden[ad] OR Wuerttemberg[ad] OR Wurttemberg[ad] OR Bayern[ad] OR Bavaria[ad] OR Berlin[ad] OR Brandenburg[ad] OR Bremen[ad] OR Oldenburg[ad] OR Mitteldeutschland[ad] OR Rhein[ad] OR Rhine[ad] OR Hannover[ad] OR Braunschweig[ad] OR Gottingen[ad]

OR Goettingen[ad] OR Nurnberg[ad] OR Nuernberg[ad] OR Ruhr[ad] OR Koln[ad] OR koeln[ad] OR Bonn[ad] OR Hamburg[ad] OR Hessen[ad] OR Hesse[ad] OR Hessia[ad] OR Mecklenburg[ad] OR Vorpommern[ad] OR Pomerania[ad] OR Niedersachsen[ad] OR Neddersassen[ad] OR Saxony[ad] OR Niederbayern[ad] OR "Northern Rhine"[ad] OR "North Rhine"[ad] OR Westphalia[ad] OR Westfalen[ad] OR "Rhineland Palatinate"[ad] OR "Rheinland Pfalz"[ad] OR Saarland[ad] OR Sachsen[ad] OR "Schleswig Holstein"[ad] OR Thuringia[ad] OR Thuringen[ad] OR Thueringen[ad] OR Munchen[ad] OR Muenchen[ad] OR Munich[ad] OR Frankfurt[ad] OR Stuttgart[ad] OR Dusseldorf[ad] OR Duesseldorf[ad] OR Dortmund[ad] OR Essen[ad] OR France[ad] OR French*[ad] OR Francais*[ad] OR Alsace[ad] OR Elsass[ad] OR Aquitaine[ad] OR Aquitania[ad] OR Akitania[ad] OR Aguiene[ad] OR Auvergne[ad] OR Auvernhe[ad] OR Auvernha[ad] OR Normandie[ad] OR Normandy[ad] OR Normaundie[ad] OR Bourgogne[ad] OR Burgundy[ad] OR Bregogne[ad] OR Borgoeagne[ad] OR Borgogne[ad] OR Brittany[ad] OR Breizh[ad] OR Bertaeyn[ad] OR Bretagne[ad] OR "Champagne Ardenne"[ad] OR Corse[ad] OR Corsica[ad] OR "Franche Comte"[ad] OR "Frantche Comte"[ad] OR "Franche Comtat"[ad] OR Guadeloupe[ad] OR Guyane[ad] OR Guiana[ad] OR "Languedoc Roussillon"[ad] OR "Lengadoc Rosselhon"[ad] OR "Llenguadoc-Rossello"[ad] OR Limousin[ad] OR Lemosin[ad] OR Lorraine[ad] OR Lothringen[ad] OR Lottringe[ad] OR Martinique[ad] OR "Midi Pyrenees"[ad] OR "Miegjorn Pireneus"[ad] OR "Mieidia Pireneus"[ad] OR "Mediodia Pirineos"[ad] OR "Pays de la Loire"[ad] OR "Broiou al Liger"[ad] OR Picardie[ad] OR Picardy[ad] OR "Poitou Charentes"[ad] OR "Peitau Charantas"[ad] OR "Poetou-Cherentes"[ad] OR Provence[ad] OR Provenca[ad] OR Prouvencof[ad] OR "Cote d Azur"[ad] OR "Cote d'Azur"[ad] OR "Costo d'Azur"[ad] OR "Costo d'Azur"[ad] OR "Costa d'Azur"[ad] OR "Costa d Azur"[ad] OR Reunion[ad] OR "Rhone Alpes"[ad] OR "Rono Arpes"[ad] OR "Rose Aups"[ad] OR Ain[ad] OR Aisne[ad] OR Allier[ad] OR "Alpes de Haute Provence"[ad] OR "Haute Alpes"[ad] OR "Alpes Maritimes"[ad] OR Ardeche[ad] OR Ardennes[ad] OR Ariège[ad] OR Aube[ad] OR Aude[ad] OR Aveyron[ad] OR "Bas Rhin"[ad] OR "Bouches du Rhone"[ad] OR Calvados[ad] OR Cantal[ad] OR Charente[ad] OR Cher[ad] OR Correze[ad] OR "Corse du Sud"[ad] OR "Cote d Or"[ad] OR "Cote d'Or"[ad] OR "Cotes d Armor"[ad] OR "Cotes d'Armor"[ad] OR Creuse[ad] OR "Deux Sevres"[ad] OR Dordogne[ad] OR Doubs[ad] OR Drome[ad] OR Essonne[ad] OR Eure[ad] OR Finistere[ad] OR Gard[ad] OR Gers[ad] OR Gironde[ad] OR "Haute Corse"[ad] OR "Haute Garonne"[ad] OR "Haute Marne"[ad] OR "Hautes Alpes"[ad] OR "Haute Saone"[ad] OR "Haute Savoie"[ad] OR "Hautes Pyrenees"[ad] OR "Haute Vienne"[ad] OR "Haut Rhin"[ad] OR "Hauts de Seine"[ad] OR Hérault[ad] OR "Ile de France"[ad] OR "Ille et Vilaine"[ad] OR Indre[ad] OR Isere[ad] OR Jura[ad] OR Landes[ad] OR Loire[ad] OR Loiret[ad] OR (Lot[ad] AND (departement[ad] OR departement[ad])) OR "Lot et Garonne"[ad] OR "Loir et Cher"[ad] OR Lozere[ad] OR Manche[ad] OR Marne[ad] OR Mayenne[ad] OR Mayotte[ad] OR "Meurthe et Moselle"[ad] OR Meuse[ad] OR Morbihan[ad] OR Moselle[ad] OR (Nord[ad] AND (departement[ad] OR departement[ad])) OR Nièvre[ad] OR Oise[ad] OR Orne[ad] OR "Pas de calais"[ad] OR "Noord-Nauw van Kales"[ad] OR Paris[ad] OR "Puy de dome"[ad] OR "Pyrenees Atlantiques"[ad] OR "Pyrenees Orientales"[ad] OR Rhone[ad] OR Sarthe[ad] OR Savoie[ad] OR "Seine et Marne"[ad] OR "Seine Maritime"[ad] OR Somme[ad] OR Tarn[ad] OR "Territoire de Belfort"[ad] OR "Val de Marne"[ad] OR "Val d Oise"[ad] OR Var[ad] OR Vaucluse[ad] OR Vendee[ad] OR Vienne[ad] OR Vosges[ad] OR Yonne[ad] OR Yvelines[ad] OR Marseille[ad] OR Lyon[ad] OR Nice[ad] OR Nantes[ad] OR Strasbourg[ad] OR Montpellier[ad] OR Bordeaux[ad] OR Lille[ad] OR Toulouse[ad] OR "Outre Mer"[ad] OR "Seine Saint Denis"[ad] OR (Finland[ad] OR Finnish*[ad] OR Finn[ad] OR Finns[ad] OR Suomif[ad] AND Suomen[ad] OR Suomalaiset[ad] OR Aland[ad] OR Ahvenanmaa[ad] OR Uusimaa[ad] OR Nyland[ad] OR Karelia[ad] OR Karjala[ad] OR Karelen[ad] OR Ostrobothnia[ad] OR Pohjanmaa[ad] OR Osterbotten[ad] OR Savonia[ad] OR Savo[ad] OR Savolax[ad] OR Kainuu[ad] OR Kajanaland*[ad] OR "Kanta Hame"[ad] OR Tavastia[ad] OR Tavastland[ad] OR Kymenlaakso[ad] OR Kymmenedalen[ad] OR Lapland[ad] OR Lappi[ad] OR Lappland[ad] OR "Paijat Hame"[ad] OR Pirkanmaa[ad] OR Birkaland[ad] OR Satakunta[ad] OR Satakunda[ad] OR Helsinki[ad] OR Helsingfors[ad] OR Espoo[ad] OR Esbo[ad] OR Tampere[ad] OR Tammerfors[ad] OR Vantaa[ad] OR Vanda[ad] OR Oulu[ad] OR Uleaborg[ad] OR Turku[ad] OR Abo[ad] OR Jyväskylä[ad] OR Kuopio[ad] OR Lahti[ad] OR Lahtis[ad] OR Kouvolaa[ad] OR (Estonia*[ad] OR Eestii[ad] OR Eestlased[ad] OR Eestlane[ad] OR Harju[ad] OR Harjumaa[ad] OR Hiiumaa[ad] OR "Ida Viru"[ad] OR "Ida Virumaa"[ad] OR Jarvamaa[ad] OR Jarva[ad] OR Jogeveamaa[ad] OR Jogevea[ad] OR Laanemaa[ad] OR Laane[ad] OR "Laane Virumaa"[ad] OR Parnu[ad] OR Parnumaa[ad] OR Polva[ad] OR Polvamaa[ad] OR Rapla[ad] OR Raplamaa[ad] OR Saare[ad] OR Saaremaa[ad] OR Tartu[ad] OR Tartumaa[ad] OR Valga[ad] OR Valgamaa[ad] OR Viljandimaa[ad] OR Viljandi[ad] OR Voru[ad] OR Vorumaa[ad] OR Tallinn[ad] OR Narva[ad] OR "Kohtla Jarve"[ad] OR Rakvere[ad] OR Maardu[ad] OR Sillamae[ad] OR Kuressaare[ad] OR (Denmark[ad] OR Danish*[ad] OR dane[ad] OR danes[ad] OR Danmark[ad] OR dansk*[ad] OR Hovedstaden[ad] OR Midtjylland[ad] OR Nordjylland[ad] OR Sjaelland[ad] OR Sealand[ad] OR "Zealand region"[ad] OR "region Zealand"[ad] OR Syddanmark[ad] OR Jutland[ad] OR Jylland[ad] OR Sonderjyllands[ad] OR Copenhagen[ad] OR Kobenhavn[ad] OR Arhus[ad] OR Aarhus[ad] OR Bornholm[ad] OR Frederiksberg[ad] OR Frederiksborg[ad] OR Ringkjobing[ad] OR Viborg[ad] OR Vejle[ad] OR Roskilde[ad] OR Storstrom[ad] OR Vestsjaellands[ad] OR "West Zealand"[ad] OR Funen[ad] OR Ribe[ad] OR "Kalaallit Nunaat"[ad] OR Gronland[ad] OR Foroyar[ad] OR Faeroerne[ad] OR "Faroe islands"[ad] OR Aalborg[ad] OR Alborg[ad] OR Odense[ad] OR Esbjerg[ad] OR Gentofte[ad] OR Gladsaxe[ad] OR Randers[ad] OR Kolding[ad] OR (Czech*[ad] OR Cesky[ad] OR Ceska[ad] OR Cech[ad] OR Cestina[ad] OR Prague[ad] OR Praha[ad] OR Prag[ad] OR Stredoces*[ad] OR Jihoces*[ad] OR Bohemia[ad] OR Bohemian[ad] OR Plzen*[ad] OR Pilsen[ad] OR Karlovars*[ad] OR "Karlovy Vary"[ad] OR Usteck*[ad] OR Usti[ad] OR Liberec*[ad] OR "Hradec Kralove"[ad] OR Kralovehradec*[ad] OR Pardubic*[ad] OR Olomouc*[ad] OR Olomoc[ad] OR Holomoc[ad] OR Moravskoslezs*[ad] OR Jihomorav*[ad] OR Moravia[ad] OR Moravian[ad] OR Morava[ad] OR Vysocina[ad] OR Zlin[ad] OR Zlinsk*[ad] OR "Ceske Budejovice"[ad] OR Budweis[ad] OR Brno[ad] OR Ostrava[ad] OR (Cyprus[ad] OR Cypriot*[ad] OR Kypros[ad] OR Kibris*[ad] OR kypriaki[ad] OR Kyprioi[ad] OR Nicosia[ad] OR Lefkosa[ad] OR Lefkosaia[ad] OR Famagusta[ad] OR Magusa[ad] OR Ammochostos[ad] OR Gazimagusa[ad] OR Kyrenia[ad] OR Girne[ad] OR Keryneia[ad] OR Larnaca[ad] OR Larnaka[ad] OR Iskele[ad] OR Limassol[ad] OR Lemesos[ad] OR Limasol[ad] OR Leymosun[ad] OR Paphos[ad] OR Pafos[ad] OR Baf[ad] OR Strovolos[ad] OR Lakatamia[ad] OR Lakadamyia[ad] OR "Kato Polemidia"[ad] OR "Kato Polemidhia"[ad] OR Aglandjia[ad] OR Eglence[ad] OR Aglantzia[ad] OR Aradhippou[ad] OR Aradippou[ad] OR Engomi[ad] OR (Croat*[ad] OR Hrvatsk*[ad] OR hrvat[ad] OR Bjelovar[ad] OR "Bjelovarsko bilogorska"[ad] OR "Brod Posavina"[ad] OR "Brodsko posavska"[ad] OR "Dubrovnik Neretva"[ad] OR "dubrovacko neretvanska"[ad] OR Zagreb[ad] OR Zagrebacka[ad] OR Istria[ad] OR Istarska[ad] OR Karlovačka[ad] OR Karlovac[ad] OR "Koprivnicko krizevacka"[ad] OR Koprivnica[ad] OR Krizevci[ad] OR "Krapina Zagorje"[ad] OR "Krapinsko zagorska"[ad] OR "Lika Senj"[ad] OR "Licko senjska"[ad] OR Medimurska[ad] OR Medimurje[ad] OR Osijek[ad] OR Baranja[ad] OR "Osjecko baranjska"[ad] OR "Pozega Slavonia"[ad] OR "Požesko slavonska"[ad] OR "Primorje Gorski Kotar"[ad] OR "Primorsko goranska"[ad] OR "Sibensko kninska"[ad] OR "Sibensko kninske"[ad] OR Sibenik[ad] OR Knin[ad] OR Sisak[ad] OR "Sisacko moslavacka"[ad] OR Moslavina[ad] OR "Splitsko dalmatinska"[ad] OR Split[ad] OR Dalmatia[ad] OR Varazdin[ad] OR Varazdinska[ad] OR Viroviticko[ad] OR podravska[ad] OR

Virovitica[ad] OR Podravina[ad] OR "Vukovarsko srijemska"[ad] OR Vukovar[ad] OR Srijem[ad] OR Zadar[ad] OR Zadarska[ad] OR Rijeka[ad] OR "Velika gorica"[ad] OR "Slavonski brod"[ad] OR Pula[ad] OR (Bulgaria*[ad] OR Balgariya[ad] OR Balgarija[ad] OR Blagoevgrad*[ad] OR "Pirin Macedonia"[ad] OR Burgas[ad] OR Dobrich[ad] OR Gabrovo[ad] OR Haskovo[ad] OR Kardzhali[ad] OR Kurdzhali[ad] OR Kyustendil[ad] OR Lovech[ad] OR Lovec[ad] OR Montana[ad] OR Pazardzhik[ad] OR Pernik[ad] OR Pleven*[ad] OR Plovdiv[ad] OR Razgrad[ad] OR Rouse[ad] OR Ruse[ad] OR Rusenka[ad] OR Shumen[ad] OR Silistra[ad] OR Sliven[ad] OR Smolyan[ad] OR Sofia[ad] OR Sofyiska[ad] OR Sofiiska[ad] OR "Stara Zagora"[ad] OR Targovishte[ad] OR Varna[ad] OR "Veliko Tarnovo"[ad] OR Vidin[ad] OR Vratsa[ad] OR Vratza[ad] OR Yambol[ad]) OR (Belgi*[ad] OR Belge*[ad] OR Belg[ad] OR Brussel*[ad] OR Bruxelles[ad] OR Bruxelloise[ad] OR Walloon*[ad] OR Wallon*[ad] OR Vlaams[ad] OR Flander*[ad] OR Flandern[ad] OR Flandre[ad] OR Flemish[ad] OR Flamand[ad] OR Flemisch[ad] OR Flamisch*[ad] OR Vlaanderen[ad] OR Flamande[ad] OR Waals[ad] OR Antwerp*[ad] OR Anvers[ad] OR Henegouwen[ad] OR Hennegau[ad] OR Hainaut[ad] OR Hainaut[ad] OR Liege[ad] OR Luik[ad] OR Luttich[ad] OR Limbourg[ad] OR Limburg[ad] OR Namur[ad] OR Namen[ad] OR Ostflandern[ad] OR Westflandern[ad] OR Ghent[ad] OR Gent[ad] OR Gand[ad] OR Charleroi[ad] OR Bruges[ad] OR Brugge*[ad] OR Schaerbeek[ad] OR Schaarbeek[ad] OR Anderlecht[ad] OR Leuven[ad] OR Louvain[ad]) OR (Austria*[ad] OR Osterreich*[ad] OR Oesterreich*[ad] OR Ostosterreich[ad] OR Ostoesterreich[ad] OR Sudosterreich[ad] OR Sudoesterreich[ad] OR Westosterreich[ad] OR Westoesterreich[ad] OR Burgenland[ad] OR Carinthia[ad] OR Karnten[ad] OR Kaernten[ad] OR Niederosterreich[ad] OR Niederosterreich[ad] OR Oberosterreich[ad] OR Oberoesterreich[ad] OR Salzburg[ad] OR Saizburg[ad] OR Styria[ad] OR Steiermark[ad] OR Tyrol[ad] OR Tirol[ad] OR Vorarlberg[ad] OR Vienna[ad] OR Wien[ad] OR Graz[ad] OR Linz[ad] OR Innsbruck[ad] OR Klagenfurt[ad] OR Villach[ad] OR Wels[ad] OR "St Polten"[ad] OR "St Poelten"[ad] OR "Sankt Polten"[ad] OR "Sankt Poelten"[ad] OR Dornbirn[ad]) OR Gibraltar[tw] OR Gibraltar[ad] OR Hebrid*[tw] OR Hebrid*[ad] OR Svalbard*[tw] OR Svalbard*[ad] OR "United States"[Mesh] OR "United States"[ad] OR USA[ad] OR US[ad] OR U.S.A.[ad] OR U.S.A.*[ad] OR U.S.A.*[tw] OR America*[ad] OR America*[tw] OR Alabama[ad] OR Alaska[ad] OR Arizona[ad] OR Arkansas[ad] OR California[ad] OR Colorado[ad] OR Connecticut[ad] OR Delaware[ad] OR Florida[ad] OR Georgia[ad] OR Hawaii[ad] OR Idaho[ad] OR Illinois[ad] OR Indiana[ad] OR Iowa[ad] OR Kansas[ad] OR Kentucky[ad] OR Louisiana[ad] OR Maine[ad] OR Maryland[ad] OR Massachusetts[ad] OR Michigan[ad] OR Minnesota[ad] OR Mississippi[ad] OR Missouri[ad] OR Montana[ad] OR Nebraska[ad] OR Nevada[ad] OR New Hampshire[ad] OR New Jersey[ad] OR New Mexico[ad] OR New York[ad] OR North Carolina[ad] OR North Carolina[ad] OR North Dakota[ad] OR Ohio[ad] OR Oklahoma[ad] OR Oregon[ad] OR Pennsylvania[ad] OR Rhode Island[ad] OR South Carolina[ad] OR South Dakota[ad] OR Tennessee[ad] OR Texas[ad] OR Utah[ad] OR Vermont[ad] OR Virginia[ad] OR Washington[ad] OR West Virginia[ad] OR Wisconsin[ad] OR Wyoming[ad] OR Alabama[tw] OR Alaska[tw] OR Arizona[tw] OR Arkansas[tw] OR California[tw] OR Colorado[tw] OR Connecticut[tw] OR Delaware[tw] OR Florida[tw] OR Georgia[tw] OR Hawaii[tw] OR Idaho[tw] OR Illinois[tw] OR Indiana[tw] OR Iowa[tw] OR Kansas[tw] OR Kentucky[tw] OR Louisiana[tw] OR Maine[tw] OR Maryland[tw] OR Massachusetts[tw] OR Michigan[tw] OR Minnesota[tw] OR Mississippi[tw] OR Missouri[tw] OR Montana[tw] OR Nebraska[tw] OR Nevada[tw] OR New Hampshire[tw] OR New Jersey[tw] OR New Mexico[tw] OR New York[tw] OR North Carolina[tw] OR North Dakota[tw] OR Ohio[tw] OR Oklahoma[tw] OR Oregon[tw] OR Pennsylvania[tw] OR Rhode Island[tw] OR South Carolina[tw] OR South Dakota[tw] OR Tennessee[tw] OR Texas[tw] OR Utah[tw] OR Vermont[tw] OR Virginia[tw] OR Washington[tw] OR West Virginia[tw] OR Wisconsin[tw] OR Wyoming[tw] OR "Canada"[Mesh] OR Canada[ad] OR Canada[tw] OR Canadian[tw] OR Canadian[ad] OR "Australia"[Mesh] OR Australia*[tw] OR Australia*[ad] OR "New Zealand"[Mesh] OR "New Zealand"[tw] OR "New Zealand"[ad] OR global[tw] OR world[tw] OR worldwide[tw]

Embase

'european union'/exp OR 'europe'/de OR europe*:ab,ti OR europa*:ab,ti OR eu:ab,ti OR eea:ab,ti OR eefta:ab,ti OR 'eu/eea':ab,ti OR 'eu/efta':ab,ti OR ecsc:ab,ti OR euratom:ab,ti OR eurozone:ab,ti OR eec:ab,ti OR ec:ab,ti OR (schengen:ab,ti AND (area:ab,ti OR countr*:ab,ti OR region*:ab,ti OR state:ab,ti OR states:ab,ti)) OR euroregion:ab,ti OR euroregion*:ab,ti OR 'eastern europe'/de OR 'western europe'/de OR 'balkan peninsula'/exp OR balkan:ab,ti OR balkans:ab,ti OR 'baltic states'/de OR baltic:ab,ti OR 'southern europe'/de OR (mediterranean:ab,ti AND (area:ab,ti OR countr*:ab,ti OR region*:ab,ti OR state:ab,ti OR states:ab,ti)) OR (alpine:ab,ti AND (area:ab,ti OR countr*:ab,ti OR region*:ab,ti OR state:ab,ti OR states:ab,ti)) OR 'scandinavia'/de OR scandinavia:ab,ti OR scandinavian:ab,ti OR (nordic NEXT/1 (countr* OR state*)):ab,ti OR danubian:ab,ti OR 'iberian peninsula':ab,ti OR 'peninsula iberica':ab,ti OR 'péninsule ibérique':ab,ti OR 'iberia penintsula':ab,ti OR iberia:ab,ti OR anatolia:ab,ti OR anatolu:ab,ti OR anatole:ab,ti OR anatolian:ab,ti OR 'yugoslavia (pre-1992)'/de OR 'yugoslavia'/exp OR yugoslavia:ab,ti OR 'czechoslovakia'/de OR czechoslovakia:ab,ti OR 'czecho slovakia':ab,ti OR ceskoslovensko:ab,ti OR 'cesko slovensko':ab,ti OR 'benelux'/exp OR benelux:ab,ti OR fennoscandia:ab,ti OR 'fenna scandinavia':ab,ti OR fennoskandi*:ab,ti OR (visegrád:ab,ti AND (group:ab,ti OR four:ab,ti OR triangle:ab,ti)) OR 'visegrádska čtyřka':ab,ti OR 'visegrádska skupina':ab,ti OR 'visegrádi egyttmúködés':ab,ti OR 'visegrádi négyek':ab,ti OR 'grupa wyszehradzka':ab,ti OR 'vyšehradská skupina':ab,ti OR 'vyšehradská štvorka':ab,ti OR 'EU citizen'/de OR 'Central European'/de OR 'Eastern European'/de OR 'Northern European'/de OR 'Southern European'/de OR 'Western European'/de OR 'austrian'/exp OR 'austria'/exp OR austria*:ab,ti OR osterreich*:ab,ti OR oesterreich*:ab,ti OR ostosterreich:ab,ti OR ostoesterreich:ab,ti OR sudosterreich:ab,ti OR sudoesterreich:ab,ti OR westosterreich:ab,ti OR westoesterreich:ab,ti OR burgenland:ab,ti OR carinthia:ab,ti OR karnten:ab,ti OR kaernten:ab,ti OR niederosterreich:ab,ti OR niederoesterreich:ab,ti OR oberosterreich:ab,ti OR oberoesterreich:ab,ti OR salzburg:ab,ti OR saizburg:ab,ti OR styria:ab,ti OR steiermark:ab,ti OR tyrol:ab,ti OR tirol:ab,ti OR vorarlberg:ab,ti OR vienna:ab,ti OR wien:ab,ti OR graz:ab,ti OR linz:ab,ti OR innsbruck:ab,ti OR klagenfurt:ab,ti OR villach:ab,ti OR wels:ab,ti OR 'st polten':ab,ti OR 'st poelten':ab,ti OR 'sankt polten':ab,ti OR 'sankt poelten':ab,ti OR dornbirn:ab,ti OR 'Belgium'/exp OR 'Belgian'/exp OR Belgi*:ti,ab OR Belge*:ti,ab OR Belg:ti,ab OR Brussel*:ti,ab OR Bruxelles:ti,ab OR Bruxelloise:ti,ab OR Walloon*:ti,ab OR Wallon*:ti,ab OR Vlaams:ti,ab OR Flander*:ti,ab OR Flandern:ti,ab OR Flandre:ti,ab OR Flemish:ti,ab OR Flamand:ti,ab OR Flemisch:ti,ab OR Flämisch*:ti,ab OR Vlaanderen:ti,ab OR Flamande:ti,ab OR Waals:ti,ab OR Antwerp*:ti,ab OR Anvers:ti,ab OR Henegouwen:ti,ab OR Hennegau:ti,ab OR Hainaut:ti,ab OR Hainaut:ti,ab OR Liege:ti,ab OR Luik:ti,ab OR Luttich:ti,ab OR Limbourg:ti,ab OR Limburg:ti,ab OR Namur:ti,ab OR Namen:ti,ab OR Ostflandern:ti,ab OR Westflandern:ti,ab OR Ghent:ti,ab OR Gent:ti,ab OR Gand:ti,ab OR Charleroi:ti,ab OR Bruges:ti,ab OR Brugge*:ti,ab OR Schaerbeek:ti,ab OR Schaarbeek:ti,ab OR Anderlecht:ti,ab OR Leuven:ti,ab OR Louvain:ti,ab OR 'bulgaria'/exp OR 'bulgarian (citizen)'/exp OR 'Bulgarian (people)'/exp OR bulgaria*:ti,ab OR balgariya:ab,ti OR balgarija:ab,ti OR blagoevgrad*:ab,ti OR 'pirin macedonia':ab,ti OR burgas:ab,ti OR dobrich:ab,ti OR gabrovo:ab,ti OR haskovo:ab,ti OR

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Connacht:ti,ab OR Connachta:ti,ab OR Drogheda:ti,ab OR 'Droichead Atha':ti,ab OR Dundalk:ti,ab OR 'Dún Dealgan':ti,ab OR Swords:ti,ab OR Sord:ti,ab OR Bray:ti,ab OR Bre:ti,ab OR Navan:ti,ab OR 'An Uaimh':ti,ab OR 'Italy'/exp OR 'Italian (citizen)'/exp OR 'Italic people'/exp OR Italy:ti,ab OR Italia*:ti,ab OR Abruzzo:ti,ab OR Abruza:ti,ab OR Basilicata:ti,ab OR Lucania:ti,ab OR Calabria:ti,ab OR Campania:ti,ab OR 'Emilia Romagna':ti,ab OR 'friuli venezia giulia':ti,ab OR Lazio:ti,ab OR Latium:ti,ab OR Liguria*:ti,ab OR Lombardy*:ti,ab OR Lombardia:ti,ab OR Marche:ti,ab OR Marches:ti,ab OR Molisano:ti,ab OR Molise:ti,ab OR Piedmont*:ti,ab OR Piemonte:ti,ab OR Bolzano:ti,ab OR Bozen:ti,ab OR Trentino:ti,ab OR Trento:ti,ab OR Puglia:ti,ab OR Apulia:ti,ab OR Sardinia:ti,ab OR Sardegna:ti,ab OR Sicily:ti,ab OR Sicilia:ti,ab OR Toscana:ti,ab OR Tuscany:ti,ab OR Umbria:ti,ab OR 'Valle d Aosta':ti,ab OR 'Vallee d Aoste':ti,ab OR 'Aosta Valley':ti,ab OR Veneto:ti,ab OR Venetia:ti,ab OR Triveneto:ti,ab OR Rome:ti,ab OR Roma:ti,ab OR Milan:ti,ab OR Milano:ti,ab OR Naples:ti,ab OR Napoli:ti,ab OR Turin:ti,ab OR Torino:ti,ab OR Palermo:ti,ab OR Genoa:ti,ab OR Genova:ti,ab OR Bologna:ti,ab OR Florence:ti,ab OR Firenze:ti,ab OR Bari:ti,ab OR Catania:ti,ab OR 'Latvia'/exp OR 'Latvian (citizen)'/exp OR 'Lett (people)'/exp OR Latvi*:ti,ab OR Riga:ti,ab OR Courland:ti,ab OR Kurzeme:ti,ab OR Kurland:ti,ab OR Latgale:ti,ab OR Lettgallia:ti,ab OR Latgola:ti,ab OR Latgalia:ti,ab OR Vidzeme:ti,ab OR Vidumo:ti,ab OR Semigallia:ti,ab OR Semigalia:ti,ab OR Zemgale:ti,ab OR Pieriga:ti,ab OR Daugavpils:ti,ab OR Dinaburg:ti,ab OR Jekabpils:ti,ab OR Jakobstadt:ti,ab OR Jelgava:ti,ab OR Jurmala:ti,ab OR Liepaja:ti,ab OR Libau:ti,ab OR Rezekne:ti,ab OR Rezne:ti,ab OR Rositten:ti,ab OR Valmiera:ti,ab OR Wolmar:ti,ab OR Ventspils:ti,ab OR Windau:ti,ab OR Ogre:ti,ab OR 'Lithuania'/exp OR 'Lithuanian (citizen)'/exp OR Lithuania*:ti,ab OR 'Lietuvos Respublika':ti,ab OR Lietuva:ti,ab OR lietuviu:ti,ab OR Alytus:ti,ab OR Alytaus:ti,ab OR Kaunas:ti,ab OR Kauno:ti,ab OR Klaipeda:ti,ab OR Klaipedos:ti,ab OR Marijampoles:ti,ab OR Marijampole:ti,ab OR Panevezys:ti,ab OR Panevezio:ti,ab OR Siauliai:ti,ab OR Siauliu:ti,ab OR Taurages:ti,ab OR Taurage:ti,ab OR Telsiu:ti,ab OR Telsiai:ti,ab OR Utenos:ti,ab OR Utena:ti,ab OR Vilnia:ti,ab OR Vilniaus:ti,ab OR Mazeikiai:ti,ab OR Mazeikiu:ti,ab OR Jonavos:ti,ab OR 'Luxembourg'/exp OR Luxembourg*:ti,ab OR Luxemburg:ti,ab OR Letzebuerg:ti,ab OR Diekirch:ti,ab OR Grevenmacher:ti,ab OR 'Esch sur Alzette':ti,ab OR 'Esch Uelzecht':ti,ab OR 'Esch an der Alzette':ti,ab OR 'Esch an der Alzig':ti,ab OR Dudelange:ti,ab OR Diddeleng:ti,ab OR Düdelingen:ti,ab OR Duëdelingen:ti,ab OR Schifflange:ti,ab OR Scheffleng:ti,ab OR Schifflingen:ti,ab OR Bettembourg:ti,ab OR Beeteburg:ti,ab OR Bettemburg:ti,ab OR Petange:ti,ab OR

Peiteng:ti,ab OR Petingen:ti,ab OR Ettelbruck:ti,ab OR Ettelbreck:ti,ab OR Ettelbrueck:ti,ab OR Diekirch:ti,ab OR Dikrech:ti,ab OR Strassen:ti,ab OR Stroossen:ti,ab OR Bertrange:ti,ab OR Bartreng:ti,ab OR Bartringen:ti,ab OR 'Malta'/exp OR 'Maltese (citizen)'/exp OR Malta:ti,ab OR Maltese*:ti,ab OR Maltin:ti,ab OR Gozo:ti,ab OR Ghawdex:ti,ab OR Valetta:ti,ab OR 'Ili Belt':ti,ab OR Birkirkara:ti,ab OR 'B Kara':ti,ab OR Bircircara:ti,ab OR Mosta:ti,ab OR Qormi:ti,ab OR 'St Paul s Bay':ti,ab OR 'Pawl il Bahar':ti,ab OR Zabbar:ti,ab OR Sliema:ti,ab OR Naxxar:ti,ab OR Gwann:ti,ab OR 'St John':ti,ab OR Zebbug:ti,ab OR 'Citta rohan':ti,ab OR Fgura:ti,ab OR 'Netherlands'/exp OR 'Dutchman'/exp OR Netherlands:ti,ab OR Nederland*:ti,ab OR Dutch*:ti,ab OR Drenthe:ti,ab OR Flevoland:ti,ab OR Friesland:ti,ab OR Fryslan:ti,ab OR Frisia:ti,ab OR Gelderland:ti,ab OR Guelders:ti,ab OR Groningen:ti,ab OR Limburg:ti,ab OR Brabant:ti,ab OR Holland:ti,ab OR Overijssel:ti,ab OR Overissel:ti,ab OR Utrecht:ti,ab OR Zeeland:ti,ab OR Amsterdam:ti,ab OR Rotterdam:ti,ab OR Hague:ti,ab OR 's-Gravenhage':ti,ab OR 'Den Haag':ti,ab OR Eindhoven:ti,ab OR Tilburg:ti,ab OR Almere:ti,ab OR Breda:ti,ab OR Nijmegen:ti,ab OR Nimeguen:ti,ab OR 'Poland'/exp OR 'Polish citizen'/exp OR 'Pole (people)'/exp OR Poland:ti,ab OR Polska:ti,ab OR Polish:ti,ab OR Pole:ti,ab OR Poles:ti,ab OR Polski:ti,ab OR Polak:ti,ab OR Polka:ti,ab OR Polacy:ti,ab OR Dolnoslaskie:ti,ab OR Silesia*:ti,ab OR Slask:ti,ab OR Pomorskie:ti,ab OR Pomerania*:ti,ab OR Kujawsko:ti,ab OR Kuyavian:ti,ab OR Lodzkie:ti,ab OR Lodz:ti,ab OR Lubelskie:ti,ab OR Lublin:ti,ab OR Lubuskie:ti,ab OR Lubusz:ti,ab OR Lubus:ti,ab OR Malopolskie:ti,ab OR Mazowieckie:ti,ab OR Mazowske:ti,ab OR Masovia:ti,ab OR Masovian:ti,ab OR Opolskie:ti,ab OR Opole:ti,ab OR Podkarpackie:ti,ab OR Subcarpathian*:ti,ab OR Podlaskie:ti,ab OR Podlachia:ti,ab OR Podlasie:ti,ab OR Slaskie:ti,ab OR Swietokrzyskie:ti,ab OR 'Warmia Mazuria':ti,ab OR 'Warmian Mazurian':ti,ab OR 'Warmia Masuria':ti,ab OR 'Warmian Masurian':ti,ab OR 'Warmia Mazury':ti,ab OR 'Warminsko Mazurskie':ti,ab OR 'Warmian Masurian':ti,ab OR Wielkopolskie:ti,ab OR Zachodniopomorskie:ti,ab OR Warsaw:ti,ab OR Warszawa:ti,ab OR Krakow:ti,ab OR Cracow:ti,ab OR Wroclaw:ti,ab OR Poznan:ti,ab OR Gdansk:ti,ab OR Szczecin:ti,ab OR Bydgoszcz:ti,ab OR Katowice:ti,ab OR 'Portugal'/exp OR 'Portuguese (citizen)'/exp OR Portugal:ti,ab OR Portugues*:ti,ab OR Azores:ti,ab OR Acores:ti,ab OR Madeira:ti,ab OR Alentejo:ti,ab OR Algarve:ti,ab OR Lisboa:ti,ab OR OR Lisbon:ti,ab OR 'Alto Tras-os-Montes':ti,ab OR (Ave NEAR/3 (community OR intermunicipal OR comunidade)):ti,ab OR Mondego:ti,ab OR Vouga:ti,ab OR Beira:ti,ab OR Cavado:ti,ab OR Lafoes:ti,ab OR Douro:ti,ab OR Porto:ti,ab OR Oporto:ti,ab OR Tejo:ti,ab OR Minho:ti,ab OR Setubal:ti,ab OR Pinhal:ti,ab OR 'Serra da Estrela':ti,ab OR Tamega:ti,ab OR Leira:ti,ab OR Santarem:ti,ab OR Beja:ti,ab OR Faro:ti,ab OR Evora:ti,ab OR Portalegre:ti,ab OR 'Castelo Branco':ti,ab OR Guarda:ti,ab OR Coimbra:ti,ab OR Aveiro:ti,ab OR Viseu:ti,ab OR Braganca:ti,ab OR Braganza:ti,ab OR Braga:ti,ab OR 'Vila real':ti,ab OR 'Viana do Castelo':ti,ab OR Gaia:ti,ab OR Amadora:ti,ab OR Funchal:ti,ab OR Coimbra:ti,ab OR Almada:ti,ab OR (Avalva:ti,ab AND Cacem:ti,ab) OR 'Romania'/exp OR 'Romanian (citizen)'/exp OR Romania*:ti,ab OR Rumania*:ti,ab OR Roumania*:ti,ab OR Romani:ti,ab OR Rumani:ti,ab OR Alba:ti,ab OR Arad:ti,ab OR Arges:ti,ab OR Bacau:ti,ab OR Bihor:ti,ab OR 'Bistrita Nasaud':ti,ab OR Botosani:ti,ab OR Braila:ti,ab OR Brasov:ti,ab OR Kronstadt:ti,ab OR Brasso:ti,ab OR Brassovia:ti,ab OR Coron:ti,ab OR Bucharest:ti,ab OR Bucuresti:ti,ab OR Buzau:ti,ab OR Buzau:ti,ab OR Cluj:ti,ab OR Cluj:ti,ab OR Klausenburg:ti,ab OR Kolozsvar:ti,ab OR Constanta:ti,ab OR Tomis:ti,ab OR Konstantia:ti,ab OR Kostence:ti,ab OR Covasna:ti,ab OR Dambovita:ti,ab OR Dolj:ti,ab OR Galati:ti,ab OR Galatz:ti,ab OR Galac:ti,ab OR Kalas:ti,ab OR Giurgiu:ti,ab OR Gorj:ti,ab OR Harghita:ti,ab OR Hunedoara:ti,ab OR Ialomita:ti,ab OR Iasi:ti,ab OR Jassy:ti,ab OR Lassy:ti,ab OR Ifov:ti,ab OR Maramures:ti,ab OR Mehedinti:ti,ab OR Mures:ti,ab OR Neamt:ti,ab OR Olt:ti,ab AND (river:ti,ab OR county:ti,ab OR region:ti,ab OR judetul:ti,ab OR Raul:ti,ab)) OR Prahova:ti,ab OR Salaj:ti,ab OR 'Satu Mare':ti,ab OR Sibiu:ti,ab OR Suceava:ti,ab OR Teleorman:ti,ab OR Timis:ti,ab OR Tulcea:ti,ab OR Valcea:ti,ab OR Vilcea:ti,ab OR Vaslui:ti,ab OR Vrancea:ti,ab OR Timisoara:ti,ab OR Temeswar:ti,ab OR Temeschburg:ti,ab OR Temeschwar:ti,ab OR Temesvar:ti,ab OR Temisvar:ti,ab OR Timisvar:ti,ab OR Temesva:ti,ab OR Craiova:ti,ab OR Ploiesti:ti,ab OR Ploesti:ti,ab OR Oradea:ti,ab OR Varad:ti,ab OR Varat:ti,ab OR 'Slovakia'/exp OR 'Slovak (citizen)'/exp OR 'Slovak (people)'/exp OR Slovakia:ti,ab OR Slovensk*:ti,ab OR Slovak*:ti,ab OR Slovaci:ti,ab OR Slovenki:ti,ab OR Bratislav*:ti,ab OR Bratislav*:ti,ab OR Presporok:ti,ab OR Pressburg:ti,ab OR Preßburg:ti,ab OR Posonium:ti,ab OR Banskobystrica*:ti,ab OR 'Banska Bystrica':ti,ab OR Neusohl:ti,ab OR Besztercebánya:ti,ab OR Kosic*:ti,ab OR Kaschau:ti,ab OR Kassa:ti,ab OR Nitrian*:ti,ab OR Nitra:ti,ab OR Neutra:ti,ab OR Nyitra:ti,ab OR Nyitria:ti,ab OR Trnav*:ti,ab OR Tyrnau:ti,ab OR Nagyszombat:ti,ab OR Tyrnavia:ti,ab OR Presov*:ti,ab OR Trencian*:ti,ab OR Trencin:ti,ab OR Trencschin:ti,ab OR Trencsén:ti,ab OR Zilina:ti,ab OR Sillein:ti,ab OR Zsolna:ti,ab OR Zylina:ti,ab OR (Martin:ti,ab AND (city:ti,ab OR Svaty:ti,ab)) OR Turócszentmárton:ti,ab OR Poprad:ti,ab OR Deutschedorf:ti,ab OR Zvolen:ti,ab OR Aragon:ti,ab OR 'Slovenia'/exp OR 'Slovenian (citizen)'/exp OR 'Slovene (people)'/exp OR Slovenia*:ti,ab OR Slovenija:ti,ab OR slovensk*:ti,ab OR Slovenci:ti,ab OR Slovene*:ti,ab OR Gorenjska:ti,ab OR Carniola:ti,ab OR Goriska:ti,ab OR Gorizia:ti,ab OR Jugovzhodna:ti,ab OR Koroska:ti,ab OR Carinthia:ti,ab OR 'Notranjsko kraska':ti,ab OR 'Obalno kraska':ti,ab OR 'Coastal karst':ti,ab OR Osrednjeslovenska:ti,ab OR Podravska:ti,ab OR Drava:ti,ab OR Pomurska:ti,ab OR Mura:ti,ab OR Savinjska:ti,ab OR Savinja:ti,ab OR Spodnjeposavska:ti,ab OR Zasavska:ti,ab OR 'Central Sava':ti,ab OR Posavska:ti,ab OR 'Lower Sava':ti,ab OR Ljubljana:ti,ab OR Laibach:ti,ab OR Lubiana:ti,ab OR Maribor:ti,ab OR 'Marburg an der Drau':ti,ab OR Kranj:ti,ab OR Carnium:ti,ab OR Creina:ti,ab OR Chreina:ti,ab OR Krainbur:ti,ab OR Koper:ti,ab OR Capodistria:ti,ab OR Kopar:ti,ab OR Celje:ti,ab OR 'Novo mesto':ti,ab OR Neustadt:ti,ab OR Domzale:ti,ab OR Velenje:ti,ab OR Wollan:ti,ab OR Woellan:ti,ab OR 'Nova Gorica':ti,ab OR Kamnik:ti,ab OR 'Spain'/exp OR 'Spaniard'/exp OR 'Basque (people)'/exp OR Spain:ti,ab OR Espana:ti,ab OR Spanish:ti,ab OR Espanol*:ti,ab OR Spaniard*:ti,ab OR Andalucia:ti,ab OR Andalusia:ti,ab OR Aragon:ti,ab OR Arago:ti,ab OR Cantabria:ti,ab OR Canarias:ti,ab OR 'Canary Islands':ti,ab OR (Canaries:ti,ab AND island*:ti,ab) OR 'Castile and leon':ti,ab OR 'Castilla y Leon':ti,ab OR 'Castile La Mancha':ti,ab OR 'Castilla La Mancha':ti,ab OR Cataluna:ti,ab OR Catalonia:ti,ab OR Ceuta:ti,ab OR Madrid:ti,ab OR Melilla:ti,ab OR Navarra:ti,ab OR Navarre:ti,ab OR Valencia*:ti,ab OR Extremadura:ti,ab OR Galicia:ti,ab OR Balears:ti,ab OR 'Balearic Islands':ti,ab OR 'Balear Islands':ti,ab OR Baleares:ti,ab OR 'La Rioja':ti,ab OR 'Pais Vasco':ti,ab OR 'Basque Country':ti,ab OR 'Baske region':ti,ab OR Euskadi:ti,ab OR Asturias:ti,ab OR Murcia:ti,ab OR Coruna:ti,ab OR Alava:ti,ab OR Araba:ti,ab OR Albacete:ti,ab OR Alicante:ti,ab OR Alacant:ti,ab OR Almeria:ti,ab OR Avila:ti,ab OR Badajoz:ti,ab OR Badajos:ti,ab OR Barcelona:ti,ab OR Burgos:ti,ab OR Caceres:ti,ab OR Cadiz:ti,ab OR Castellon:ti,ab OR Castello:ti,ab OR 'Ciudad Real':ti,ab OR Cordoba:ti,ab OR Cuenca:ti,ab OR Eivissa:ti,ab OR Ibiza:ti,ab OR Formentera:ti,ab OR 'El Hierro':ti,ab OR Fuerteventura:ti,ab OR Galiza:ti,ab OR Girona:ti,ab OR Gerona:ti,ab OR 'Gran Canaria':ti,ab OR Granada:ti,ab OR Guadalajara:ti,ab OR Guipuzcoa:ti,ab OR Gipuzkoa:ti,ab OR Huelva:ti,ab OR Huesca:ti,ab OR Jaen:ti,ab OR 'La Gomera':ti,ab OR 'La Palma':ti,ab OR Lanzarote:ti,ab OR Leon:ti,ab OR Lleida:ti,ab OR Lerida:ti,ab OR Lugo:ti,ab OR Malaga:ti,ab OR Mallorca:ti,ab OR Majorca:ti,ab OR Menorca:ti,ab OR Minorca:ti,ab OR Murcia:ti,ab OR Ourense:ti,ab OR Orense:ti,ab OR Palencia:ti,ab OR Pontevedra:ti,ab OR Salamanca:ti,ab OR Segovia:ti,ab OR Sevilla:ti,ab OR Seville:ti,ab OR Soria:ti,ab OR Tarragona:ti,ab OR Tenerife:ti,ab OR Teruel:ti,ab OR Toledo:ti,ab OR Valladolid:ti,ab OR Vizcaya:ti,ab OR Biscay:ti,ab OR Zamora:ti,ab OR Zaragoza:ti,ab OR Saragossa:ti,ab OR 'Las Palmas':ti,ab OR Bilbao:ti,ab OR Bilbo:ti,ab OR

'Sweden'/exp OR 'Swedish citizen'/exp OR 'Swede (people)'/exp OR Sweden:ti,ab OR Sverige:ti,ab OR Swedish:ti,ab OR Svenska:ti,ab OR svenskar:ti,ab OR Swede:ti,ab OR Swedes:ti,ab OR Norrland:ti,ab OR Mellansverige:ti,ab OR Smaland:ti,ab OR Stockholm*:ti,ab OR Sydsverige:ti,ab OR Vastsverige:ti,ab OR Blekinge:ti,ab OR Dalarna:ti,ab OR Gavleborg*:ti,ab OR Gotland*:ti,ab OR Halland*:ti,ab OR Jamtland*:ti,ab OR Jonkoping*:ti,ab OR Kalmar:ti,ab OR Kronoberg*:ti,ab OR Norrbotten*:ti,ab OR Orebro:ti,ab OR Ostergotland*:ti,ab OR Skane:ti,ab OR Sodermanlands:ti,ab OR Uppsala:ti,ab OR Varmland*:ti,ab OR Vasterbotten*:ti,ab OR Vasternorrland*:ti,ab OR Vastmanland*:ti,ab OR vastergotland*:ti,ab OR Gotaland*:ti,ab OR Gothenburg:ti,ab OR Goteborg:ti,ab OR Malmo:ti,ab OR Vasteras:ti,ab OR Linkoping:ti,ab OR Helsingborg:ti,ab OR Halsingborg:ti,ab OR Norrkoping:ti,ab OR 'United Kingdom'/exp OR 'British citizen'/exp OR 'GB':ti,ab OR 'United kingdom':ti,ab OR 'UK':ti,ab OR Britain:ti,ab OR British:ti,ab OR England:ti,ab OR English:ti,ab OR Scotland:ti,ab OR Scottish:ti,ab OR Scots:ti,ab OR Wales:ti,ab OR Cymru:ti,ab OR Welsh:ti,ab OR 'North Ireland':ti,ab OR 'Northern Ireland':ti,ab OR Irish:ti,ab OR Avon:ti,ab OR Bedfordshire:ti,ab OR Berkshire:ti,ab OR Bristol:ti,ab OR Buckinghamshire:ti,ab OR Cambridgeshire:ti,ab OR 'Isle of Ely':ti,ab OR Cheshire:ti,ab OR Cleveland:ti,ab OR Cornwall:ti,ab OR Cumberland:ti,ab OR Cumbria:ti,ab OR Derbyshire:ti,ab OR Devon:ti,ab OR Dorset:ti,ab OR Durham:ti,ab OR Essex:ti,ab OR Gloucestershire:ti,ab OR Hampshire:ti,ab OR Southampton:ti,ab OR (Hereford:ti,ab AND Worcester:ti,ab) OR Hertfordshire:ti,ab OR Herefordshire:ti,ab OR Humberside:ti,ab OR Huntingdon:ti,ab OR Huntingdonshire:ti,ab OR 'Isle of Wight':ti,ab OR Kent:ti,ab OR Lancashire:ti,ab OR Leicestershire:ti,ab OR Lincolnshire:ti,ab OR London:ti,ab OR Manchester:ti,ab OR Merseyside:ti,ab OR Middlesex:ti,ab OR Norfolk:ti,ab OR Northamptonshire:ti,ab OR Northumberland:ti,ab OR Nottinghamshire:ti,ab OR Oxfordshire:ti,ab OR Peterborough:ti,ab OR Rutland:ti,ab OR Shropshire:ti,ab OR Salop:ti,ab OR Somerset:ti,ab OR Yorkshire:ti,ab OR Staffordshire:ti,ab OR Suffolk:ti,ab OR Surrey:ti,ab OR Sussex:ti,ab OR (Tyne:ti,ab AND Wear:ti,ab) OR Warwickshire:ti,ab OR Midlands:ti,ab OR Westmorland:ti,ab OR Wiltshire:ti,ab OR Worcestershire:ti,ab OR 'Isle of Man':ti,ab OR Jersey:ti,ab OR Guernsey:ti,ab OR 'Channel Islands':ti,ab OR Aberdeen:ti,ab OR Aberdeenshire:ti,ab OR Angus:ti,ab OR Forfarshire:ti,ab OR Argyll:ti,ab OR Ayrshire:ti,ab OR Banffshire:ti,ab OR Berwickshire:ti,ab OR Bute:ti,ab OR Caithness:ti,ab OR Clackmannanshire:ti,ab OR Cromartyshire:ti,ab OR Dumfriesshire:ti,ab OR Dunbartonshire:ti,ab OR Dumbarton:ti,ab OR Dundee:ti,ab OR Lothian:ti,ab OR Haddingtonshire:ti,ab OR Edinburgh:ti,ab OR Fife:ti,ab OR Glasgow:ti,ab OR Inverness-shire:ti,ab OR Kincardineshire:ti,ab OR Kinross-shire:ti,ab OR Kirkcudbrightshire:ti,ab OR Lanarkshire:ti,ab OR Midlothian:ti,ab OR Moray:ti,ab OR Elginshire:ti,ab OR Nairnshire:ti,ab OR Orkney:ti,ab OR Peebleshire:ti,ab OR Perthshire:ti,ab OR Renfrewshire:ti,ab OR (Ross:ti,ab AND Cromarty:ti,ab) OR Ross-shire:ti,ab OR Roxburghshire:ti,ab OR Selkirkshire:ti,ab OR Shetland:ti,ab OR Zetland:ti,ab OR Stirlingshire:ti,ab OR Sutherland:ti,ab OR Linlithgowshire:ti,ab OR Wigtownshire:ti,ab OR Anglesey:ti,ab OR Brecknockshire:ti,ab OR Caernarfonshire:ti,ab OR Carmarthenshire:ti,ab OR Cardiganshire:ti,ab OR Ceredigion:ti,ab OR Cwlyd:ti,ab OR Denbighshire:ti,ab OR Dyfed:ti,ab OR Flintshire:ti,ab OR Glamorgan:ti,ab OR Gwent:ti,ab OR Gwynedd:ti,ab OR Merionethshire:ti,ab OR Montgomeryshire:ti,ab OR Monmouthshire:ti,ab OR Pembrokeshire:ti,ab OR Powys:ti,ab OR Radnorshire:ti,ab OR Antrim:ti,ab OR Aontroim:ti,ab OR 'Contae Aontroma':ti,ab OR Anthrim:ti,ab OR Antrim:ti,ab OR Entrim:ti,ab OR Armagh:ti,ab OR 'Ard Mhacha':ti,ab OR Airmagh:ti,ab OR Belfast:ti,ab OR (Down:ti,ab AND (district:ti,ab OR council:ti,ab OR County:ti,ab)) OR 'An Dún':ti,ab OR 'an Duin':ti,ab OR Doon:ti,ab OR Doun:ti,ab OR Fermanagh:ti,ab OR 'Fear Manach':ti,ab OR 'Fhear Manach':ti,ab OR Fermanay:ti,ab OR Londonderry:ti,ab OR Doire:ti,ab OR Dhoire:ti,ab OR Lunnonderrrie:ti,ab OR Derry:ti,ab OR Birmingham:ti,ab OR Leeds:ti,ab OR Sheffield:ti,ab OR Bradford:ti,ab OR Liverpool:ti,ab OR 'Albania'/exp OR 'Albanian (citizen)'/exp OR 'Albanian (people)'/exp OR Albania*:ti,ab OR Shqiperi*:ti,ab OR Schqipt*:ti,ab OR Berat:ti,ab OR Beratit:ti,ab OR Diber:ti,ab OR Dibres:ti,ab OR Durres:ti,ab OR Durresit:ti,ab OR Elbasan:ti,ab OR Elbasanit:ti,ab OR Fier:ti,ab OR Fierit:ti,ab OR Gjirokaster:ti,ab OR Gjirokastres:ti,ab OR Korce:ti,ab OR Korces:ti,ab OR Kukes:ti,ab OR Kukesit:ti,ab OR Lezhes:ti,ab OR Lezhe:ti,ab OR Shkoder:ti,ab OR Shkoder:ti,ab OR Tirana:ti,ab OR Tirane*:ti,ab OR Vlore:ti,ab OR Vlores:ti,ab OR Kamez:ti,ab OR Beraz:ti,ab OR Beraz:ti,ab OR Lushnje:ti,ab OR Macedonia (republic)/exp OR 'Macedonian (citizen)'/exp OR 'Macedonian (people)'/exp OR Makedon*:ti,ab OR Macedon*:ti,ab OR FYrom:ti,ab OR Istocen:ti,ab OR Severoistocen:ti,ab OR Jugoistocen:ti,ab OR Jugozapaden:ti,ab OR Pelagonski:ti,ab OR Pelagonia:ti,ab OR Poloski:ti,ab OR Polog:ti,ab OR Skopski:ti,ab OR Skopje:ti,ab OR Ckonje:ti,ab OR Vardar*:ti,ab OR Bitola:ti,ab OR Kumanovo:ti,ab OR Prilep:ti,ab OR Tetovo:ti,ab OR Tetova:ti,ab OR Tetove:ti,ab OR Veles:ti,ab OR Stip:ti,ab OR Shtip:ti,ab OR Ohrid:ti,ab OR Gostivar:ti,ab OR Gostivari:ti,ab OR Strumica:ti,ab OR 'Icelander'/exp OR 'Icelandic'/exp OR Icelander:ti,ab OR Icelandic*:ti,ab OR islenska*:ti,ab OR Icelander*:ti,ab OR Islendinga*:ti,ab OR Islendigar:ti,ab OR Inslenska:ti,ab OR Reykjavik:ti,ab OR Reykjavikurborg:ti,ab OR Hofudborgarsvaedi:ti,ab OR Sudurnes:ti,ab OR Vesturland:ti,ab OR Vestfiridir:ti,ab OR Westfjords:ti,ab OR Nordurland:ti,ab OR Austurland:ti,ab OR Sudurland:ti,ab OR Kopavogur:ti,ab OR Hafnarfjordur:ti,ab OR Akureyri:ti,ab OR Gardabaer:ti,ab OR Mosfellsbaer:ti,ab OR Keflavik:ti,ab OR Akranes:ti,ab OR Selfoss:ti,ab OR Seltjarnarnes:ti,ab OR 'Montenegro (republic)'/exp OR Montenegr*:ti,ab OR 'Crna Gora':ti,ab OR Crnogorci:ti,ab OR Andrijevica:ti,ab OR (Bar:ti,ab AND (Opstina:ti,ab OR municipality:ti,ab OR city:ti,ab OR town:ti,ab)) OR Berane:ti,ab OR 'Bijelo polje':ti,ab OR Budva:ti,ab OR Cetinje:ti,ab OR Danilovgrad:ti,ab OR Gusinje:ti,ab OR 'herceg Novi':ti,ab OR Kolasin:ti,ab OR Kotor:ti,ab OR Mojkovac:ti,ab OR Niksic:ti,ab OR Petnija:ti,ab OR Plav:ti,ab OR Pluzine:ti,ab OR Pljevlja:ti,ab OR Podgorica:ti,ab OR Rozaje:ti,ab OR Savnik:ti,ab OR Tivat:ti,ab OR Ulcinj:ti,ab OR Zabljak:ti,ab OR 'Serbia'/exp OR 'Serbian (citizen)'/exp OR 'Serb (people)'/exp OR Serbia*:ti,ab OR Srbija:ti,ab OR Serb:ti,ab OR Serbs:ti,ab OR Srbi:ti,ab OR Vojvodina:ti,ab OR Belgrade:ti,ab OR Beograd:ti,ab OR Sumadija:ti,ab OR Kolubara:ti,ab OR Kolubarski:ti,ab OR Macva:ti,ab OR Macvanski:ti,ab OR Moravica:ti,ab OR Moravicki:ti,ab OR Pomoravlje:ti,ab OR Pomoravski:ti,ab OR Rasinski:ti,ab OR Rasina:ti,ab OR Raska:ti,ab OR Raski:ti,ab OR Sumadijski:ti,ab OR Zlatibor:ti,ab OR Zlatiborski:ti,ab OR Bor:ti,ab OR Borski:ti,ab OR Branicevo:ti,ab OR Branicevski:ti,ab OR Jablanica:ti,ab OR Jablanicki:ti,ab OR Nisava:ti,ab OR Nisavski:ti,ab OR Pcinja:ti,ab OR Pcinjski:ti,ab OR Pirot:ti,ab OR Pirotski:ti,ab OR Podunavlje:ti,ab OR Podunavski:ti,ab OR OR Toplica:ti,ab OR OR Toplicki:ti,ab OR OR Zajecar:ti,ab OR OR Zajecarski:ti,ab OR OR Banat:ti,ab OR OR Srendjebanatski:ti,ab OR OR Backa:ti,ab OR OR Severnobački:ti,ab OR OR Severnobański:ti,ab OR OR Juznobački:ti,ab OR OR Juznobański:ti,ab OR OR Srem:ti,ab OR OR Sremski:ti,ab OR OR Zapadnobački:ti,ab OR OR 'Novi Sad':ti,ab OR OR 'Novy Sad':ti,ab OR Újvidék:ti,ab OR Nis:ti,ab OR Nish:ti,ab OR Nissa:ti,ab OR Kragujevac:ti,ab OR Subotica:ti,ab OR Szabadka:ti,ab OR Zrenjanin:ti,ab OR Pancevo:ti,ab OR Cacak:ti,ab OR Kraljevo:ti,ab OR 'Novi Pazar':ti,ab OR OR 'Novy Pazar':ti,ab OR 'Turkey (republic)'/exp OR 'Turkish citizen'/exp OR Turkey:ti,ab OR Turkiye:ti,ab OR Turkish:ti,ab OR Turk:ti,ab OR Turck*:ti,ab OR Adana:ti,ab OR Adiyaman:ti,ab OR Ayfon*:ti,ab OR Agri:ti,ab OR Aksaray:ti,ab OR Aksaray:ti,ab OR Amasya:ti,ab OR Ankara:ti,ab OR Antalya:ti,ab OR Ardahan:ti,ab OR Artvin:ti,ab OR Aydin:ti,ab OR Balikesir:ti,ab OR Bartin:ti,ab OR Batman:ti,ab OR Bayburt:ti,ab OR Bilecik:ti,ab OR Bingol:ti,ab OR Bitlis:ti,ab OR Bolu:ti,ab OR Burdur:ti,ab OR Bursa:ti,ab OR Canakkale:ti,ab OR Cannkiri:ti,ab OR Corum:ti,ab OR Denizli:ti,ab OR Diyarbakir:ti,ab OR Duzce:ti,ab OR Edirne:ti,ab OR Elazig:ti,ab OR Erzincan:ti,ab OR Erzurum:ti,ab OR Eskishir:ti,ab OR Gaziantep:ti,ab OR Giresun:ti,ab OR Gumushane:ti,ab OR Hakkari:ti,ab OR Hatay:ti,ab OR Igdirdir:ti,ab OR Isparta:ti,ab OR

Istanbul:ti,ab OR Izmir:ti,ab OR Kahramanmaras:ti,ab OR Karabuk:ti,ab OR Karaman:ti,ab OR Kars:ti,ab OR Kastamonu:ti,ab OR Kayseri:ti,ab OR Kirikkale:ti,ab OR Kirklarely:ti,ab OR Kirklareli:ti,ab OR Kirsheir:ti,ab OR Kocaeli:ti,ab OR Konya:ti,ab OR Kutahya:ti,ab OR Malatya:ti,ab OR Manisa:ti,ab OR Mardin:ti,ab OR Mersin:ti,ab OR Mugla:ti,ab OR Mus:ti,ab OR Nevsehir:ti,ab OR Nigde:ti,ab OR Ordu:ti,ab OR Osmaniye:ti,ab OR Rize:ti,ab OR Sakarya:ti,ab OR Samsun:ti,ab OR Sanliurfa:ti,ab OR Siirt:ti,ab OR Sinop:ti,ab OR Sivas:ti,ab OR Sirnak:ti,ab OR Tekirdag:ti,ab OR Tokat:ti,ab OR Trabzon:ti,ab OR Tunceli:ti,ab OR Usak:ti,ab OR (Van:ti,ab AND (province:ti,ab OR ili:ti,ab)) OR Yalova:ti,ab OR Yozgat:ti,ab OR Kilis:ti,ab OR 'Bosnia and Herzegovina'/exp OR 'Bosnian (citizen)'/exp OR 'Bosniak (people)'/exp OR Bosnia*:ti,ab OR Herzegov*:ti,ab OR Herzegonine:ti,ab OR Bosna:ti,ab OR Bosne:ti,ab OR Bosanski:ti,ab OR Bosanac:ti,ab OR Bosanci:ti,ab OR Srpska:ti,ab OR Brcko:ti,ab OR Posavski:ti,ab OR Posavina:ti,ab OR posavska:ti,ab OR Tuzlanski:ti,ab OR Tuzla:ti,ab OR Tuzlanska:ti,ab OR 'Zenicko dobojski':ti,ab OR 'Zenicko dobojska':ti,ab OR Zenica:ti,ab OR 'Bosansko Podrinjski':ti,ab OR 'Bosansko Podrinjska':ti,ab OR Srednjobosanski:ti,ab OR hercegovacko:ti,ab OR Zapadnohercegovacki:ti,ab OR Zapadnohercegovacka:ti,ab OR Sarajevo:ti,ab OR Sarajevska:ti,ab OR 'Kanton 10':ti,ab OR '10 kanton':ti,ab OR Hercegbosanska:ti,ab OR 'Unsko sanski':ti,ab OR 'Una Sana':ti,ab OR 'Banja Luka':ti,ab OR Bijeljina:ti,ab OR Mostar:ti,ab OR Prijedor:ti,ab OR Cazin:ti,ab OR Doboj:ti,ab OR Zupanja:ti,ab OR 'Kosovo'/exp OR 'Kosovar'/exp OR Kosov*:ti,ab OR Ferizaj*:ti,ab OR Urosevac*:ti,ab OR Gjakov*:ti,ab OR Dakovic*:ti,ab OR Gjilan*:ti,ab OR Ngjilan*:ti,ab OR Mitrovic*:ti,ab OR Pejes:ti,ab OR Peja:ti,ab OR Peje:ti,ab OR Pecki:ti,ab OR Pec:ti,ab OR Pristin*:ti,ab OR Prishtin*:ti,ab OR Pristinski:ti,ab OR Prizrenit:ti,ab OR Prizreni:ti,ab OR Prizrenski:ti,ab OR Prizen:ti,ab OR Prizreni:ti,ab OR Produjev*:ti,ab OR Vucitrn:ti,ab OR Vushtrri*:ti,ab OR 'Suva reka':ti,ab OR Suhareka:ti,ab OR Besiana:ti,ab OR Metohija:ti,ab OR Dukagjini:ti,ab OR Dukagjinit:ti,ab OR 'Liechtenstein'/exp OR Liechtenstein:ti,ab OR Lienchtensteiner*:ti,ab OR Balzers:ti,ab OR Eschen:ti,ab OR Gamprin:ti,ab OR Mauren:ti,ab OR Planken:ti,ab OR Ruggell:ti,ab OR Schaan:ti,ab OR Schellenberg:ti,ab OR Triesen:ti,ab OR Triesenberg:ti,ab OR Vaduz:ti,ab OR 'Norway'/exp OR 'Norwegian (citizen)'/exp OR 'Norwegian (people)'/exp OR Norway:ti,ab OR Norwegian*:ti,ab OR Norge:ti,ab OR Noreg:ti,ab OR Norgga:ti,ab OR Akershus:ti,ab OR 'Aust Agder':ti,ab OR Buskerud:ti,ab OR Finnmark:ti,ab OR Hedmark:ti,ab OR Hordaland:ti,ab OR 'More og Romsdal':ti,ab OR 'More and Romsdal':ti,ab OR 'More Romsdal':ti,ab OR Nordland:ti,ab OR Trondelag:ti,ab OR Oppland:ti,ab OR Oslo:ti,ab OR Ostfold:ti,ab OR Rogaland:ti,ab OR 'Sogn og fjordane':ti,ab OR 'Sogn and fjordane':ti,ab OR 'sogn fjordane':ti,ab OR Telemark:ti,ab OR Troms:ti,ab OR Troms:ti,ab OR Romsa:ti,ab OR Romssa:ti,ab OR 'Vest Agder':ti,ab OR Vestfold:ti,ab OR Bergen:ti,ab OR Stavanger:ti,ab OR Sandnes:ti,ab OR Trondheim:ti,ab OR Trondhem:ti,ab OR Kaupangen:ti,ab OR Nidaros:ti,ab OR Drammen:ti,ab OR Fredrikstad:ti,ab OR Skien:ti,ab OR Tromso:ti,ab OR Sarpsborg:ti,ab OR 'Switzerland'/exp OR 'Swiss'/exp OR Switzerland:ti,ab OR Schweiz:ti,ab OR Schweizerische:ti,ab OR Swiss:ti,ab OR Suisse*:ti,ab OR Svizzera:ti,ab OR Svizzeri:ti,ab OR Svizzers:ti,ab OR Svizra:ti,ab OR Helvetica:ti,ab OR Aargau:ti,ab OR Argovia:ti,ab OR Ausserrhoden:ti,ab OR 'Outer Rhodes':ti,ab OR Innerrhoden:ti,ab OR 'Inner Rhodes':ti,ab OR Basel:ti,ab OR Bale:ti,ab OR Basilea:ti,ab OR Bern:ti,ab OR Berne:ti,ab OR Berna:ti,ab OR Fribourg:ti,ab OR Freiburg:ti,ab OR Friburg:ti,ab OR Geneve:ti,ab OR Geneva:ti,ab OR Geneve:ti,ab OR Genf:ti,ab OR Ginevra:ti,ab OR Genevra:ti,ab OR Glarus:ti,ab OR Graubunden:ti,ab OR Graubuenden:ti,ab OR Grisons:ti,ab OR Grigioni:ti,ab OR Grischun:ti,ab OR jura:ti,ab OR Lucerne:ti,ab OR Luzern:ti,ab OR Losanna:ti,ab OR Neuchatel:ti,ab OR Nidwalden:ti,ab OR Nidwald:ti,ab OR Obwalden:ti,ab OR Obwald:ti,ab OR Schaffhausen:ti,ab OR Schaffhouse:ti,ab OR Schwyz:ti,ab OR Solothurn:ti,ab OR Soleure:ti,ab OR Thurgau:ti,ab OR Thurgovia:ti,ab OR Ticino:ti,ab OR Tessin:ti,ab OR Uri:ti,ab OR Valais:ti,ab OR Wallis:ti,ab OR Vaud:ti,ab OR Zug:ti,ab OR Zurich:ti,ab OR Zuerich:ti,ab OR Zurigo:ti,ab OR Lausanne:ti,ab OR Losanna:ti,ab OR Winterthur:ti,ab OR Winterthour:ti,ab OR 'St Gallen':ti,ab OR 'Saint Gallen':ti,ab OR 'Sankt Gallen':ti,ab OR 'Saint Gall':ti,ab OR 'San Gallo':ti,ab OR 'Son Gagl':ti,ab OR Turigt:ti,ab OR europe*:ad OR europa*:ad OR eu:ad OR eea:ad OR eefta:ad OR 'eu/eea':ad OR 'eu/efta':ad OR ecss:ad OR euratom:ad OR eurozone:ad OR eec:ad OR ec:ad OR (schengen:ad AND (area:ad OR countr*:ad OR region*:ad OR state:ad OR states:ad)) OR euroregion:ad OR euroregions:ad OR balkan:ad OR balkans:ad OR balkanic:ad OR (mediterranean:ad AND (area:ad OR countr*:ad OR region*:ad OR state:ad OR states:ad)) OR (alpine:ad AND (area:ad OR countr*:ad OR region*:ad OR state:ad OR states:ad)) OR scandinavia:ad OR scandinavian:ad OR (nordic NEXT/1 (countr* OR state*)):ad OR danubian:ad OR 'iberian peninsula':ad OR 'peninsula iberica':ad OR 'péninsule ibérique':ad OR 'iberiar penintsula':ad OR iberia:ad OR anatolia:ad OR anadolu:ad OR anatole:ad OR anatolian:ad OR yugoslavia:ad OR czechoslovakia:ad OR 'czecho slovakia':ad OR ceskoslovensko:ad OR 'cesko slovensko':ad OR benelux:ad OR fennoscandia:ad OR 'fennes scandinavia':ad OR fennoscandi*:ad OR (visegrád:ad AND (group:ad OR four:ad OR triangle:ad)) OR 'visegrádska čtyřka':ad OR 'visegrádska skupina':ad OR 'visegrádi együttműködés':ad OR 'visegrádi négyek':ad OR 'grupa wyszehradzka':ad OR 'vyšehradská skupina':ad OR 'vyšehradská štvorka':ad OR austria*:ad OR osterreich*:ad OR oesterreich*:ad OR ostosterreich:ad OR ostoesterreich:ad OR sudosterreich:ad OR sudoesterreich:ad OR westosterreich:ad OR westoesterreich:ad OR burgenland:ad OR carinthia:ad OR karnten:ad OR kaernten:ad OR niederosterreich:ad OR niederoesterreich:ad OR oberosterreich:ad OR oberoesterreich:ad OR salzburg:ad OR saizburg:ad OR styria:ad OR steiermark:ad OR tyrol:ad OR tirol:ad OR vorarlberg:ad OR vienna:ad OR wien:ad OR graz:ad OR linz:ad OR innsbruck:ad OR klagenfurt:ad OR villach:ad OR wels:ad OR 'st polten':ad OR 'st poelten':ad OR 'sankt polten':ad OR 'sankt poelten':ad OR dornbirn:ad OR Belgi*:ad OR Belge*:ad OR Belg:ad OR Brussel*:ad OR Bruxelles:ad OR Bruxelloise:ad OR Walloon*:ad OR Wallon*:ad OR Vlaams:ad OR Flander*:ad OR Flandern:ad OR Flandre:ad OR Flemish:ad OR Flamand:ad OR Flemisch:ad OR Flämisch*:ad OR Vlaanderen:ad OR Flamande:ad OR Waals:ad OR Antwerp*:ad OR Anvers:ad OR Henegouwen:ad OR Hennegau:ad OR Hainault:ad OR Hainaut:ad OR Liege:ad OR Luik:ad OR Luttich:ad OR Limbourg:ad OR Limburg:ad OR Namur:ad OR Namen:ad OR Ostflandern:ad OR Westflandern:ad OR Ghent:ad OR Gent:ad OR Gand:ad OR Charleroi:ad OR Bruges:ad OR Brugge*:ad OR Schaerbeek:ad OR Schaarbeek:ad OR Anderlecht:ad OR Leuven:ad OR Louvain:ad OR Bulgaria:ad OR balgariya:ad OR balgarija:ad OR blagoevgrad*:ad OR 'pirin macedonia':ad OR burgas:ad OR dobrich:ad OR gabrovo:ad OR haskovo:ad OR kardzhali:ad OR kurdzhali:ad OR kystendil:ad OR lovech:ad OR lovec:ad OR montana:ad OR pazardzhik:ad OR pernik:ad OR pleven*:ad OR plovdiv:ad OR razgrad:ad OR rousse:ad OR ruse:ad OR rusenka:ad OR shumen:ad OR silistra:ad OR sliven:ad OR smolyan:ad OR sofia:ad OR sofyiska:ad OR sofiiska:ad OR 'stara zagora':ad OR targovishte:ad OR varna:ad OR 'veliko tarnovo':ad OR vidin:ad OR vratsa:ad OR vratza:ad OR yambol:ad OR croat*:ad OR hrvatsk*:ad OR hrvati:ad OR bjelovar:ad OR 'bjelovarsko bilogorska':ad OR 'brod posavina':ad OR 'brodsko posavska':ad OR 'dubrovnik neretva':ad OR 'dubrovacko neretvanska':ad OR zagreb:ad OR zagrebacka:ad OR istria:ad OR istarska:ad OR karlovacka:ad OR karlovac:ad OR 'koprivnicko krizevacka':ad OR 'koprivnica:ad OR krizevci:ad OR 'krapina zagorje':ad OR 'krapinsko zagorska':ad OR 'lika senj':ad OR 'licko senjska':ad OR medimurska:ad OR medimurje:ad OR osijek:ad OR baranja:ad OR 'osjecko baranjska':ad OR 'pozega slavinia':ad OR 'pozesko slavonska':ad OR 'primorje gorski kotar':ad OR 'primorsko goranska':ad OR 'sibensko kninska':ad OR 'sibensko kninske':ad OR sibenik:ad OR knin:ad OR sisak:ad OR 'sisacko moslavacka':ad OR moslavina:ad OR 'splitsko dalmatinska':ad OR split:ad OR dalmatia:ad OR varazdin:ad OR varazdinska:ad OR

viroviticko:ad OR podravska:ad OR virovitica:ad OR podravina:ad OR 'vukovarsko srijemska':ad OR vukovar:ad OR srijem:ad OR
 zadar:ad OR zadarska:ad OR rijeka:ad OR 'velika gorica':ad OR 'slavonski brod':ad OR pula:ad OR cyprus:ad OR cyriot*:ad OR
 kypros:ad OR kibris*:ad OR kypriaki:ad OR kyprioi:ad OR nicosia:ad OR lefkosa:ad OR lefkosia:ad OR famagusta:ad OR
 magusa:ad OR ammochostos:ad OR gazimagusa:ad OR kyrenia:ad OR girne:ad OR keryneia:ad OR larnaca:ad OR larnaka:ad OR
 iskele:ad OR limassol:ad OR lemesos:ad OR limasol:ad OR leymosun:ad OR paphos:ad OR pafos:ad OR baf:ad OR strovolos:ad
 OR lakatamia:ad OR lakadamyia:ad OR 'kato polemidia':ad OR 'kato polemidhia':ad OR aglandjia:ad OR eglence:ad OR
 aglantzia:ad OR aradhippou:ad OR aradippou:ad OR engomi:ad OR czech*:ad OR cesky:ad OR ceska:ad OR cech:ad OR
 cestina:ad OR prague:ad OR praha:ad OR prag:ad OR stredoces*:ad OR jihoces*:ad OR bohemia:ad OR bohemian:ad OR
 plzen*:ad OR pilsen:ad OR karlovars*:ad OR 'karlovy vary':ad OR usteck*:ad OR usti:ad OR liberec*:ad OR 'hradec kralove':ad
 OR kralovehradec*:ad OR pardubic*:ad OR olomouc*:ad OR olomoc:ad OR holomoc:ad OR moravskoslezs*:ad OR jihomorav*:ad
 OR moravia:ad OR moravian:ad OR morava:ad OR vysocina:ad OR zlin:ad OR zlinsk*:ad OR 'ceske budejovice':ad OR budweis:ad
 OR brno:ad OR ostrava:ad OR Denmark:ad OR Danish*:ad OR dane:ad OR danes:ad OR Danmark:ad OR dansk*:ad OR
 Hovedstaden:ad OR Midtjylland:ad OR Nordjylland:ad OR Sjælland:ad OR Sealand:ad OR 'Zealand region':ad OR 'region
 Zealand':ad OR Syddanmark:ad OR Jutland:ad OR Jylland:ad OR Sønderjyllands:ad OR Copenhagen:ad OR København:ad OR
 Århus:ad OR Aarhus:ad OR Bornholm:ad OR Frederiksberg:ad OR Frederiksborg:ad OR Ringkjøbing:ad OR Viborg:ad OR Vejle:ad
 OR Roskilde:ad OR Storstrøm:ad OR Vestsjællands:ad OR 'West Zealand':ad OR Funen:ad OR Ribe:ad OR 'Kalaallit Nunaat':ad
 OR Gronland:ad OR Foroyar:ad OR Faeroerne:ad OR 'Faroe islands':ad OR Aalborg:ad OR Ålborg:ad OR Odense:ad OR
 Esbjerg:ad OR Gentofte:ad OR Gladsaxe:ad OR Randers:ad OR Kolding:ad OR Estonia*:ad OR Eesti:ad OR Eestlased:ad OR
 Eestlane:ad OR Harju:ad OR Harjumaa:ad OR Hiiumaa:ad OR Hiiu:ad OR Hiiumaa:ad OR 'Ida Viru':ad OR 'Ida Virumaa':ad OR Jarvamaa:ad OR
 Jarva:ad OR Jõgevamaa:ad OR Jõgeva:ad OR Laanemaa:ad OR Laane:ad OR 'Laane Virumaa':ad OR Pärnu:ad OR Parnumaa:ad
 OR Polva:ad OR Polvamaa:ad OR Rapla:ad OR Raplamaa:ad OR Saare:ad OR Saaremaa:ad OR Tartu:ad OR Tartumaa:ad OR
 Valga:ad OR Valgamaa:ad OR Viljandimaa:ad OR Viljandi:ad OR Voru:ad OR Vorumaa:ad OR Tallinn:ad OR Narva:ad OR 'Kohtla
 Jarve':ad OR Rakvere:ad OR Maardu:ad OR Sillamäe:ad OR Kuressaare:ad OR Finland:ad OR Finnish*:ad OR Finn:ad OR Finns:ad
 OR Suomi:ad Suomen:ad OR Suomalaiset:ad OR Åland:ad OR Ahvenanmaa:ad OR Uusimaa:ad OR Nyland:ad OR Karelia:ad OR
 Karjala:ad OR Karelän:ad OR Ostrobothnia:ad OR Pohjanmaa:ad OR Osterbotten:ad OR Savonia:ad OR Savo:ad OR Savolax:ad
 OR Kainuu:ad OR Akajaland*:ad OR 'Kanta-Häme':ad OR Tavastia:ad OR Tavastia:ad OR Tavastland:ad OR Kymenlaakso:ad OR
 Kymmenedalen:ad OR Lapland:ad OR Lappi:ad OR Lapland:ad OR 'Paijat Häme':ad OR Pirkanmaa:ad OR Birkaland:ad OR
 Satakunta:ad OR Satakunda:ad OR Helsinki:ad OR Helsingfors:ad OR Espoo:ad OR Esbo:ad OR Tampere:ad OR Tammerfors:ad
 OR Vantaa:ad OR Vanda:ad OR Oulu:ad OR Uleåborg:ad OR Turku:ad OR Åbo:ad OR Jyväskylä:ad OR Kuopio:ad OR Lahti:ad OR
 Lahtis:ad OR Kouvola:ad OR France:ad OR French*:ad OR Française*:ad OR Alsace:ad OR Elsass:ad OR Aquitaine:ad OR
 Aquitania:ad OR Akitania:ad OR Aguiéne:ad OR Auvergne:ad OR Auvergne:ad OR Auvergne:ad OR Auvergne:ad OR Normandie:ad OR
 Normandy:ad OR Normandie:ad OR Bourgogne:ad OR Burgundy:ad OR Bregogne:ad OR Borgoëgne:ad OR Borgogne:ad OR
 Bretagne:ad OR Breizh:ad OR Bertaëyn:ad OR Bretagne:ad OR 'Champagne Ardenne':ad OR Corse:ad OR Corsica:ad OR 'Franche
 Comte':ad OR 'Franche Comté':ad OR 'Franche Comtat':ad OR Guadeloupe:ad OR Guyane:ad OR Guiana:ad OR 'Languedoc
 Roussillon':ad OR 'Lengadoc Rosselhon':ad OR 'Llenguadoc-Rossello':ad OR Limousin:ad OR Lemosin:ad OR Lorraine:ad OR
 Lothringen:ad OR Martinique:ad OR 'Midi Pyrenées':ad OR 'Midi Pyrenées':ad OR 'Miègjorn Pirenèus':ad OR
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 'Peitau Charantas':ad OR 'Poitou-Cherentes':ad OR Provence:ad OR Provenca:ad OR Prouvenco:ad OR 'Cote d Azur':ad OR 'Costo
 d Azur':ad OR 'Costa d Azur':ad OR Reunion:ad OR 'Rhone Alpes':ad OR 'Rono Arpes':ad OR 'Rose Aups':ad OR Ain:ad OR
 Aisne:ad OR Allier:ad OR 'Alpes de Haute Provence':ad OR 'Haute Alpes':ad OR 'Alpes Maritimes':ad OR Ardeche:ad OR
 Ardennes:ad OR Ariège:ad OR Aube:ad OR Aude:ad OR Aveyron:ad OR 'Bas Rhin':ad OR 'Bouches du Rhone':ad OR Calvados:ad
 OR Cantal:ad OR Charente:ad OR Cher:ad OR Correze:ad OR 'Corse du Sud':ad OR 'Cote d Or':ad OR 'Cotes d Armor':ad OR
 Creuse:ad OR 'Deux Sevres':ad OR Dordogne:ad OR Doubs:ad OR Drome:ad OR Essonne:ad OR Eure:ad OR Finistere:ad OR
 Gard:ad OR Gers:ad OR Gironde:ad OR 'Haute Corse':ad OR 'Haute Garonne':ad OR 'Haute Marne':ad OR 'Hautes Alpes':ad OR
 'Haute Saone':ad OR 'Haute Savoie':ad OR 'Hautes Pyrenées':ad OR 'Haute Vienne':ad OR 'Haut Rhin':ad OR 'Hauts de Seine':ad
 OR Herault:ad OR 'Ille de France':ad OR 'Ille et Vilaine':ad OR Indre:ad OR Iser:ad OR Jura:ad OR Landes:ad OR Loire:ad OR
 Loiret:ad OR (Lot NEAR/3 (departement OR departement)):ad OR 'Lot et Garonne':ad OR 'Loir et Cher':ad OR Lozere:ad OR
 Manche:ad OR Marne:ad OR Mayenne:ad OR Mayotte:ad OR 'Meurthe et Moselle':ad OR Meuse:ad OR Morbihan:ad OR
 Moselle:ad OR (Nord NEAR/3 (departement OR departement)):ad OR Nièvre:ad OR Oise:ad OR Orne:ad OR 'Pas de calais':ad OR
 'Noord-Nauw van Kales':ad OR Paris:ad OR 'Puy de dome':ad OR 'Pyrenées Atlantiques':ad OR 'Pyrenées Orientales':ad OR
 Rhone:ad OR Sarthe:ad OR Savoie:ad OR 'Seine et Marne':ad OR 'Seine Maritime':ad OR Somme:ad OR Tarn:ad OR 'Territoire de
 Belfort':ad OR 'Val de Marne':ad OR 'Val d Oise':ad OR Var:ad OR Vaucluse:ad OR Vendee:ad OR Vienne:ad OR Vosges:ad OR
 Yonne:ad OR Yvelines:ad OR Marseille:ad OR Lyon:ad OR Nice:ad OR Nantes:ad OR Strasbourg:ad OR Montpellier:ad OR
 Bordeaux:ad OR Lille:ad OR Toulouse:ad OR 'Outre Mer':ad OR 'Seine Saint Denis':ad OR German*:ad OR Deutsch*:ad OR
 Bundesrepublik:ad OR Westdeutschland:ad OR Ostdeutschland:ad OR Baden:ad OR Württemberg:ad OR Württemberg:ad OR
 Bayern:ad OR Bavaria:ad OR Berlin:ad OR Brandenburg:ad OR Bremen:ad OR Oldenburg:ad OR Mitteldeutschland:ad OR
 Rhein:ad OR Rhine:ad OR Hannover:ad OR Braunschweig:ad OR Göttingen:ad OR Goettingen:ad OR Nurnberg:ad OR
 Nuernberg:ad OR Ruhr:ad OR Köln:ad OR koeln:ad OR Bonn:ad OR Hamburg:ad OR Hessen:ad OR Hesse:ad OR Hestia:ad OR
 Mecklenburg:ad OR Vorpommern:ad OR Pomerania:ad OR Niedersachsen:ad OR Neddersassen:ad OR Saxony:ad OR
 Niederbayern:ad OR 'Northern Rhine':ad OR 'North Rhine':ad OR Westphalia:ad OR Westfalen:ad OR 'Rhineland Palatinate':ad OR
 'Rheinland Pfalz':ad OR Saarland:ad OR Sachsen:ad OR 'Schleswig Holstein':ad OR Thuringia:ad OR Thuringen:ad OR
 Thuringen:ad OR München:ad OR Muenchen:ad OR Munich:ad OR Frankfurt:ad OR Stuttgart:ad OR Dusseldorf:ad OR
 Duesseldorf:ad OR Dortmund:ad OR Essen:ad OR Greece:ad OR 'Hellenic republic':ad OR Greek*:ad OR Ellada:ad OR Elladas:ad
 OR 'Elliniki Dimokratia':ad OR Hellas:ad OR Hellenes:ad OR Attica:ad OR Attiki:ad OR Makedonia*:ad OR Macedonia:ad OR
 Thraki:ad OR Thrace:ad OR Crete:ad OR Kriti:ad OR 'Ionia Nisia':ad OR 'Ionian neson':ad OR 'Ionion nIson':ad OR 'Ionian
 islands':ad OR 'Ionian island':ad OR Epirus:ad OR Ipeiros:ad OR 'Periféreia Ipeirou':ad OR 'North aegean':ad OR 'Northern
 Aegean':ad OR 'Aegean islands':ad OR 'Aegean island':ad OR 'Nisoi Agaïou':ad OR 'Notio Aigaió':ad OR Peloponnese:ad OR
 Peloponniso*:ad OR Thessaly:ad OR Thessalia:ad OR Thessalian:ad OR Petthalia:ad OR 'Voreio Aigaió':ad OR 'Voreio Aigaiou':ad
 OR 'South aegean':ad OR 'Southern Aegean':ad OR 'Mount athos':ad OR 'Oros Athos':ad OR Cyclades:ad OR Cyklades:ad OR
 Kiklades:ad OR Dodecanese:ad OR Dodekanisa:ad OR Athens:ad OR Athina:ad OR Thessaloniki:ad OR Thessalonica:ad OR
 Patras:ad OR Patra:ad OR Pireas:ad OR Piraeus:ad OR Larissa:ad OR Larisa:ad OR Heraklion:ad OR Heraclion:ad OR Iraklion:ad

OR Irakleion:ad OR Iraklio:ad OR Volos:ad OR Rhodes:ad OR Rodos:ad OR Ioannina:ad OR Janina:ad OR Yannena:ad OR Chania:ad OR Chalcis:ad OR Chalkida:ad OR Hungar*:ad OR Magyarorszag:ad OR Magyar*:ad OR Dunantuli:ad OR Transdanubia:ad OR Dunantul:ad OR 'Great Plain':ad OR 'Eszak Alföld':ad OR 'Del Alföld':ad OR 'Alfold es eszak':ad OR 'Northern Alföld':ad OR 'North Alföld':ad OR 'South Alföld':ad OR 'Southern Alföld':ad OR Bacs:ad OR Kiskun:ad OR Baranya:ad OR Bekes:ad OR Borsod:ad OR Abauj:ad OR Zemplen:ad OR OR Budapest:ad OR Csongrad:ad OR Fejer:ad OR gyor:ad OR moson:ad OR sopron:ad OR hajdu:ad OR bihar:ad OR Heves:ad OR 'jasz nagykun szolnok':ad OR komarom:ad OR esztergom:ad OR Nograd:ad OR (Pest NEXT/3 (megye OR county)):ad OR Somogy:ad OR szabolcs:ad OR szatmar:ad OR bereg:ad OR Tolna:ad OR Vas:ad OR Veszprem:ad OR Zala:ad OR Debrecen:ad OR Miskolc:ad OR Szeged:ad OR Pecs:ad OR Gyor:ad OR Nyiregyhaza:ad OR Kecskemet:ad OR Szekesfehervar:ad OR Szombathely:ad OR Ireland:ad OR Eire:ad OR Irish*:ad OR Fingal:ad OR 'Fine Gall':ad OR OR Dublin:ad OR 'Ath Cliath':ad OR 'Dun Laoghaire':ad OR OR Wicklow:ad OR 'Cill Mhantain':ad OR 'Chill Mhantain':ad OR Wexford:ad OR 'Loch Garman':ad OR OR Carlow:ad OR OR Ceatharlach:ad OR OR Kildare:ad OR 'Cill Dara':ad OR 'Chill Dara':ad OR Meath:ad OR 'An Mhi':ad OR 'Contae na Mi':ad OR Louth:ad OR 'Contae Lu':ad OR Monaghan:ad OR Muineachán:ad OR Mhuineacháin:ad OR Cavan:ad OR 'An Cabhan':ad OR 'An Cabhain':ad OR Longford:ad OR 'An Longfort':ad OR 'an Longfoirt':ad OR Langfurd:ad OR Westmeath:ad OR 'An Iarmhi':ad OR 'na Iarmhi':ad OR Offaly:ad OR 'Uibh Fhaili':ad OR Laois:ad OR Laoise:ad OR Kilkenny:ad OR 'Chill Chainnigh':ad OR 'Cill Chainnigh':ad OR Waterford:ad OR 'Port Lairge':ad OR Watterford:ad OR OR Cork:ad OR Corcaigh:ad OR OR Chorcai:ad OR OR Kerry:ad OR OR Ciarrai:ad OR OR Chiarrai:ad OR OR Limerick:ad OR Luimneach:ad OR Luimnigh:ad OR Tipperary:ad OR 'Tiobraid Arann':ad OR 'Thiobraid Arann':ad OR Clare:ad OR 'An Clar':ad OR 'an Chlair':ad OR Galway:ad OR Gaillimh:ad OR 'na Gaillimhe':ad OR Mayo:ad OR 'Maigh Eo':ad OR 'Mhaigh Eo':ad OR Roscommon:ad OR 'Ros comain':ad OR Sligo:ad OR Sligeach:ad OR Shligigh:ad OR Leitrim:ad OR Liatroim:ad OR Liatroma:ad OR Donegal:ad OR 'Dhún na nGall':ad OR Dinnygal:ad OR Dunnyga:ad OR Leinster:ad OR Laighin:ad OR 'Cúige Laighean':ad OR OR Munster:ad OR Mumhain:ad OR 'Cúige Mumhan':ad OR OR Connacht:ad OR OR Connachta:ad OR OR Drogheda:ad OR 'Droichead Atha':ad OR OR Dundalk:ad OR 'Dún Dealgan':ad OR OR Swords:ad OR OR Sord:ad OR OR Bray:ad OR OR Bre:ad OR OR Navan:ad OR 'An Uaimh':ad OR OR Italy:ad OR Italia*:ad OR OR Abruzzo:ad OR OR Abruzzi:ad OR OR Basilicata:ad OR OR Lucania:ad OR OR Calabria:ad OR OR Campania:ad OR 'Emilia Romagna':ad OR 'friuli venezia giulia':ad OR OR Lazio:ad OR OR Latium:ad OR OR Liguria*:ad OR OR Lombardy:ad OR OR Lombardia:ad OR OR Marche:ad OR OR Marches:ad OR OR Molisano:ad OR OR Molise:ad OR OR Piedmont*:ad OR OR Piemonte:ad OR OR Bolzano:ad OR OR Bozen:ad OR OR Trentino:ad OR OR Trento:ad OR OR Puglia:ad OR OR Apulia:ad OR OR Sardinia:ad OR OR Sardegna:ad OR OR Sicily:ad OR OR Sicilia:ad OR OR Toscana:ad OR OR Tuscany:ad OR OR Umbria:ad OR 'Valle d Aosta':ad OR 'Vallee d Aoste':ad OR 'Aosta Valley':ad OR OR Veneto:ad OR OR Venetia:ad OR OR Triveneto:ad OR OR Rome:ad OR OR Roma:ad OR OR Milan:ad OR OR Milano:ad OR OR Naples:ad OR OR Napoli:ad OR OR Turin:ad OR OR Torino:ad OR OR Palermo:ad OR OR Genoa:ad OR OR Genova:ad OR OR Bologna:ad OR OR Florence:ad OR OR Firenze:ad OR OR Bari:ad OR OR Catania:ad OR OR Latvi*:ad OR OR Riga:ad OR OR Courland:ad OR OR Kurzeme:ad OR OR Kurland:ad OR OR Latgale:ad OR OR Lettgallia:ad OR OR Latgola:ad OR OR Latgalia:ad OR OR Vidzeme:ad OR OR Vidumo:ad OR OR Semigallia:ad OR OR Semigale:ad OR OR Zemgale:ad OR OR Pieriga:ad OR OR Daugavpils:ad OR OR Dinaburg:ad OR OR Jekabpils:ad OR OR Jakobstadt:ad OR OR Jelgava:ad OR OR Jurmala:ad OR OR Liepaja:ad OR OR Libau:ad OR OR Rezekne:ad OR OR Rezne:ad OR OR Rositten:ad OR OR Valmiera:ad OR OR Wolmar:ad OR OR Ventpils:ad OR OR Windau:ad OR OR Ogre:ad OR OR Lithuania*:ad OR 'Lietuvos Respublika':ad OR OR Lietuva:ad OR OR lietuviu:ad OR OR Alytus:ad OR OR Alytaus:ad OR OR Kaunas:ad OR OR Kauno:ad OR OR Klaipeda:ad OR OR Klaipedos:ad OR OR Marijampoles:ad OR OR Marijampole:ad OR OR Panevezys:ad OR OR Panevezio:ad OR OR Siauliai:ad OR OR Siauliu:ad OR OR Taurages:ad OR OR Taurage:ad OR OR Telsiu:ad OR OR Telsiai:ad OR OR Utenos:ad OR OR Utena:ad OR OR Vilnius:ad OR OR Vilniaus:ad OR OR Mazeikiai:ad OR OR Jonava:ad OR OR Mazeikiu:ad OR OR Jonavos:ad OR OR Luxembourg*:ad OR OR Luxemburg:ad OR OR Letzebuerg:ad OR OR Diekirch:ad OR OR Grevenmacher:ad OR OR 'Esch sur Alzette':ad OR OR 'Esch Uelzecht':ad OR OR 'Esch an der Alzette':ad OR OR 'Esch an der Alzig':ad OR OR Dudelange:ad OR OR Diddeleng:ad OR OR Dúdelingen:ad OR OR Duédelingen:ad OR OR Schifflange:ad OR OR Scheffleng:ad OR OR Schifflingen:ad OR OR Bettembourg:ad OR OR Beetebuerg:ad OR OR Bettemburg:ad OR OR Petange:ad OR OR Peiteng:ad OR OR Petingen:ad OR OR Ettelbruck:ad OR OR Ettelbreck:ad OR OR Ettelbrueck:ad OR OR Diekirch:ad OR OR Dikrech:ad OR OR Strassen:ad OR OR Stroossen:ad OR OR Bertrange:ad OR OR Bartreng:ad OR OR Bartringen:ad OR OR Malta:ad OR OR Maltese*:ad OR OR Maltin:ad OR OR Gozo:ad OR OR Ghawdex:ad OR OR Valletta:ad OR 'Ill Belt':ad OR OR Birkirkara:ad OR OR 'B Kara':ad OR OR Bircircara:ad OR OR Mosta:ad OR OR Qormi:ad OR OR 'St Paul s Bay':ad OR OR 'Pawl il Bahar':ad OR OR Zabbar:ad OR OR Sliema:ad OR OR Naxxar:ad OR OR Gwann:ad OR OR 'St John':ad OR OR Zebbug:ad OR OR 'Citta rohan':ad OR OR Fgura:ad OR OR Netherlands:ad OR OR Nederland*:ad OR OR Dutch*:ad OR OR Drenthe:ad OR OR Flevoland:ad OR OR Friesland:ad OR OR Fryslan:ad OR OR Frisia:ad OR OR Gelderland:ad OR OR Guelders:ad OR OR Groningen:ad OR OR Limburg:ad OR OR Brabant:ad OR OR Holland:ad OR OR Overijssel:ad OR OR Overijssel:ad OR OR Utrecht:ad OR OR Zeeland:ad OR OR Amsterdam:ad OR OR Rotterdam:ad OR OR Hague:ad OR OR 's-Gravenhage':ad OR OR 'Den Haag':ad OR OR Eindhoven:ad OR OR Tilburg:ad OR OR Almere:ad OR OR Breda:ad OR OR Nijmegen:ad OR OR Nimeguen:ad OR OR Poland:ad OR OR Polska:ad OR OR Polish:ad OR OR Pole:ad OR OR Poles:ad OR OR Polski:ad OR OR Polak:ad OR OR Polka:ad OR OR Polacy:ad OR OR Dolnoslaskie:ad OR OR Silesia*:ad OR OR Slask:ad OR OR Pomorskie:ad OR OR Pomerania*:ad OR OR Kujawsko:ad OR OR Kuyavian:ad OR OR Lodzkie:ad OR OR Lodz:ad OR OR Lubelskie:ad OR OR Lublin:ad OR OR Lubuskie:ad OR OR Lubus:ad OR OR Lubus:ad OR OR Malopolskie:ad OR OR Mazowskie:ad OR OR Mazowieckie:ad OR OR Masovia:ad OR OR Masovian:ad OR OR Opolskie:ad OR OR Opole:ad OR OR Podkarpackie:ad OR OR Subcarpathian*:ad OR OR Podlaskie:ad OR OR Podlachia:ad OR OR Podlasie:ad OR OR Slaskie:ad OR OR Swietokrzyskie:ad OR OR 'Warmia Mazuria':ad OR OR 'Warmian Mazurian':ad OR OR 'Warmia Masuria':ad OR OR 'Warmian Masurian':ad OR OR 'Warmia Mazury':ad OR OR 'Warminsko Mazurskie':ad OR OR 'Warmian Masurian':ad OR OR Wielkopolskie:ad OR OR Zachodniopomorskie:ad OR OR Warsaw:ad OR OR Warszawa:ad OR OR Krakow:ad OR OR Cracow:ad OR OR Wroclaw:ad OR OR Poznan:ad OR OR Szczecin:ad OR OR Bydgoszcz:ad OR OR Katowice:ad OR OR Portugal:ad OR OR Portugues*:ad OR OR Azores:ad OR OR Acores:ad OR OR Madeira:ad OR OR Alentejo:ad OR OR Algarve:ad OR OR Lisboa:ad OR OR Lisbon:ad OR OR 'Alto Tras-os-Montes':ad OR OR (Ave NEAR/3 (community OR intermunicipal OR comunidade)):ad OR OR Mondego:ad OR OR Vouga:ad OR OR Beira:ad OR OR Cavado:ad OR OR Lafoes:ad OR OR Douro:ad OR OR Porto:ad OR OR Oporto:ad OR OR Tejo:ad OR OR Minho:ad OR OR Setubal:ad OR OR Pinhal:ad OR OR 'Serra da Estrela':ad OR OR Tamega:ad OR OR Leira:ad OR OR Santarem:ad OR OR Beja:ad OR OR Faro:ad OR OR Evora:ad OR OR Portalegre:ad OR OR 'Castelo Branco':ad OR OR Guarda:ad OR OR Coimbra:ad OR OR Aveiro:ad OR OR Viseu:ad OR OR Braganca:ad OR OR Braganza:ad OR OR Braga:ad OR OR 'Vila real':ad OR OR 'Viana do Castelo':ad OR OR Gaia:ad OR OR Amadora:ad OR OR Funchal:ad OR OR Coimbra:ad OR OR Almada:ad OR OR (Aguilva:ad AND Cacem:ad) OR OR Romania*:ad OR OR Rumania*:ad OR OR Roumania*:ad OR OR Romani:ad OR OR Rumani:ad OR OR Alba:ad OR OR Arad:ad OR OR Arges:ad OR OR Bacau:ad OR OR Bihor:ad OR OR 'Bistrita Nasaud':ad OR OR Botosani:ad OR OR Braila:ad OR OR Brasov:ad OR OR Kronstadt:ad OR OR Brasso:ad OR OR Brassovia:ad OR OR Coron:ad OR OR Bucharest:ad OR OR Bucuresti:ad OR OR Buzau:ad OR OR Calarasi:ad OR OR 'Caras-Severin':ad OR OR Cluj:ad OR OR Klausenburg:ad OR OR Kolozsvar:ad OR OR Constanta:ad OR OR Tomis:ad OR OR Konstantia:ad OR OR Kostence:ad OR OR Covasna:ad OR OR Dambovita:ad OR OR Dolj:ad OR OR Galati:ad OR OR Galatz:ad OR OR Galac:ad OR OR Kalas:ad OR OR Giurgiu:ad OR OR Gorj:ad OR OR Harghita:ad OR OR Hunedoara:ad OR OR Ialomita:ad OR OR Iasi:ad OR OR Jassy:ad OR OR Lassy:ad OR OR Ilfov:ad OR OR Maramures:ad OR OR Mehedinti:ad OR OR Mures:ad OR OR Neamt:ad OR OR (Olt:ad AND (river:ad OR county:ad OR region:ad OR judetul:ad OR Raul:ad)) OR OR Prahova:ad OR OR Salaj:ad OR OR 'Satu Mare':ad OR OR Sibiu:ad OR OR Suceava:ad OR OR Teleorman:ad OR OR Timis:ad OR OR Tulcea:ad OR OR Valcea:ad OR OR Vilcea:ad OR OR Vaslui:ad OR OR Vrancea:ad

OR Timisoara:ad OR Temeswar:ad OR Temeschburg:ad OR Temeschwar:ad OR Temesvar:ad OR Temisvar:ad OR Timisvar:ad
OR Temesva:ad OR Craiova:ad OR Ploiesti:ad OR Ploesti:ad OR Oradea:ad OR Varad:ad OR Varat:ad OR Slovakia:ad
OR Slovensk*:ad OR Slovak*:ad OR Slovaci:ad OR Slovenki:ad OR Bratislav*:ad OR Presporok:ad OR Pressburg:ad OR
Preßburg:ad OR Posenium:ad OR Banskobystri*:ad OR 'Banska Bystrica':ad OR Neusohl:ad OR Besztercebánya:ad OR Kosic*:ad
OR Kaschau:ad OR Kassa:ad OR Nitrán*:ad OR Nitra:ad OR Neutra:ad OR Nyitra:ad OR Nyitria:ad OR Trnav*:ad OR Tyrnau:ad
OR Nagyszombat:ad OR Tyrnavia:ad OR Presov*:ad OR Trencian*:ad OR Trencin:ad OR Trentschin:ad OR Trencsén:ad OR
Zilina:ad OR Sillein:ad OR Zsolna:ad OR Zylina:ad OR (Martin:ad AND (city:ad OR Svaty:ad)) OR Turócszentmárton:ad
OR Poprad:ad OR Deutschendorf:ad OR Zvolen:ad OR Slovenia*:ad OR Slovenija:ad OR slovensk*:ad OR Slovenci:ad OR
Slovene*:ad OR Gorenjska:ad OR Carniola:ad OR Goriska:ad OR Gorizia:ad OR Jugovzhodna:ad OR Koroska:ad OR Carinthia:ad
OR 'Notranjsko kraska':ad OR 'Obalno kraska':ad OR 'Coastal karst':ad OR Osrednjeslovenska:ad OR Podravska:ad OR
Drava:ad OR Pomurska:ad OR Mura:ad OR Savinjska:ad OR Savinja:ad OR Spodnjeposavska:ad OR Zasavska:ad OR 'Central
Sava':ad OR Posavska:ad OR 'Lower Sava':ad OR Ljubljana:ad OR Laibach:ad OR Lubiana:ad OR Maribor:ad OR 'Marburg an der
Drau':ad OR Kranj:ad OR Carnium:ad OR Creina:ad OR Chreina:ad OR Krainbur:ad OR Koper:ad OR Capodistria:ad OR Kopar:ad
OR Celje:ad OR 'Novo mesto':ad OR Neustadt:ad OR Domžale:ad OR Velenje:ad OR Wollan:ad OR Woellan:ad OR 'Nova
Gorica':ad OR Kamnik:ad OR Spain:ad OR Espana:ad OR Spanish:ad OR Espanol*:ad OR Spaniard*:ad OR Andalucia:ad
OR Andalusia:ad OR Aragon:ad OR Arago:ad OR Cantabria:ad OR Canarias:ad OR 'Canary Islands':ad OR (Canaries:ad AND
island*:ad) OR 'Castile and leon':ad OR 'Castilla y Leon':ad OR 'Castile La Mancha':ad OR 'Castilla La Mancha':ad OR Cataluna:ad
OR Catalonia:ad OR Ceuta:ad OR Madrid:ad OR Melilla:ad OR Navarra:ad OR Navarre:ad OR Valencia*:ad OR Extremadura:ad
OR Galicia:ad OR Balears:ad OR 'Balearic Islands':ad OR 'Balear Islands':ad OR Baleares:ad OR 'La Rioja':ad OR 'Pais Vasco':ad
OR 'Basque Country':ad OR 'Baske region':ad OR Euskadi:ad OR Asturias:ad OR Murcia:ad OR Coruna:ad OR Alava:ad
OR Araba:ad OR Albacete:ad OR Alicante:ad OR Alacant:ad OR Almeria:ad OR Avila:ad OR Badajoz:ad OR Badajos:ad
OR Barcelona:ad OR Burgos:ad OR Caceres:ad OR Cadiz:ad OR Castellon:ad OR Castello:ad OR 'Ciudad Real':ad OR Cordoba:ad
OR Cuenca:ad OR Eivissa:ad OR Ibiza:ad OR Formentera:ad OR 'El Hierro':ad OR Fuerteventura:ad OR Galiza:ad OR Girona:ad
OR Gerona:ad OR 'Gran Canaria':ad OR Granada:ad OR Guadalajara:ad OR Guipuzcoa:ad OR Gipuzkoa:ad OR Huelva:ad
OR Huesca:ad OR Jaen:ad OR 'La Gomera':ad OR 'La Palma':ad OR Lanzarote:ad OR Leon:ad OR Lleida:ad OR Lerida:ad
OR Lugo:ad OR Malaga:ad OR Mallorca:ad OR Majorca:ad OR Menorca:ad OR Minorca:ad OR Murcia:ad OR Ourense:ad OR
Orense:ad OR Palencia:ad OR Pontevedra:ad OR Salamanca:ad OR Segovia:ad OR Sevilla:ad OR Seville:ad OR Soria:ad
OR Tarragona:ad OR Tenerife:ad OR Teruel:ad OR Toledo:ad OR Valladolid:ad OR Vizcaya:ad OR Biscay:ad OR Zamora:ad
OR Zaragoza:ad OR Saragossa:ad OR 'Las Palmas':ad OR Bilbao:ad OR Bilbo:ad OR Sweden:ad OR Sverige:ad OR
Swedish:ad OR Svenska:ad OR svenskar:ad OR Swede:ad OR Swedes:ad OR Norrland:ad OR Mellansverige:ad
OR Smaland:ad OR Stockholm*:ad OR Sydsverige:ad OR Vastverige:ad OR Blekinge:ad OR Dalarna:ad OR Gavlberg*:ad OR
Gotland*:ad OR Halland*:ad OR Jamtland*:ad OR Jonkoping*:ad OR Kalmar:ad OR Kronoberg*:ad OR Norrbotten*:ad OR
Orebro:ad OR Ostergotland*:ad OR Skane:ad OR Sodermanlands:ad OR Uppsala:ad OR Varmland*:ad OR Vasterbotten*:ad OR
Vasternorrland*:ad OR Vastmanland*:ad OR vastergotland*:ad OR Gotaland*:ad OR Gothenburg:ad OR Goteborg:ad
OR Malmo:ad OR Vasteras:ad OR Linkoping:ad OR Helsingborg:ad OR Halsingborg:ad OR Norrkoping:ad OR 'GB':ad OR 'United
kingdom':ad OR 'UK':ad OR Britain:ad OR British:ad OR England:ad OR English:ad OR Scotland:ad OR Scottish:ad OR Scots:ad
OR Wales:ad OR Cymru:ad OR Welsh:ad OR 'North Ireland':ad OR 'Northern Ireland':ad OR Irish:ad OR Avon:ad OR
Bedfordshire:ad OR Berkshire:ad OR Bristol:ad OR Buckinghamshire:ad OR Cambridgeshire:ad OR 'Isle of Ely':ad OR
Cheshire:ad OR Cleveland:ad OR Cornwall:ad OR Cumberland:ad OR Cumbria:ad OR Derbyshire:ad OR Devon:ad OR Dorset:ad
OR Durham:ad OR Essex:ad OR Gloucestershire:ad OR Hampshire:ad OR Southampton:ad OR (Hereford:ad AND Worcester:ad)
OR Hertfordshire:ad OR Herefordshire:ad OR Humberside:ad OR Huntingdon:ad OR 'Isle of Wight':ad OR
Kent:ad OR Lancashire:ad OR Leicestershire:ad OR Lincolnshire:ad OR London:ad OR Manchester:ad OR Merseyside:ad OR
Middlesex:ad OR Norfolk:ad OR Northamptonshire:ad OR Northumberland:ad OR Nottinghamshire:ad OR Oxfordshire:ad OR
Peterborough:ad OR Rutland:ad OR Shropshire:ad OR Salop:ad OR Somerset:ad OR Yorkshire:ad OR Staffordshire:ad OR
Suffolk:ad OR Surrey:ad OR Sussex:ad OR (Tyne:ad AND Wear:ad) OR Warwickshire:ad OR Midlands:ad OR Westmorland:ad
OR Wiltshire:ad OR Worcestershire:ad OR 'Isle of Man':ad OR Jersey:ad OR Guernsey:ad OR 'Channel Islands':ad OR
Aberdeen:ad OR Aberdeenshire:ad OR Angus:ad OR Forfarshire:ad OR Argyll:ad OR Ayrshire:ad OR Banffshire:ad OR
Berwickshire:ad OR Bute:ad OR Caithness:ad OR Clackmannanshire:ad OR Cromartyshire:ad OR Dumfriesshire:ad OR
Dunbartonshire:ad OR Dumbarton:ad OR Dundee:ad OR Lothian:ad OR Haddingtonshire:ad OR Edinburgh:ad OR Fife:ad OR
Glasgow:ad OR Inverness-shire:ad OR Kincardineshire:ad OR Kinross-shire:ad OR Kirkcudbrightshire:ad OR Lanarkshire:ad OR
Midlothian:ad OR Moray:ad OR Elginshire:ad OR Nairnshire:ad OR Orkney:ad OR Peeblesshire:ad OR Perthshire:ad OR
Renfrewshire:ad OR (Ross:ad AND Cromarty:ad) OR Ross-shire:ad OR Roxburghshire:ad OR Selkirkshire:ad OR Shetland:ad OR
Zetland:ad OR Stirlingshire:ad OR Sutherland:ad OR Linlithgowshire:ad OR Wigtownshire:ad OR Anglesey:ad OR
Brecknockshire:ad OR Caernarfonshire:ad OR Carmarthenshire:ad OR Cardiganshire:ad OR Ceredigion:ad OR Clwyd:ad OR
Denbighshire:ad OR Dyfed:ad OR Flintshire:ad OR Glamorgan:ad OR Gwent:ad OR Gwynedd:ad OR Merionethshire:ad OR
Montgomeryshire:ad OR Monmouthshire:ad OR Pembrokeshire:ad OR Powys:ad OR Radnorshire:ad OR Aontrrim:ad OR
Aontroim:ad OR 'Contae Aontroma':ad OR Antrim:ad OR Antrim:ad OR Entrim:ad OR Armagh:ad OR 'Ard Mhacha':ad OR
Airmagh:ad OR Belfast:ad OR (Down:ad AND (district:ad OR council:ad OR County:ad)) OR 'An Dún':ad OR 'an Dúin':ad OR
Doon:ad OR Doun:ad OR Fermanagh:ad OR 'Fear Manach':ad OR 'Fhear Manach':ad OR Fermanay:ad OR Londonderry:ad OR
Doire:ad OR Dhoire:ad OR Lunnonderrie:ad OR Derry:ad OR Birmingham:ad OR Leeds:ad OR Sheffield:ad OR Bradford:ad OR
Liverpool:ad OR Albania*:ad OR Shqiperi*:ad OR Schqipt*:ad OR Berat:ad OR Beratit:ad OR Diber:ad OR Dibres:ad OR
Durrës:ad OR Durrësit:ad OR Elbasan:ad OR Elbasanit:ad OR Fier:ad OR Fierit:ad OR Gjirokaster:ad OR Gjirokastres:ad OR
Korce:ad OR Korces:ad OR Kukes:ad OR Kukesit:ad OR Lezhes:ad OR Lezhe:ad OR Shkodres:ad OR Shkoder:ad OR Tirana:ad OR
Tirane*:ad OR Vlore:ad OR Vlores:ad OR Kamez:ad OR Beraz:ad OR Lushnje:ad OR Makedon*:ad OR Macedon*:ad OR Fyrom:ad
OR Istocen:ad OR Severoistocen:ad OR Jugoistocen:ad OR Jugozapaden:ad OR Pelagonski:ad OR Pelagonia:ad OR Poloski:ad OR
Polog:ad OR Skopski:ad OR Skopje:ad OR Kconje:ad OR Vardar*:ad OR Bitola:ad OR Kumanovo:ad OR Prilep:ad OR Tetovo:ad
OR Tetova:ad OR Tetove:ad OR Veles:ad OR Stip:ad OR Shtip:ad OR Ohrid:ad OR Gostivar:ad OR Gostivari:ad OR Strumica:ad
OR Iceland:ad OR Icelandic*:ad OR islenska*:ad OR Icelander*:ad OR islendiga*:ad OR Islendigar:ad OR Inslenska:ad
OR Reykjavik:ad OR Reykjavíkurborg:ad OR Hofudborgarsvaedi:ad OR Sudurnes:ad OR Vesturland:ad OR Vestfirðir:ad
OR Westfjords:ad OR Nordurland:ad OR Austurland:ad OR Sudurland:ad OR Kopavogur:ad OR Hafnarfjörður:ad OR Akureyri:ad
OR Gardabaer:ad OR Mosfellsbaer:ad OR Keflavik:ad OR Akranes:ad OR Selfoss:ad OR Seltjarnarnes:ad OR Montenegro*:ad OR

'Crna Gora':ad OR Crnogorci:ad OR Andrijevica:ad OR (Bar:ad AND (Opstina:ad OR municipality:ad OR city:ad OR town:ad)) OR Berane:ad OR 'Bijelo polje':ad OR Budva:ad OR Cetinje:ad OR Danilovgrad:ad OR Gusinje:ad OR 'herceg Novi':ad OR Kolasin:ad OR Kotor:ad OR Mojkovac:ad OR Niksic:ad OR Petinja:ad OR Plav:ad OR Pluzine:ad OR Pljevlja:ad OR Podgorica:ad OR Rozaje:ad OR Savnik:ad OR Tivat:ad OR Ulcinj:ad OR Zabljak:ad OR Serbia*:ad OR Srbija:ad OR Serb:ad OR Serbs:ad OR Srbi:ad OR Vojvodina:ad OR Belgrade:ad OR Beograd:ad OR Sumadija:ad OR Kolubara:ad OR Kolubarski:ad OR Macva:ad OR Macvanski:ad OR Moravica:ad OR Moravicki:ad OR Pomoravlje:ad OR Pomoravski:ad OR Rasinski:ad OR Rasina:ad OR Raska:ad OR Raski:ad OR Sumadijski:ad OR Zlatibor:ad OR Zlatiborski:ad OR Bor:ad OR Borski:ad OR Branicevo:ad OR Branicevski:ad OR Jablanica:ad OR Jablanicki:ad OR Nisava:ad OR Nisavski:ad OR Pcinja:ad OR Pcinjski:ad OR Pirot:ad OR Pirotski:ad OR Podunavlje:ad OR Podunavski:ad OR Toplica:ad OR Toplicki:ad OR Zajecar:ad OR Zajecarski:ad OR Banat:ad OR Sredjebanatski:ad OR Backa:ad OR Severnbacki:ad OR Severnbanatski:ad OR Juznbacki:ad OR Juznbanatski:ad OR Srem:ad OR Sremski:ad OR Zapadnbacki:ad OR 'Novi Sad':ad OR 'Novy Sad':ad OR Ujvidek:ad OR Nis:ad OR Nish:ad OR Nissa:ad OR Kragujevac:ad OR Subotica:ad OR Szabadka:ad OR Zrenjanin:ad OR Pancevo:ad OR Cacak:ad OR Kraljevo:ad OR 'Novi Pazar':ad OR 'Novy Pazar':ad OR Turkey:ad OR Turkiye:ad OR Turkish:ad OR Turk:ad OR Turkc*:ad OR Adana:ad OR Adiyaman:ad OR Ayfon*:ad OR Agri:ad OR Aksaray:ad OR Amasya:ad OR Ankara:ad OR Antalya:ad OR Ardahan:ad OR Artvin:ad OR Aydin:ad OR Balikesir:ad OR Bartin:ad OR Batman:ad OR Bayburt:ad OR Bilecik:ad OR Bingol:ad OR Bitlis:ad OR Bolu:ad OR Burdur:ad OR Bursa:ad OR Canakkale:ad OR Cannkiri:ad OR Corum:ad OR Denizli:ad OR Diyarbakir:ad OR Duzce:ad OR Edirne:ad OR Elazig:ad OR Erzincan:ad OR Erzurum:ad OR Eskishir:ad OR Gaziantep:ad OR Giresun:ad OR Gumushane:ad OR Hakkari:ad OR Hatay:ad OR Igdir:ad OR Isparta:ad OR Istanbul:ad OR Izmir:ad OR Kahramanmaras:ad OR Karabuk:ad OR Karaman:ad OR Kars:ad OR Kastamonu:ad OR Kayseri:ad OR Kirikkale:ad OR Kirklarely:ad OR Kirklareli:ad OR Kirsheir:ad OR Kocaeli:ad OR Konya:ad OR Kutahya:ad OR Malatya:ad OR Manisa:ad OR Mardin:ad OR Mersin:ad OR Mugla:ad OR Mus:ad OR Nevsehir:ad OR Nigde:ad OR Ordu:ad OR Osmaniye:ad OR Rize:ad OR Sakarya:ad OR Samsun:ad OR Sanliurfa:ad OR Siirt:ad OR Sinop:ad OR Sivas:ad OR Sirnak:ad OR Tekirdag:ad OR Tokat:ad OR Trabzon:ad OR Tunceli:ad OR Usak:ad OR (Van:ad AND (province:ad OR ili:ad)) OR Yalova:ad OR Yozgat:ad OR Killis:ad OR Bosnia*:ad OR Herzegov*:ad OR Herzegonine:ad OR Bosna:ad OR Bosne:ad OR Bosanski:ad OR Bosanac:ad OR Bosanci:ad OR Srpska:ad OR Brcko:ad OR Posavski:ad OR Posavina:ad OR posavska:ad OR Tuzlanski:ad OR Tuzla:ad OR Tuzlanska:ad OR 'Zenicko dobojski':ad OR 'Zenicko dobojska':ad OR Zenica:ad OR 'Bosansko Podrinjski':ad OR 'Bosansko Podrinjska':ad OR Srednjobosanski:ad OR hercegovacko:ad OR Zapadnohercegovacki:ad OR Zapadnohercegovacka:ad OR Sarajevo:ad OR Sarajevska:ad OR 'Kanton 10':ad OR '10 kanton':ad OR Hercegbosanska:ad OR 'Unsko sanski':ad OR 'Una Sana':ad OR 'Banja Luka':ad OR bijeljina:ad OR Mostar:ad OR Prijedor:ad OR Cazin:ad OR Dobojski:ad OR Zupanja:ad OR Kosov*:ad OR Ferizaj*:ad OR Urosevac*:ad OR Gjakov*:ad OR Dakovic*:ad OR Gjilan*:ad OR Gnjilan*:ad OR Mitrovic*:ad OR Pejes:ad OR Peja:ad OR Peje:ad OR Pecki:ad OR Pec:ad OR Pristin*:ad OR Prishtin*:ad OR Pristinski:ad OR Prizrenit:ad OR Prizrenski:ad OR Prizen:ad OR Prizen:ad OR Prizeni:ad OR Produjev*:ad OR Vucitrn:ad OR Vushtrri*:ad OR 'Suva reka':ad OR Suhareka:ad OR Besiana:ad OR Metohija:ad OR Dukagjini:ad OR Dukagjinit:ad OR Liechtenstein:ad OR Lienchtensteiner*:ad OR Balzers:ad OR Eschen:ad OR Gamprin:ad OR Mauren:ad OR Planken:ad OR Ruggell:ad OR Schaan:ad OR Schellenberg:ad OR Triesen:ad OR Triesenberg:ad OR Vaduz:ad OR Norway:ad OR Norwegian*:ad OR Norge:ad OR Noreg:ad OR Norgga:ad OR Akershus:ad OR 'Aust Agder':ad OR Buskerud:ad OR Finnmark:ad OR Hedmark:ad OR Hordaland:ad OR 'More og Romsdal':ad OR 'More and Romsdal':ad OR Nordland:ad OR Trondelag:ad OR Oppland:ad OR Oslo:ad OR Ostfold:ad OR Rogaland:ad OR 'Sogn og fjordane':ad OR 'Sogn and fjordane':ad OR 'sogn fjordane':ad OR Telemark:ad OR Troms:ad OR Romsa:ad OR Romssa:ad OR 'Vest Agder':ad OR Vestfold:ad OR Bergen:ad OR Stavanger:ad OR Sandnes:ad OR Trondheim:ad OR Trondhjem:ad OR Kaupangen:ad OR Nidaros:ad OR Drammen:ad OR Fredrikstad:ad OR Skien:ad OR Tromso:ad OR Sarpsborg:ad OR Switzerland:ad OR Schweiz:ad OR Schweizerische:ad OR Swiss:ad OR Suisse*:ad OR Svizzera:ad OR Svizzeri:ad OR Svizzers:ad OR Svizra:ad OR Helvetica:ad OR Aargau:ad OR Argovia:ad OR Ausserrhoden:ad OR 'Outer Rhodes':ad OR Innerrhoden:ad OR 'Inner Rhodes':ad OR Basel:ad OR Bale:ad OR Basilea:ad OR Bern:ad OR Berne:ad OR Berna:ad OR Fribourg:ad OR Freiburg:ad OR Friburg:ad OR Geneva:ad OR Geneve:ad OR Genf:ad OR Ginevra:ad OR Geneva:ad OR Glarus:ad OR Graubunden:ad OR Graubuenden:ad OR Grisons:ad OR Grigioni:ad OR Grischun:ad OR jura:ad OR Lucerne:ad OR Luzern:ad OR Losanna:ad OR Neuchatel:ad OR Nidwalden:ad OR Nidwald:ad OR Obwalden:ad OR Obwald:ad OR Schaffhausen:ad OR Schaffhouse:ad OR Schwyz:ad OR Solothurn:ad OR Soleure:ad OR Thurgau:ad OR Thurgovia:ad OR Ticino:ad OR Tessin:ad OR Uri:ad OR Valais:ad OR Wallis:ad OR Vaud:ad OR Zug:ad OR Zurich:ad OR Zuerich:ad OR Zurigo:ad OR Lausanne:ad OR Losanna:ad OR Winterthur:ad OR Winterthour:ad OR 'St Gallen':ad OR 'Saint Gallen':ad OR 'Sankt Gallen':ad OR 'Saint Gall':ad OR 'San Gallo':ad OR 'Son Gagl':ad OR Turtig:ad OR Gibraltar:ad OR Gibraltar*:ad OR Hebrid*:ad OR Hebrid*:ad OR Svalbard*:ad OR 'United States/exp OR "United States":ad OR USA:ad OR US:ad OR U.S.A.:ad OR America*:ad OR "United States":ad OR USA:ad OR US:ad OR U.S.A.:ad OR America*:ad OR Alabama:ad OR Alaska:ad OR Arizona:ad OR Arkansas:ad OR California:ad OR Colorado:ad OR Connecticut:ad OR Delaware:ad OR Florida:ad OR Georgia:ad OR Hawaii:ad OR Idaho:ad OR Illinois:ad OR Indiana:ad OR Iowa:ad OR Kansas:ad OR Kentucky:ad OR Louisiana:ad OR Maine:ad OR Maryland:ad OR Massachusetts:ad OR Michigan:ad OR Minnesota:ad OR Mississippi:ad OR Missouri:ad OR Montana:ad OR Nebraska:ad OR Nevada:ad OR "New Hampshire":ad OR "New Jersey":ad OR "New Mexico":ad OR "New York":ad OR "North Carolina":ad OR "North Dakota":ad OR Ohio:ad OR Oklahoma:ad OR Oregon:ad OR Pennsylvania:ad OR "Rhode Island":ad OR "South Carolina":ad OR "South Dakota":ad OR Tennessee:ad OR Texas:ad OR Utah:ad OR Vermont:ad OR Virginia:ad OR Washington:ad OR "West Virginia":ad OR Wisconsin:ad OR Wyoming:ad OR Alabama:ad OR Alaska:ad OR Arizona:ad OR Arkansas:ad OR California:ad OR Colorado:ad OR Connecticut:ad OR Delaware:ad OR Florida:ad OR Georgia:ad OR Hawaii:ad OR Idaho:ad OR Illinois:ad OR Indiana:ad OR Iowa:ad OR Kansas:ad OR Kentucky:ad OR Louisiana:ad OR Maine:ad OR Maryland:ad OR Massachusetts:ad OR Michigan:ad OR Minnesota:ad OR Mississippi:ad OR Missouri:ad OR Montana:ad OR Nebraska:ad OR Nevada:ad OR "New Hampshire":ad OR "New Jersey":ad OR "New Mexico":ad OR "New York":ad OR "North Carolina":ad OR "North Dakota":ad OR Ohio:ad OR Oklahoma:ad OR Oregon:ad OR Pennsylvania:ad OR "Rhode Island":ad OR "South Carolina":ad OR "South Dakota":ad OR Tennessee:ad OR Texas:ad OR Utah:ad OR Vermont:ad OR Virginia:ad OR Washington:ad OR "West Virginia":ad OR Wisconsin:ad OR Wyoming:ad OR 'Canada'/exp OR Canada:ad OR Canada:ad OR Canadian:ad OR Canadian:ad OR 'Australia'/exp OR Australia*:ad OR Australia*:ad OR 'New Zealand'/exp OR "New Zealand":ad OR "New Zealand":ad OR global:ad OR world:ad OR worldwide:ad OR world:ad

Annex 3. Quality appraisal checklists other than NICE

Cross-sectional study

Code as - - / - / + - / + / ++ or NA if not applicable

Author	
Countries	
Internal validity	
The study addresses an appropriate and clearly focused question	
The study population is clearly described	
The population is a representative sample of the source population	
The outcome measures are described	
The assessment of outcome is made blind to exposure status	
Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the outcome assessment	
Exposure status is measured in a standard, valid and reliable way	
The measurement of outcome is clearly described (e.g., written questionnaire, face-to-face interview, internet survey)	
The main potential confounders are identified and taken into account in the design and analysis	
Comparison is made between participants and non-participants to establish their similarities/ differences	
Confidence intervals are provided	
If study is carried out at more than one site, results are comparable for all site	
Overall assessment of the study	
How well was study done to minimise confounding/ bias, and to establish a causal relationship?	
If coded + or -, what is the likely direction in which bias might affect the study results?	
Was the likelihood of bias due to measuring exposure and outcome at the same moment, taken into account by the authors?	
Are you certain that the overall effect is due to the exposure being investigated?	
Are the results of the study applicable to the patient group targeted in the search question?	
Comments	
Include or exclude	
If exclusion, give reason	

Surveillance study

Code as - / - / + / + / ++ or NA if not applicable

Author	
Countries	
Internal validity	
The study addresses an appropriate and clearly focused question	
The population being studied is selected from a data source that is representative for the overall population of interest	
The outcomes are clearly defined	
The main potential confounders are identified and taken into account in the design and analysis	
Additional questions	
Are epidemiological outcomes described that can be used in this review, e.g. incidences or rates per 100,000 or proportion of cases?	
Is the study population large enough to be a representative sample of the source population?	
Is the disease of interest the main subject of the paper?	
Are the outcomes of the study based on observed cases (and not on assumptions or models?)	
The surveillance period is long enough to detect new cases and to accurately calculate prevalence/incidence rates	
Overall assessment of the study	
Are the results valid?	
Are the results applicable to the population targeted in the search question?	
Comments	
Include or exclude	
If exclusion, give reason	

Other research (applied to outbreak studies)

Code as - / - / + / + / ++ or NA if not applicable

Author	
Countries	
Internal validity	
The study addresses an appropriate and clearly focused question	
The study population is clearly described	
The population is representative of the source population	
Exposure status is measured in a standard, valid and reliable way	
The outcomes are clearly defined	
Variation (e.g. range, SD) in outcome of interest is provided	
The diagnosis of interest the main subject of the paper	
Overall assessment of the study	
Are the results valid?	
Are the results applicable to the population targeted in the search question?	
Comments	
Include or exclude	
If exclusion, give reason	

Annex 4. Expert panel members and ECDC/EMCDDA staff

Expert panel members

Name	Organisation	Country
Viktor Mravcik	Government of Czech Republic	Czech Republic
Fadi Meroueh	Association des Professionnels de Santé Exerçant en Prison	France
Laurent Michel	Centre Pierre Nicole, Croix Rouge Française	France
Heino Stöver	HA-REACT	Germany
Ruth Zimmerman	Robert Koch Institute	Germany
Erica Cardoso	Direcção-Geral de Reinserção e Serviços Prisionais (DGRSP), Ministério de Justiça	Portugal
Teresa Galhardo	Direcção-Geral de Reinserção e Serviços Prisionais (DGRSP)	Portugal
Rui Morgado	Direcção-Geral de Reinserção e Serviços Prisionais (DGRSP), Ministério de Justiça	Portugal
Lucia Mihailescu	Formerly with Romanian National Administration of Penitentiaries	Romania
Jose-Manuel Arroyo-Cobo	General Secretariat of Penitentiary Institutions	Spain
Stefan Eggist	Federal Office of Public Health	Switzerland
Hans Wolff	University of Geneva	Switzerland
Sharon Hutchinson	NHS National Services Scotland & Glasgow Caledonian University	UK
Eamonn O'Moore	Public Health England	UK
Alison Hannah	Penal Reform International	International
Jan Malinowski	Council of Europe	International
Lars Møller	WHO	International
Ehab Salah	United Nations on Drugs and Crime	International

ECDC and EMCDDA staff who attended expert panel meetings

Name	Organisation
Dagmar Hedrich	EMCDDA
Marialinda Montanari	EMCDDA
Liesbeth Vandam	EMCDDA
Helena de Carvalho Gomes	ECDC
Lara Tavoschi	ECDC

Annex 5. Exclusion table peer-reviewed literature and corresponding reference list

Exclusion table second selection step

Exclusion reason (number of articles)	References
No data on objectives (n=126)	[1-123]
Narrative reviews (n=31)	[124-154]
Insufficient (description of) methodology (n=27)	[155-181]
Non-pertinent publication types (n=19)	[182-200]
Case report/small cases series (n=14)	[201-214]
Systematic review (n=12) (checked for possibly missed relevant individual articles)	[215-226]
Incorrect population (n=9) (e.g. inmates in a police detention centre or juvenile detention centre, women of incarcerated men)	[227-235]
Duplicate articles (n=5)	[236-240]
Modelling studies (n=2)	[241, 242]
More recent data available (n=2)	[243, 244]
Not country of interest (n=2)	[245, 246]

Reference list of excluded articles during second selection step

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Annex 7. Report on field researchers for grey literature

Field researchers

A field researcher was appointed through HWBs in each of the following countries where the federation is active, namely UK, Germany, Spain, France and Italy. Several attempts have been made to find a field researcher for the Netherlands, through an e-mail exchange with Dr Michel Westra (member of HWBs) and Dr Kim van Rooy.

The European field researchers appointed as responsible for each country were:

- Ruth Gray, UK
- Sofia Victoria Casado Hoces, Antonio Gonzalez Gomez, Spain
- Leon Weichert, Germany
- Deborah Iwanikow, France
- Giordano Madeddu, Italy (coordinator)

Materials

The grey literature research officially started on 18th April 2016, with an official letter and call to the researchers sent by HWBs' Secretariat. The definitive deadline for the collection of materials regarding the three macro areas (HIV, viral hepatitis, injecting-related infections) was settled on 31st July 2016. A call for paper (see below) was issued by HWBs and translated in the relevant language by the field researcher. It was up to the field researcher whether to work in team with any other expert they wished to involve, or to perform the research on their own.

Results

The following are the results concerning the three macro areas:

1. UK

The first batch of documents has been received on 10th May 2016. A total of 2 documents with related evidence tables has been sent to HWBs.

2. Spain

The first batch of documents has been received on 28th April 2016. A further batch was received from HWB on 30th July 2016, and was sent to the coordinator on July 14th, 2017. A total of 57 documents with related evidence tables has been sent to HWBs.

3. Germany

The first batch of documents has been received on 24th May 2016. A further batch was received from HWB on 30th July 2016, and sent to the coordinator on July 14th, 2017. A total of 4 documents with related evidence tables has been sent to HWBs. The number of documents might seem limited. This is due to the fact that the prison healthcare system in Germany is not managed by central headquarters, instead is handled by the single Länder, thus jeopardising the planning and introduction of general guidelines. This issue has affected negatively the research, which methodology has been described by Dr. Weichert in a specific document.

4. France

The first batch of documents has been received on 6th June 2016. A total of 2 documents not including the related evidence tables has been sent to HWBs.

5. Italy

The first batch of documents has been received on 24th May 2016. A further batch of documents was received by HWB on 9th June 2017 and a third batch on 12th July 2017 and was sent to the coordinator on 14th July 2017. A total of 28 documents were received.

Call for papers

This guidance will support field researchers work in researching and collecting relevant grey literature documents in the following prioritized macro areas:

- Macro area 4: Prevention, care and treatment of HIV, including throughcare
- Macro area 5: Prevention, care and treatment of viral hepatitis, with a focus on treatment for hepatitis C, including throughcare
- Macro area 6: Prevention and control of injecting-related infections among current or former drug users, including throughcare.

Who is the focus?

Prison population: adult people aged 18 years or older in prison settings (i.e. those detained or in remand and those 'going through the gate').

Which is the setting?

Prison setting: prisons and other custodial settings which function as prison excluding migrant centers and police detention rooms

Key issues and scoping questions

The key issues and scoping questions are useful to guide the systematic review of the grey literature.

Macro area 4

Key issue: prevention, care and treatment of HIV, including throughcare

Scoping questions

- Which prevention interventions for HIV are effective in prison settings?
- Which care and/or treatment interventions aimed at control of HIV are effective in prison settings?
- Which service models for prevention, care and/or treatment of HIV are effective in prison settings?
- Which prevention interventions for HIV are cost-effective in prison settings?
- Which care and/or treatment interventions aimed at control of HIV are cost-effective in prison settings?
- Which service models for prevention, care and/or treatment of HIV are cost-effective in prison settings?
- What is the acceptance/uptake/coverage of prevention, care and/or treatment of HIV in prison settings?
- How to improve the acceptance/uptake/coverage of prevention, care and/or treatment of HIV in prison settings?
- Who should be targeted for prevention, care and/or treatment of HIV in prison settings?

Macro area 5

Key issue: prevention, care and treatment of viral hepatitis, with a focus on treatment for hepatitis C, including throughcare

Scoping questions

- Which prevention interventions for viral hepatitis are effective in prison settings?
- Which care and/or treatment interventions aimed at control of viral hepatitis are effective in prison settings?
- Which service models for prevention, care and/or treatment of viral hepatitis are effective in prison settings?
- Which prevention interventions for viral hepatitis are cost-effective in prison settings?
- Which care and/or treatment interventions aimed at control of viral hepatitis are cost-effective in prison settings?
- Which service models for prevention, care and/or treatment of viral hepatitis are cost-effective in prison settings?
- What is the acceptance/uptake/coverage of prevention, care and/or treatment of viral hepatitis in prison settings?
- How to improve the acceptance/uptake/coverage of prevention, care and/or treatment of viral hepatitis in prison settings?
- Who should be targeted for prevention, care and/or treatment of viral hepatitis in prison settings?

Macro area 6

Key issue: prevention and control of injecting-related infections among current or former drug users, including throughcare

Scoping questions

- Which prevention interventions for injecting-related infections among current drug users are effective in prison settings?
- Which interventions aimed at control of injecting-related infections among current or former drug users are effective in prison settings?
- Which service models for prevention and control of injecting-related infections among current or former drug users are effective in prison settings?
- Which prevention interventions for injecting-related infections among current or drug users are cost-effective in prison settings?
- Which interventions aimed at control of injecting-related infections among current or former drug users are cost-effective in prison settings?

- Which service models for prevention and control of injecting-related infections among current or former drug users are cost-effective in prison settings?
- What is the acceptance/uptake/coverage of prevention and control of injecting-related infections among current or former drug users in prison settings?
- How to improve the acceptance/uptake/coverage of prevention and control of injecting-related infections among current or former drug users in prison settings?

What kind of papers?

National field researchers were asked to collect and summarise (in a short pre-defined format):

Existing documents describing:

- National guidelines
- Institutional protocols
- Unpublished research reports/national conference abstracts

Summaries of:

- Intervention case studies
- Service models

regarding the macro areas of this specific contract (prevention, care and treatment of HIV and viral hepatitis, and prevention and control of injecting-related infections among current or former drug users).

Inclusion and exclusion criteria

The following inclusion and exclusion criteria were applied for the grey literature search:

Table A. Inclusion and exclusion criteria

	Inclusion	Exclusion
Period of publication	Conference abstracts: from 2010 onwards Other documents: from 2005 onwards	
Content of document	<ul style="list-style-type: none"> • Conference abstracts • Guidelines • Intervention or clinical protocols • Unpublished research results • Case studies/service models, including measures of effectiveness 	
Document quality	Only grey literature documents with a methods section or an overview of sources. This means that when information relevant to our objectives is retrieved from a grey literature document, it must be clear what the source of this information is	Document without a clear source/reference for the relevant information
Document population	Adults in prisons, jails and other custodial settings that function as a prison <ul style="list-style-type: none"> • Detained persons, including persons in remand • Persons 'going through the gate' (e.g. prison guards, healthcare workers, etc.) 	<ul style="list-style-type: none"> • Children (<18 years) • Persons in police custody • Persons in migrant centres
Subject of the document	<ul style="list-style-type: none"> • Prevention, care and treatment of HIV • Prevention, care and treatment of viral hepatitis • Prevention and control of injecting-related infections among current or former drug users 	
Geographical area	<ul style="list-style-type: none"> • EU/EEA 	
Specific outcomes of interest	<ul style="list-style-type: none"> • Quantitative outcomes • Qualitative outcomes 	<ul style="list-style-type: none"> • No exclusion based on outcomes

Data extraction and summary

Relevant data will be extracted from included documents in order to create evidence tables, or case studies/service models are summarised according to the template described below. The tables/summaries were compiled by each field researcher and reviewed by the HWBs researcher responsible for the grey literature.

Ad 1. Existing national guidelines, institutional protocols and unpublished research reports/conference abstracts

The included documents were summarised by collecting, per individual record, relevant information in a standardised data extraction format (Evidence table, see Annex below).

Ad 2. Intervention case studies and service models

Case studies and service models can be summarised according to pre-defined format, including:

- Source
- Setting
- Target population(s) (country, prison setting, risk groups)
- Clearly described accounts of their intervention/service model related to the relevant macro area (see also scoping questions above)
- Elements of evaluation/monitoring or evidence of success (e.g. prevention intervention, pre- and post-intervention infection rate)
- Resource requirements
- Linkage to care

Case studies/service models can be included when at least the third and fourth item on the list are met.

Table B: Evidence table for national guidelines, institutional protocol and unpublished research reports/conference abstracts

Reference	Source	Type of document	Setting, population	Intervention	Results	Comments
Author, title, year, web link (when available)	Institute/company, etc. that prepared the document	National guideline, institutional protocol unpublished research, report/conferences abstract	Country, prison setting, risk groups, etc. to which the results apply	Type of intervention or service model: brief description	Relevant results on the objectives given in the document: per objectives	Any additional information that is relevant for interpreting the results

Annex 8. Exclusion table grey literature and corresponding reference list

Exclusion table second selection step

Exclusion reason (number of articles)	References
No data on objectives (n=60)	[1-74]
No country of interest (n=6)	[75-81]
More recent data available (n=1)	[82]
Duplicate with included in PRL (n=1)	[83]
Outside data range (n=1)	[84]

Reference list of excluded articles during second selection step

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Annex 9. Summary tables and guideline summaries – Prevention of BBVs

General BBVs prevention

Effectiveness

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
Intervention: condom distribution								
Non-EU/EEA PRL	Dolan, 2004 [45] Australia Cross-sectional study	23 NSW male correctional centres November 1997 – September 1998	Installation of 150 condom vending machines - since November 1997 - free use - boxes containing 1 condom, 1 sachet of lubricant, 1 sealable disposal bag and an information card	n=556 inmates and n=50 staff NR No comparator	NR	Use condom machine: 28% (n/N NR) - Every now and then: 52% - Once a week: 21% - Every couple of weeks: 9% - Only once: 15% 40% used condoms for sex, 19% used the sealable disposal bags for storage of substances (e.g. tobacco), 25% used the contents of the box for self-masturbation (n/N NR) The frequency of condom use since programme introduction among sexually active inmates for anal and oral intercourse (n=44, n=54) was every time (52%, 28%), often (7%, 2%), sometimes (16%, 22%), never (21%, 44%) and no sex since condom availability (4%, 4%) 294,853 condoms dispensed during study period; 24,571 per month	NR	Very low
Intervention: safe tattooing programme								
EU/EAA GL	Humet, 2012 [46] Spain	Correctional facilities in Catalunya September 2011 –	Safe tattooing programme	n=86 inmates NR No comparator	NR	66% (57/86) inmates requested safe tattoos 68% (39/57) performed safe tattooing	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
	Retrospective study	February 2012				<ul style="list-style-type: none"> - 30.5% (12/39) did not perform tattoos before and 69.5% (27/39) had previously been tattooed - Of the latter group 85% (23/27) were tattooed using uncontrolled equipment, 43% (10/23) of these during imprisonment <ul style="list-style-type: none"> 32% (18/57) did not perform safe tattoos - 50% (9/18) because of lack of money and 50% (9/18) because of release from prison 		
Group behaviour intervention vs. control								
Non-EU/EEA PRL	Lehman, 2015 [47] USA RCT	8 prison facilities in 2 states NR	<p>WaySafe:</p> <ul style="list-style-type: none"> - 6 weekly 1-hr sessions by a trained counsellor in groups of 10-20 inmates - Variety of group-based and participatory activities¹ - Added to TAU by focusing on decision making in an engaging and highly interactive format <p>TAU:</p> <ul style="list-style-type: none"> - Modified therapeutic community programming (group and individual) - Didactic, lecture format covering basic HIV information - Offenders were required to attend 20 hours in total 	<p>n=653 WaySafe vs. n=604 TAU</p> <p>In last phase of prison-based substance abuse treatment; sufficient time left before release (from 2-3 months) to complete the study</p> <p>WaySafe vs. TAU</p>	NR	<ul style="list-style-type: none"> * WaySafe higher mean score at post-test (1 week after end of intervention, in prison) than TAU for all 5 measures (all p<0.001), effect sizes: <ul style="list-style-type: none"> - HIV knowledge confidence: 0.424 - Avoiding risky sex: 0.416 - Avoiding risky drug use: 0.270 - HIV services and testing: 0.346 - Risk reduction skills: 0.381 *Significant pre-test to post-test (1 week after end of intervention) increases on all 5 scales for both the TAU and WaySafe groups, although there were larger changes for the WaySafe group on each scale: <ul style="list-style-type: none"> - WaySafe: post-test/pre-test difference score ranges 2.7-5.3, effect sizes 0.491-0.795 - TAU: post-test/pre-test difference score ranges 1.3-2.6, effect sizes 0.232 to 0.352 	<p>Study focuses solely on inmates receiving substance abuse treatment</p> <p>There were significant differences between WaySafe and TAU participants on all 5 scales in 4 facilities, and significant differences for part of the scales in the other 4 facilities</p>	Low
Group skills-building intervention vs. discussion intervention								
Non-EU/EEA PRL	St. Lawrence, 1997 [50] USA RCT	State women's prison NR	<p>SCT intervention:</p> <ul style="list-style-type: none"> - 4 sessions provided specific skills training using instruction, modelling and skill rehearsal 	<p>n=90 inmates</p> <p>Females</p> <p>SCT vs. TGP</p>	NR	<ul style="list-style-type: none"> - Greater improvements in acknowledging a partner's request in SCT group than in TGP group (p<0.02), directly post-intervention - Women in the TGP group showed greater improvements in commitment to change than women in the SCT group (p<0.02), 	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
			<p>TGP intervention:</p> <ul style="list-style-type: none"> - 4 sessions promoted unstructured discussion between participants and included no skill training or rehearsal of risk reduction skills - 4 cohort groups in each intervention condition with 8-15 participants in each group - Group sessions for each condition met once a week for 6 weeks and lasted 90 minutes - Sessions 1 and 2 were identical in both conditions and provided information about HIV/AIDS and other STIs, disease transmission, and local epidemiology; last 4 sessions were parallel in their content emphasis but differed in format and methods, consistent with the theoretical models² 			<p>both directly post-intervention and at 6 months follow-up</p> <ul style="list-style-type: none"> - Women in the SCT group showed greater increases in condom application skills than women in the TGP group ($p < 0.003$), both directly post-intervention and at 6 months follow-up - No significant difference in proposing a safe alternative, refusing unprotected sex/needle sharing, providing a reason for refusal, using 'I' messages, and overall behavioural skill effectiveness rating (all during role-play assessments), and furthermore no difference in perceived HIV risk, self-efficacy, self-esteem, attitudes towards prevention, AIDS knowledge, intentions to use condoms and condom communication 		

AIDS: acquired immunodeficiency syndrome, GL: grey literature, HIV: human immunodeficiency virus, NR: not reported, NSW: New South Wales, PRL: peer-reviewed literature, RCT: randomised controlled trial, SCT: social cognitive theory, STI: sexually transmitted infection, TAU: treatment as usual, TGP: theory of gender and power, USA: United States of America

¹ Sessions: 1. Introduction to mapping, 2. Risk and reasons, 3. Information about the transmittal and prevention of HIV, 4. Should/want problem, 5. Risk scenes, 6. Planning for risks

² SCT: Session 3 - training in correct condom use, Sessions 4-5 - training in refusal, partner negotiation, and information provision skills, Session 6 - connection between drug use and HIV risk and training in correct needle-cleaning and drug refusal skills; TGP: Session 3 - women and condoms, Sessions 4-5 - discussion on sexual communication, Session 6 - discussion about the connection between drug use and high-risk sexual behaviour

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
Intervention: condom distribution										
Non-EU/EEA PRL	Dolan, 2004 [45] Australia Cross-sectional study	23 NSW male correctional centres n=556 inmates and n=50 staff November 1997 – September 1998	Installation of 150 condom vending machines - since November 1997 - free use - boxes containing 1 condom, 1 sachet of lubricant, 1 sealable disposal bag and an information card	Location of machines (n/N NR): - Appropriate: 69% of inmates - Prefer alternative location: NR *More privacy: 65% of inmates *Improved access: 16% of inmates *Preferred alternative locations: shower blocks, within accommodation wings and laundries	Support condom provision: - Inmates: 84% (467/556) - Commissioned/senior officers: 85% (11/13) - Prison officers: 43% (16/37)	NR	NR	Harassment for obtaining condoms (n/N NR): - No: 68% of inmates - Yes, other inmates: 15% of inmates - Yes, officers: 7% of inmates No incidents comprising prison safety/security or incidents of drug concealment Condom availability increases incidence of rape (n/N NR): - Yes: 14% of inmates - No: 72% of inmates	NR	Very low
Non-EU/EEA PRL	May, 2002 [49] USA Cross-sectional study	Central Detention Facility, city jail for Washington DC n=307 inmates and n=200 staff October 2000 – October 2001	Condoms provided by public health and AIDS service organisations during weekly health education classes on HIV prevention, HIV pre- or post-test counselling, or upon request to healthcare staff - since 1993 - free use	11% (34/303) of inmates have been given a condom while being in jail 200 condoms distributed each month	55% (168/303) of inmates and 64% (126/197) of staff think distributing condoms is a good idea as condoms are an effective and low-risk method to prevent the transmission of HIV or STIs Those objecting mentioned: concern	NR	NR	42% of inmates believed condoms would increase likelihood of sex in jail 13% (27/200) of staff reported occurrence of problems caused by condom distribution (not further defined)	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
					of institutional and personal safety; intervention as an endorsement of same gender relationships; inconsistent message of condom availability given that sexual activity in the jail is prohibited by institutional policy			No major security infractions involving condoms No evidence that sexual activity has increased on the basis of disciplinary reports and interviews with jail administrators		
Intervention: safe tattooing programme										
EU/EAA GL	Humet, 2012 [46] Spain Retrospective study	Correctional facilities in Catalunya N=86 inmates September 2011 – February 2012	Safe tattooing programme	NR	68% (39/57) of accepted requests performed safe tattooing	NR	NR	32% (18/57) did not perform safe tattoos: 50% (9/18) because of lack of money and 50% (9/18) because of release from prison	NR	Conference abstract
Group behaviour intervention vs. control										
Non-EU/EEA PRL	Lehman, 2015 [47] USA RCT	8 prison facilities in 2 states n=653 WaySafe vs. n=604 TAU NR	WaySafe: - 6 weekly 1-hr sessions by a trained counsellor in groups of 10-20 inmates - Variety of group-based and participatory activities ¹ - Added to TAU by focusing on decision making in an engaging and highly interactive format TAU:	In last phase of prison-based substance abuse treatment; sufficient time left before release (from 2-3 months) to complete the study	NR	NR	9.8% (136/1393) of those who completed the pre-test survey did not complete a post-test survey (study includes only those 1257 with ≥1 post-test assessment)	NR	Study focuses solely on inmates receiving substance abuse treatment	Low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
			<ul style="list-style-type: none"> - Modified therapeutic community programming (group and individual) - Didactic, lecture format covering basic HIV information - Offenders were required to attend 20 hours in total 							

AIDS: acquired immunodeficiency syndrome, HIV: human immunodeficiency virus, NR: not reported, NSW: New South Wales, PRL: peer-reviewed literature, RCT: randomised controlled trial, STI: sexually transmitted infection, TAU: treatment as usual, USA: United States of America

¹ Sessions: 1. Introduction to mapping, 2. Risk and reasons, 3. Information about the transmittal and prevention of HIV, 4. Should/want problem, 5. Risk scenes, 6. Planning for risks

Cost-effectiveness

Region Source	Reference, country, study design	Prison setting, sample	Perspective, time horizon	Scenarios	Conclusions	Sub-group specific considerations	Level of evidence
Intervention: condom distribution							
Non-EU/EEA PRL	Leibowitz, 2013 [48] USA Cost-effectiveness study	K6G protective custody unit of the LA County Men's Central Jail n=NR gay and transgender inmates	Societal perspective 32 years	Condom distribution: staff visit the unit once a week, at which time inmates line up and may receive a single condom vs. No condom distribution	- 25% of HIV transmissions averted, reducing the number of new infections from 0.8 to 0.6 per month - cost savings over the next 32 years of \$74,777	This study focuses solely on gay and transgender inmates	Low

HIV: human immunodeficiency virus, LA: Los Angeles, NR: not reported, PRL: peer-reviewed literature, USA: United States of America

Guidelines

Nine guidelines that reported on BBVs prevention were included, of which seven were specific to the prison setting (three supranational and four national guidelines) and two were supranational not specific to prison settings.

Summary of guidelines on BBV prevention in prisons settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	<ul style="list-style-type: none"> Health education Information is not enough to prevent the transmission of HIV or hepatitis but it is an essential precondition to the implementation of HIV prevention measures in prisons. The main principle is that <u>all information on blood borne diseases that is available to the community should be tailored to the needs, cultural and educational backgrounds and languages of the prison population, both staff and prisoners.</u> Prevention of sexual transmission and provision of condoms and lubricants <u>Condoms and lubricant should be easily, discreetly and freely accessible. Staff in each prison should identify the best locations for making them accessible, taking into account the layout of the building, leadership and the movement of prisoners within the premises.</u> In addition, it is essential to make condoms available in the intimate visit rooms. <u>Measures to prevent sexual violence,</u> such as proper classification, protection of the most vulnerable, rooms for conjugal visits and reporting systems <u>must also be put in place by prison management.</u> Safe tattooing and piercing equipment <u>Tattooing or piercing is highly prevalent in prisons and closely linked to the prison sub-culture.</u> Research has demonstrated that injecting drug users tend to get tattooed in prison more frequently than other prisoners. Tattooing workshops, with professionals well-trained to give information and show how to operate safely, can be held. Alternatively, professional tattooists could be invited to offer their services. Information, needles and bleach can be distributed to the prisoners. Non-governmental organisations can also play an important role in the implementation of such programmes. Prevention of mother-to-child transmission Prevention of the transmission of (HIV) virus to children begins with access to reproductive health and contraception. As with pregnant women outside prison, pregnant women in prisons need access to the full range of interventions for the prevention of mother-to-child transmission, including family planning and ART prophylaxis for pregnant and breastfeeding mothers. Children born to women living with HIV should be followed up according to national guidelines. Universal precautions and safe health services Universal precautions are essential to ensure a safe workplace for staff and to prevent accidental or iatrogenic transmission of HIV and hepatitis in prisons. In addition to the transmission through blood transfusion of infected blood or through transplantations, HIV and hepatitis can be transmitted through used needles or dental and gynaecological equipment or any medical equipment that can be in contact with blood. Up-to-date sterilisation measures, the safe collection and disposal of sharps and disposal of medical waste, based on guidelines for health (and dental) settings in the community, apply in prisons. Post-exposure prophylaxis Both prisoners and staff can be accidentally exposed to body fluids potentially infected by HIV. Post-exposure prophylaxis is short-term (one month) ART to reduce the likelihood of HIV infection after potential exposure, either through sexual activity or blood. <u>Post-exposure prophylaxis should only be offered for exposure that has the potential for HIV transmission and must be initiated within 72 hours after exposure.</u> It is, therefore, essential that clear guidelines and standard procedures to follow in case of suspected accidental exposure are produced and disseminated. These guidelines, based on national guidelines for post-exposure prophylaxis, should include first aid measures, reporting mechanisms, persons to contact, support and counselling measures.
UNAIDS, 2014 [51]	<p>Condoms need to be easily and discreetly available, ideally in areas such as toilets, shower areas, waiting rooms, workshops or day rooms where prisoners can pick up a condom without being seen by others. Distribution can be carried out by health staff, dispensing machines, trained prisoners (peers) or through a combination of any of these ways. Each prison should determine how best to make condoms available to ensure easy and discreet access. Prisoners should not have to ask for condoms, since few prisoners will do so because they do not want to disclose that they engage in same-sex sexual activity. Condoms should be provided free of charge, and can be made available to all prisoners in a health kit given to them upon entry to the facility. The health kit can also contain HIV and other health information, as well as other items such as a shaving kit, toothbrush, soap, etc. A water-based lubricant should also be provided since it reduces the probability of condom breakage and/or rectal tearing, both of which contribute to the risk of HIV transmission.</p>

	<p>Gender-specific services are often unavailable. Reproductive and general health-care services should be available to all women and available from a female physician if so desired. Some women are pregnant or become pregnant while in detention. Some women give birth or are nursing infants while in prison. The needs related to HIV prevention, treatment, care and support for women and their children are often neglected. Similarly, transgendered people in prisons have special needs that should be addressed, including protection from sexual violence.</p> <p>Women in prisons are especially vulnerable to sexual abuse, including rape, by both male staff and male prisoners. The risks are particularly high when women are detained in facilities adjacent to or within male prisons or when women's quarters are supervised by male prison staff. Women are also susceptible to sexual exploitation and may engage in sex in exchange for goods such as food, drugs, cigarettes and toiletries. In the case of sexual violence, women should have access to the full range of services, including emergency contraception, post-exposure prophylaxis and support.</p>
WHO, 2007 [53]	<p>The proper (correct) and consistent (every time) use of condoms for sexual intercourse, vaginal, anal or oral can greatly reduce a person's risk of acquiring or transmitting sexually transmitted infections, including HIV infection.</p> <p>To be comprehensive, HIV programmes in prisons should include the following components:</p> <ul style="list-style-type: none"> • Preventing new infections through, in particular: (1) reducing sexual transmission by improving life-skills (especially among younger prisoners), providing easy, anonymous access to condoms and lubricants, controlling sexually transmitted infections, notifying partners and implementing measures aimed at reducing sexual abuse and rape; (2) ensuring blood safety by testing transfused blood for HIV, reducing the number of non-vital blood transfusions and enrolling donors at lower risk; and (3) reducing transmission through sharing contaminated injecting equipment by implementing needle and syringe programmes, substitution therapy and peer-based education. • Although tattooing is prohibited in prisons in many countries, it is a very common activity. <u>Tattoos are often applied in unclean conditions using pencils, pens, straight pins or needles</u>. The pigments injected can include carbon, soot, mascara, charcoal and dirt. Dirty tattooing equipment can act as an efficient vehicle for transmitting bloodborne infections. Tattooing is associated with the risk of acquiring HIV, HBV and HCV. • Piercing is also prevalent in many prisons. The body parts that are most commonly pierced are the earlobe and ear cartilage, eyebrow, lip, nose, tongue, nipple, navel and genitals. Preventing the transmission of bloodborne diseases through tattooing requires efforts at individual, institution and population level.
<i>Specific to prison setting – national guidelines</i>	
NICE, 2016 [54]	<p>Offer people in prison information about sexually transmitted infections and available sexual health services.</p> <p>Ensure that people in prison have discreet access to condoms, dental dams and water-based lubricants without the need to ask for them.</p> <p>The potential cost savings of preventing transmission of infectious diseases such as HIV and HCV are very high, and so the prevention of a single case of these diseases by the increased availability of condoms would offset the costs of providing tens of thousands of condoms.</p> <p>Given the prevalence of BBVs in UK prisons, an increase in condom use would be expected to prevent additional infections.</p> <p>Therefore the Guideline Development Group (GDG) considered that improved accessibility of free condoms, dental dams and lubricants, leading to increased use, would be quite likely to be cost saving, and very likely to be cost-effective at a threshold of GBP 20 000 per QALY gained.</p>
UK Department of Health, 2011_a [55]	<p>HIV prevention advice for prisoners</p> <ul style="list-style-type: none"> • Never share injecting drug equipment; this includes syringes, filters, spoons and water as well as needles. • Always use a condom during sex. • Never share tattooing or body piercing equipment. • Use disinfecting tablets to clean injecting equipment, razors etc. <p>Post-exposure prophylaxis (PEP)</p> <p>If someone has been exposed to HIV, there is treatment available which can stop them from becoming infected. It is a four week course of antiretroviral drugs and should be taken as soon as possible (but no later than 72 hours) after potential exposure to HIV to have a chance of stopping infection occurring. It is important to note that PEP can have significant side effects.</p>
UK Department of Health, 2011_b [56]	<p>Prevention</p> <ul style="list-style-type: none"> • There is no vaccine available for the prevention of HIV infection. • The general guidance for prevention of BBVs should be followed to reduce the risk of infection. • Condoms should be used for all sexual contact with a partner whose HIV status is unknown. • Individuals who undergo body piercing/ tattooing should ensure that disposable sterile needles are used. • Sharing of personal items like toothbrushes, injecting equipment and razors should be avoided.

	<ul style="list-style-type: none"> • In a healthcare setting, standard infection control precautions should be adhered to; all blood, body fluids and body tissues should be treated as potentially infectious at all times. • Post exposure prophylactic (PEP) antiviral drugs begun within hours (and certainly no later than 48 to 72 hours after exposure) of a significant exposure to HIV virus may prevent infection occurring. Information, support and advice can be obtained from genitourinary medicine clinics and the Health Protection Unit. Prison healthcare should have a policy for access to PEP and advice. • All pregnant women are now offered an HIV test during pregnancy which has greatly reduced the risk of children being born with HIV infection.
SIMIT/Ministero della Salute (Italy), 2016 [57]	<p>In order to reduce HIV transmission the panel recommends:</p> <ul style="list-style-type: none"> • Free distribution of sterile tattooing equipment. • Free distribution of condoms and condoms vending machines in freely accessible but reserved areas within the prison. • Provide PEP by the prison Infectious Disease Specialist, if needed. • Assure the continuation of Opioid Substitution Treatment (OST) since it is highly effective in reducing HIV transmission among PWID.
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	<p>In addition to the recommended interventions for people in the community, interventions relevant to closed settings include:</p> <ul style="list-style-type: none"> • Prevention of HIV transmission through medical and dental services. • Prevention of transmission of HIV and other bloodborne diseases through tattooing, piercing and other forms of skin penetration. <p>Some other interventions are important and should not be overlooked, such as the distribution of toothbrushes and shavers in basic hygiene kits.</p> <p>The correct and consistent use of condoms with condom-compatible lubricants is recommended for all key populations to prevent sexual transmission of HIV and STIs. (strong recommendation, moderate quality level of evidence)</p> <p>Sexual activity takes place in prisons and other closed settings, but general access to condoms there is limited. It is important to introduce, and expand to scale, condom and lubricant distribution programmes in prisons and other closed settings, without quantity restriction, with anonymity and in an easily accessible manner (e.g. condom vending machines).</p> <p>It is important to provide people in prisons and other closed settings with prevention measures, such as condoms and clean injecting equipment, and not just with information about avoiding risks. People in prisons and other closed settings should have easy, confidential access to needle and syringe programmes.</p> <ul style="list-style-type: none"> • Prison systems should pilot-test and evaluate safer tattooing initiatives to assess whether they reduce the sharing and re-use of tattooing equipment and, thereby, reduce infections. <p>Oral PrEP (containing tenofovir disoproxil fumarate) should be offered as an additional prevention choice for key populations (including prisoners) at substantial risk for HIV infection as part of combination prevention approaches (strong recommendation, high quality of evidence)</p> <p>PEP is given to reduce the likelihood of acquiring HIV infection after possible exposure. WHO PEP guidelines were updated in 2014 and are relevant for all populations. The current recommended duration of PEP is 28 days; the first dose should be taken as soon as possible and within 72 hours after exposure.</p> <p>PEP should be made accessible to all people in prisons and other closed settings who have possibly been exposed to HIV, just as in non-prison settings.</p> <p>VMMC (voluntary medical male circumcision) is not one of the recommended interventions in the prison package.</p> <p>Special consideration should be given to ensuring that pregnant female prisoners have ready access to PMTCT services, as women often face greater barriers to HIV testing, counselling, care and treatment in prison than outside prison.</p>
European AIDS Clinical Society, 2017 [30]	<p>Effective measures to reduce sexual transmission of HIV include:</p> <p>Male condom or female condom use</p> <ul style="list-style-type: none"> • Effective in treated and untreated HIV-positive persons <p>PEP</p> <ul style="list-style-type: none"> • Consider after situations of unprotected anal or vaginal intercourse, if one partner has detectable HIV-VL and the other partner is seronegative • Start as soon as possible and within 48/72 hours post sexual exposure <p>Pre-exposure prophylaxis (PrEP)</p> <ul style="list-style-type: none"> • Effective in HIV-negative persons with high risk sexual behaviour <p>ART for HIV-positive partner</p> <ul style="list-style-type: none"> • Considered effective from 6 months of fully suppressive ART if no active STIs • Consider in e.g. sero-discordant couples

Prevention of injecting-related infections among PWID

Effectiveness

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	Seroconversion	Adverse events	Other outcomes	Level of evidence
Intervention: needles and syringes programmes								
EU/EEA PRL	Stark, 2006 [62] Germany Longitudinal study	1 male and 1 female prison in Berlin October 1998 – June 2001	- Female prison: 3 automatic dispensers, providing a sterile syringe, needle and skin disinfection pad in exchange for a used syringe, or a dummy handed out to new entrants - Male prison: social workers from a NGO exchanged sterile syringes and needles for used equipment 3 times a week	n=174 inmates who had ever used illicit drugs Ever used illicit drugs (injection, inhalational or intranasal use of heroin or cocaine) No comparator	During follow-up (median 12 months): - No HIV or HBV seroconversions - 4 out of 22 HCV seronegative at baseline developed HCV antibodies (incidence 18/100 person-years)	No adverse events possibly related to the project were observed (e.g. overall increase in injection drug use, violence involving needles against staff or other inmates)	All IDUs who seroconverted denied tattooing, piercing, sexual risk behaviour or sharing syringes while in prison, but 3 reported 'frontloading' (dividing up drug doses between ≥2 IDUs involving a used syringe) or sharing of spoons for drug preparation on several occasions in the months preceding seroconversion - 3383 syringes delivered to the female prison (October 1998 to June 2001) - 4571 syringes delivered to the male prison (February 1999 to June 2001)	Very low
EU/EEA PRL	Heinemann, 2001 [61] Germany Cross-sectional study and longitudinal study	1 prison for males and females April 1996 – July 1997	Syringe vending machines, with 1:1 exchange Several machines installed in different stations, partly in locations not accessible by staff	Cross-sectional study: - n=191 intravenous drug using inmates questionnaire/n=22 interview - n=81 prison employees questionnaire/n=9 interview Longitudinal study: - n=231 intravenous drug using inmates No comparator	- 12 HBV and 11 HCV seroconversions observed between M0 (1-12 weeks before the start of the intervention) and M1 (1-10 months after the start of the intervention), of which at least 5 HBV and 2 HCV seroconversions probably occurred during imprisonment - No seroconversions were observed during the intervention period	NR	- Despite the installation of the machines, almost all subjects described the frequency of needle sharing as unchanged or only slightly decreased, so no clear success of the project could be recorded - 10,439 syringes were exchanged during the study period	Very low
EU/EEA GL	Arroyo, 2015 [63] Spain Longitudinal study	Spanish prison system 1997-2014	Needle exchange programme	n=NR - Participating centres increased from 1 in 1997	Prevalence of HCV infection in Spanish prison system decreased from 48.6% in 1998 to 20% in 2014.	NR	Number of syringes exchanged rose from 2,582 to nearly 23,000 in 2004 and decreased since then to 4,393 in 2014	Conference abstract

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	Seroconversion	Adverse events	Other outcomes	Level of evidence
				to 38 in 2003 and decreased since then to 22 in 2014 No comparator	Prevalence of HIV infection in Spanish prison system decreased from 12.1% in 2003 to 5.8% in 2014.			
Intervention: opioid substitution treatment								
Non-EU/EEA PRL	Dolan, 2005 [60] Australia 4- year follow-up of RCT (Dolan, 2003)	NSW prisons August 1997 – December 2002	OST: methadone treatment immediately (30 mg with increase of 5 mg/3 days until 60 mg) Control: 4-month delay with guaranteed access after that period At end of RCT, all were offered OST (97% had received OST at some time during/since RCT)	n=191 OST vs. n=191 control in original RCT 218 (57%) with follow-up serostatus Males, suitable for OST according to medical staff confirming heroin problem, sentence >4 months at baseline Direct OST versus delayed OST	After median 4.2 years follow-up: - HCV: 39 of 95 HCV-negative subjects seroconverted (incidence rate 21.3/100 person-years, 95% CI 15.6-29.2) p=ns between original RCT groups - HIV: 2 HIV seroconverters (seronegative at baseline NR; incidence rate 0.276/100 person-years, 95% CI 0.033-0.996)	NR	Periods of imprisonment of <2 months (p≤0.001) and OST periods of <5 months (p=0.01) were significantly associated with increased risk of HCV seroconversion	Very low
Non-EU/EEA PRL	Dolan, 2003 [59] Australia RCT (4 months follow-up)	NSW prisons August 1997 – October 1998	OST: methadone treatment immediately (30 mg with increase of 5 mg/3 days until 60 mg) Control: 4-month delay with guaranteed access after that period	n=191 OST vs. n=191 control (follow-up data of 129 (67.5%) vs. 124 (64.9%)) Males, suitable for OST according to medical staff confirming heroin problem, sentence >4 months at baseline Direct OST versus delayed OST	After ~4 months follow-up: - HIV: 0 at baseline and follow-up - HCV: of 32 OST and 35 control HCV-negative subjects at baseline, 4 subjects in each group had seroconverted at follow-up (12.5% and 11.4%, respectively, p=ns)	NR	NR	Very low

HBV: hepatitis B virus, HCV: hepatitis C virus, HIV: human immunodeficiency virus, IDU: injecting drug user, NGO: non-governmental organisation, NR: not reported, NSW: New South Wales, OST: opioid substitution treatment, PRL: peer-reviewed literature, RCT: randomised controlled trial

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/access	Acceptance	Attrition	Sub-group considerations	Level of evidence
Intervention: needles and syringes programmes								
EU/EEA PRL	Stark, 2006 [62] Germany Longitudinal study	1 male and 1 female prison in Berlin n=174 inmates who had ever used illicit drugs October 1998 – June 2001	- Female prison: 3 automatic dispensers, providing a sterile syringe, needle and skin disinfection pad in exchange for a used syringe, or a dummy handed out to new entrants - Male prison: social workers from a NGO exchanged sterile syringes and needles for used equipment 3 times a week	NR	NR	28.7% lost to follow-up (50/174), primarily due to pre-term release or transfer	NR	Very low
EU/EEA PRL	Heinemann, 2001 [61] Germany Cross-sectional study and longitudinal study	1 prison for males and females Cross-sectional study: - n=191 intravenous drug using inmates questionnaire/n=22 interview - n=81 prison employees questionnaire /n=9 interview Longitudinal study: - n=231 intravenous drug using inmates April 1996 – July 1997	Syringe vending machines, with 1:1 exchange Several machines installed in different stations, partly in locations not accessible by staff	Over 90% of the consumers reported unreliability of the syringe vending machines. Other challenges were: not enough needles, insufficient anonymity, poor supply of dummies, and lack of special cannulas (n/N NR)	- In the survey, the acceptance (not defined) of the overall project among the drug-using inmates was significantly more positive than in the case of the non-consuming inmates (p-value NR) - A stable proportion (58-61%) of the prison employees evaluated the project 'bad' or 'very bad'. At the end of the project, the majority of the employees is still not convinced of the need of an automatic spin-off device	NR	NR	Very low
Intervention: opioid substitution treatment								
Non-EU/EEA PRL	Dolan, 2003 [59] Australia RCT (4 months follow-up)	NSW prisons n=191 OST vs. n=191 control (follow-up data of 129 (68%) vs. 124 (65%)) August 1997 – October 1998	OST: methadone treatment immediately (30 mg with increase of 5 mg/3 days until 60 mg) Control: 4-month delay with guaranteed access after that period	Male Assessed as suitable for OST by a detailed interview with medical staff Prison sentences >4 months at baseline	OST group: - 68.2% (88/129) remained in treatment - 9.3% (12/129) did not start treatment (reasons NR) Control group: - 19% commenced OST during the study period; 9% for the intended study	22.5% (29/129) in OST and 26.6% (33/124) in control group were lost to follow-up due to release from prison	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/access	Acceptance	Attrition	Sub-group considerations	Level of evidence
					period, 11% for part of the intended study period (n/N NR)			
Non-EU/EEA PRL	Dolan, 2005 [60] Australia 4-year follow-up of RCT (Dolan, 2003)	NSW prisons n=191 OST vs. n=191 control in original RCT; 218 (57%) with follow-up serostatus; 341 (89%) with follow-up OST status August 1997 – December 2002	OST: methadone treatment immediately (30 mg with increase of 5 mg/3 days until 60 mg) Control: 4-month delay with guaranteed access after that period At end of RCT, all were offered OST (97% had received OST at some time during/since RCT)	Male Assessed as suitable for OST by a detailed interview with medical staff Prison sentences >4 months at baseline	97% had received OST at some time either during or since the original RCT (n/N NR)	80.6% (275/341) dropped out of their first OST episode over 436 person-years at risk (attrition rate 63.1 per 100 person-years, 95% CI 56.1–71.0) - OST dropout risk was 10 times higher during short prison sentences (≤ 1 month) compared to when subjects were in the community ($p < 0.001$), although after 4 months imprisonment was significantly protective for OST dropout ($p \leq 0.002$)	NR	Very low

IDU: injecting drug user, NGO: non-governmental organisation, NSW: New South Wales, OST: opioid substitution treatment, PRL: peer-reviewed literature, RCT: randomised controlled trial

Cost-effectiveness

Region Source	Reference, country, study design	Prison setting, sample	Perspective, time horizon	Scenarios	Conclusions	Sub-group considerations	Level of evidence
Intervention: opioid substitution treatment							
Non-EU/EEA PRL	Warren, 2006 [64] Australia Cost-effectiveness study	NSW prisons n=NR	Provider/funder of prison services NR	OST programme (see Dolan, 2003 and 2005) for one year vs. No OST programme	- Incremental cost per additional heroin-free day: AUD \$38 - Incremental cost per death avoided: AUD \$458,074 - Incremental cost per HCV case avoided: AUD \$40,428 - OST programme in prison is no more costly than community programmes	NR	Low

AUD: Australian dollar, HCV: hepatitis C virus, NR: not reported, NSW: New South Wales, OST: opioid substitution treatment, PRL: peer-reviewed literature

Guidelines

Six guidelines on prevention of BBVs infection in PWID were included, of which three were specific to prison settings (two supranational and one national guideline), and the other three were supranational guidelines not specific to prison setting.

Summary of guidelines for injecting-related infections in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	<p>Prevention of transmission through needles shared by injecting drug users Different modalities have been adopted in several countries to make safe injection equipment available in prisons through health staff, by peers or through dispensing machines. There is evidence that these programmes are effective and not the source of security problems. To prevent hepatitis C, the injection kits should contain (in addition to the syringes) filters, water and cups. Bleach, especially in the prison context, is barely or not effective for disinfecting injection equipment and preventing the transmission of HIV and hepatitis. Whichever system is chosen to provide needles and syringes or kits, the method should include a component for the safe disposal of used needles and syringes.</p> <p>Drug dependence treatment <u>Drug dependence treatment, including opioid substitution therapy for maintenance, is an essential component of the prevention of transmission through injection equipment.</u></p>
WHO, 2007 [53]	Prevention is based on blocking transmission caused by using contaminated syringes. At the population level, adopting pragmatic policies to reduce risk creates the most favourable conditions for preventing transmission. If such policies are in place, the institutions can promote safe injecting practices by interventions ranging from health education to needle and syringe programmes. The individual drug user should avoid sharing injecting equipment and, when needle and syringe programmes are available, take part. If clean needles and syringes are not available, bleach should be used to reduce the risk of transmission, but this will not eliminate the risk. To prevent infection with HBV and HCV, PWID should avoid sharing any part of their injecting materials, including syringe, cotton, water and cooker.
<i>Specific to prison setting – national guidelines</i>	
UK Department of Health, 2011 [55]	<p>HBV and HCV prevention advice for prisoners</p> <ul style="list-style-type: none"> • Be vaccinated against HBV • Never share injecting drug equipment; this includes syringes, filters, spoons, tourniquets, swabs and water as well as needles • Never share tattooing or body piercing equipment • Use disinfecting tablets to clean injecting equipment, razors, and any other items that may have come into contact with blood or body fluids
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	<p>All people from key populations who are dependent on opioids should be offered opioid substitution therapy in keeping with WHO guidance (strong recommendation, low quality of evidence), including those in prison and other closed settings. People in prisons should have access to the same evidence-based treatment options for substance dependence as people in the community. Prison authorities in countries where OST is available in the community should urgently introduce OST programmes and expand them to scale as soon as possible. Countries should affirm and strengthen the principle of providing treatment, education and rehabilitation as an alternative to conviction and punishment for drug-related offences Care should be taken to see that people on OST before entering prisons or other closed settings can continue OST without interruption while imprisoned and when transferred between settings and can be linked to community-based OST upon release. Provision of OST before release can help reduce overdose-related mortality.</p>
ECDC/EMCDDA, 2011 [25]	<p>Based on the most robust evidence available, expert opinion, and best practice used within the EU/EEA, the following key intervention components should be applied and, if possible, be combined to achieve the maximum prevention effect through synergy.</p> <ul style="list-style-type: none"> • Injection equipment: <u>Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes, free of charge,</u> as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes. • Vaccination: Hepatitis A and B, tetanus, influenza vaccines, and, in particular for HIV-positive individuals, pneumococcal vaccine

	<ul style="list-style-type: none"> • Drug dependence treatment: Opioid substitution treatment and other effective forms of drug dependence treatment • Testing: Voluntary and confidential testing with informed consent for HIV, hepatitis C (hepatitis B for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment. • Infectious disease treatment: Antiviral treatment based on clinical indications for those who are HIV, HBV or HCV infected. Anti-TB treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated. • Health promotion: Health promotion focused on safer injecting behaviour; sexual health, including condom use; and disease prevention, testing and treatment. • Targeted delivery of services: Services should be organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings, offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services. <p>Whenever possible, interventions should be combined to achieve synergistic effects.</p>
EMCDDA, 2010 [65]	<p>Reducing or stopping the use of drugs is the safest way to prevent drug-related infectious diseases. This goal, however, may not always be realistic and counselling should therefore include information on how to reduce the risk of acquiring infections.</p> <p>In order to prevent the spread on the prevention of blood-borne and bacterial infections injecting drug users should:</p> <ul style="list-style-type: none"> • Always use a new (sterile) needle and syringe every single time they inject. Syringes and needles are not designed to be used more than once. • Never share needles, syringes, water, cooker, filters or cotton with anyone. • Never re-use needles, syringes, water, cooker, filters or cotton. • If you are sometimes forced to re-use or share needles and syringes, clean them thoroughly each time. • If available, use treatment facilities and harm reduction measures such as: <ul style="list-style-type: none"> - needle exchange programmes and other sources of sterile injecting materials; - drug-assisted rehabilitation or opioid substitution programmes (e.g. methadone programmes or other drug treatment services); - medically supervised injection facilities. • Try to reduce or stop using drugs. Replace injecting practices with non-injecting practices such as smoking and sniffing, and if possible, reduce the frequency of injecting. <p>Recommended vaccines for IDUs are: hepatitis A and B combination vaccine (or separate hepatitis A and hepatitis B vaccines)</p>

Annex 10. Summary tables and guideline summaries – HIV treatment

Effectiveness

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
HIV treatment in prison – usual care										
EU/EEA PRL	Herraiz, 2008 [68] Spain Longitudinal study	Men's Prison of Barcelona October 2003 – January 2005	Provision of ART, not further specified	n=75 HIV+ inmates receiving ART (convenience sample) Likely to be incarcerated for >6 months No comparator	NR	Definition 1 ¹ (n/N NR, p=ns): - At baseline: 72% - At 3 months: 68% - At 6 months: 77% Definition 2 ² (n/N NR, p=ns): - At baseline: 77% - At 3 months: 82% - At 6 months: 77%	NR	NR	NR	Very low
EU/EEA PRL	Inés, 2008 [69] Spain Cross-sectional study	Topas Prison March 2001 – January 2002	Provision of ART Drugs were dispensed on a monthly basis to each inmate and medication was self-administered without supervision	n=50 HIV+ inmates starting ART during study period ART-naïve or receiving <3 drugs, started ART over 10 consecutive months within study period, and completed 6 months of therapy No comparator	Viral load: - 46.0% (23/50) achieved undetectable viral load after 6 months of therapy - -1.43 log ₁₀ copies/ml change from baseline to 6 months (p<0.001) CD4 count: - +119.71 count/mm ³ change from baseline to 6 months (p<0.001) - this change differed significantly between adherent and non-adherent inmates (p=0.48)	42.0% (21/50) ³	NR	<i>Predictors undetectable viral load:</i> - adherence (OR 5.85, 95% CI: 1.56-21.88; p=0.009)	NR	Very low
EU/EEA PRL	Orly de Labry Lima, 2007 [70] Spain	3 prisons (Córdoba, Huelva, Granada)	Provision of ART, not further specified	n=281 HIV+ inmates receiving ART NR	Viral load – non-significant difference in mean viral load between baseline, 6 and 12 months	- At baseline: 45.2% (127/281) - At 6 months: 43.5% (80/184) - At 12 months: 42.3% (58/137)	NR	Inmates without psychological morbidity showed a significant	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
	Longitudinal study	May 2002 – April 2003		No comparator	CD4 count – significant difference mean CD4 count at baseline vs. 6 months (p=0.014)	(p=ns) At all 3 visits: 18% (n/N NR) ⁴		reduction in viral load (p=0.017)		
EU/EEA GL	Prestileo, 2006 [71] Italy Cross-sectional study	7 prisons in eastern Sicily NR	Provision of ART, not further specified	n=144 current or previous HIV+ PWID NR No comparator	60% (21/35) had HIV RNA <400 copies/ml Inmates receiving ART showed a mean increase of 52 (range 19-104) CD4 cells/mm ³ after 12 weeks of treatment	NR	NR	NR	NR	Conference abstract
EU/EEA GL	Gallego, 2010 [67] Spain Cross-sectional study	5 prisons in Catalunya NR	Provision of ART, not further specified	n=769 HIV-infected prisoners - 600 (78%) of these were receiving ART NR No comparator	HIV RNA was <50 copies/ml in 82.8% (497/600) HIV RNA was >1000 copies/ml in 10.5% (63/600) of cases	NR	NR	NR	45% of ART treated inmates were receiving OST with methadone	Conference abstract
EU/EEA GL	Botana Pazos, 2012 [66] Spain Cross-sectional study	1 Penitentiary centre (Madrid VI de Aranjuez) NR	Provision of ART, not further specified	n=102 HIV-infected prisoners - 85 (83.3%) received ART NR No comparator	HIV RNA was: - <50 copies/ml in 69.6% (71/102) - >50 and ≤200 copies/ml in 2.9% (3/102) - >200 and ≤1,000 copies/ml in 9.8% (10/102) - <1,000 and ≤10,000 copies/ml in 5.9% (6/102) - >10,000 in 5.9% (6/102) CD4 cell count was: - ≥500 cells/mm ³ in 43.1% (44/102)	NR	NR	NR	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
					- <500 and ≥350 cells/mm ³ in 23.5% (24/102) - <350 and ≥200 cells/mm ³ in 17.6% (18/102) - <200 cells/mm ³ in 12.7% 13/102					
HIV treatment in prison – usual care (partly DOT and/or transitional care)										
EU/EEA PRL	Soto Blanco, 2005 [77] Spain Cross-sectional study	2 prisons (Huelva, Granada) 1 July 2000 – 31 August 2000	Provision of ART ART freely provided on daily basis in sealed envelopes at prison pharmacy	n=177 HIV+ inmates on ART No impairing physical/psychological circumstances No comparator	NR	75.7% (134/177) ⁵	NR	NR	NR	Very low
Non-EU/EEA PRL	Altice, 2001 [72] USA Cross-sectional study	2 minimum- and 2 maximum-security prisons April – October 1996	Provision of ART Patients to choose between weekly pills packages or DOT On-site dedicated HIV nurse specialist ensures ART regimen is followed, continuity of care, discharge planning	n=205 consecutive HIV+ inmates receiving care by the HIV specialist Asymptomatic individuals eligible for ART (CD4<500; elevated viral load) No comparator	NR	83.5% of those currently accepting ART (137/164) ⁶	NR	NR	NR	Very low
Non-EU/EEA PRL	Kirkland, 2002 [73] USA Longitudinal study	5 prisons April 1998 – March 2000	Provision of ART (old combination treatment) Twice per day under DOT or at dispensing site	n=108 HIV+ inmates Adult ART-naive with HIV-1 infection (viral load >400 copies/	Viral load – After 24 weeks therapy: - 62.0% (67/108) undetectable viral load - The median HIV-1 RNA level was 2.41	Overall self-reported: 94.1% (n/N NR) Mean weeks 2-24: 93.4-98.6% (n/N NR) ⁷	NR	<i>Significant predictors of virologic response:</i> - baseline HIV-1 RNA level (p<0.001)	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
			for medication at specified times twice per day Change of treatment possible due to toxicity, hypersensitivity, or virologic failure	ml, CD4 count ≥ 50 cells/mm ³ within 14 days before study); no AIDS, pregnancy, breastfeeding, considering having a child, various clinical reasons, in another investigational drug study, non-compliant with study schedule No comparator	log ₁₀ copies less than the baseline (p NR) CD4 count – During the 24 weeks, the median CD4 cell count remained at 377–441 cells/mm ³			- black (vs. other races; p=0.049) - heterosexual contact (vs. other risk factors; p=0.039) - adherence (p=0.0037), after adjusting for baseline HIV-1 RNA level (p=0.0002), CD4 cell count (p=0.0339), and demographic covariates, such as ethnicity, sex, and age		
Non-EU/EEA PRL	Meyer, 2014 [75] USA Longitudinal study	CTDOC, an integrated system of 15 male and 1 female facility (pre-trial and sentenced) March 2005 – June 2012	Provision of ART Managed by Infection Control nurse and provided by Infectious Diseases specialists DOT or SAT (based on patient/provider preference) Transitional case management 30 days before release to 3 months after release; 14 days of medication upon release	n=882 HIV+ inmates on ART Confirmed HIV seropositive, in CTDOC for ≥ 90 days, prescribed ART, ≥ 2 sets of laboratory data during incarceration available 90 days apart, pharmacy data available No comparator	Viral load - HIV-1 RNA level (copies/ml): mean change -46379 (p<0.0001) from baseline to release - Viral suppression <400 copies/ml: 29.8% at baseline, 70.0% at discharge (p NR) - Maximal viral suppression <50 copies/ml: 6.2% at baseline, 23.1% at release (p NR) CD4 count - CD4 count (cells/ μ l): mean change +98.0 (p<0.0001) from baseline to release - CD4 count <200 cells/ μ l: 29.5% at	NR	NR	<i>Viral suppression at release correlated with:</i> - Female sex (AOR 1.81; 95%CI 1.26-2.59) - Lower psychiatric disorder severity (AOR 1.50; 95% CI 1.12-1.99)	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
					baseline, 16.5% at discharge (p NR)					
Non-EU/EEA PRL	Mostashari, 1998 [76] USA Cross-sectional study	Connecticut's sole correctional facility for women in Niantic July 1993 – January 1994 & April 1995 – October 1995	Provision of ART Comprehensive care from infectious disease specialist at regularly scheduled clinic visits Primarily through weekly package dispensation, minority through DOT	n=102 HIV+ female inmates CD4 counts <500 cells/ μ l No comparator	NR	61.8% (47/76) of current ART users were adherent ⁸ , 27.6% (21/76) missed their prescribed doses for ≥ 2 days/week and 10.5% (8/76) reported taking some medication for ≥ 6 days/week, but missing ≥ 1 dose/day on average	NR	63.7% (65/102) were first offered ART in prison	NR	Very low
Non-EU/EEA PRL	Springer, 2004 [78] USA Longitudinal study	CTDOC, an integrated system of 15 male and 1 female facility (pre-trial and sentenced) January 1997 – December 2002	Provision of ART HIV nurse specialist available at each facility Majority self-administer medication, in select cases ordered as DOT by HIV specialist Transitional case management 3 months before release to minimum of 30 days after release; 2-week medication supply, medical appointment with	n=1099 HIV+ inmates on ART Prescribed ART for ≥ 6 consecutive months during prison sentence, available baseline and follow-up HIV RNA levels and CD4 counts, and with ART pharmacy prescriptions No comparator	Viral load – Significant mean reduction from baseline to end of incarceration in HIV-1 RNA level of 0.93 log ₁₀ copies/ml (p<0.0001) CD4 count – Significant mean increase from baseline to end of incarceration in CD4 count of 74 lymphocytes/ml (p<0.0001)	NR	NR	<i>Predictors of viral load:</i> Women significantly greater reductions in viral load (p<0.0001)	26.5% (292/1099) inmates were reincarcerated after having spent ≥ 3 months in community): CD4 count was significantly lower and viral load significantly higher at re-incarceration as compared to at time of release (p<0.0001)	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
			HIV care provider, emergency housing and food, other assistance							
EU/EAA GL	Manzano, 2010 [74] Spain Cross-sectional study	Puerto II penitentiary center (Cadiz) 2004 – 2009	Provision of ART, Not further specified Evaluation of an ART implementation programme	n=170 - 73.5% (125/170) received ART No comparator	HIV RNA: - <50 copies/ml in 18.8% (32/170) at entry - <50 copies/ml In 60.5% (103/170) at release CD4 cell count: - <200 cells/mm ³ in 27.6% (47/170) at entry and in 21.7% (37/170) at release - <350 cells/mm ³ in 57.0% (97/170) at entry and in 45.8% (78/170) at release - >350 cells/mm ³ in 42.9% (73/170) at entry and in 54.1% (92/170) at release	NR	NR	NR	NR	Conference abstract
HIV treatment in prison – usual care (comparison DOT vs SAT)										
EU/EEA PRL	Babudieri, 2000 [81] Italy Longitudinal observational study	18 Italian prison facilities; 9 offering DOT, 9 not offering DOT April 1997-September 1998	DOT: Every medication dose was administered by a nurse overseeing the intake SAT: nurse delivers medications to the patients daily but do not oversee intake	84 patients consecutively enrolled on HIV treatment; 37 on DOT; 47 on SAT All individuals were injecting drug users	All patients in the DOT group had significant decrease in viral load (>2 log) after therapy; and 23 (62.1%) had viral load <400 copies/ml compared with 16 patients (34.0%) in the SAT group (odds ratio, 3.18; 95% confidence interval, 1.18-8.67; $\chi^2=5.49$; P=.01)	NR	NR	2 patients in the DOT group (5.4%), had a CD4 cell count that remained less than 200 \times 106/L vs 15 patients in the SAT group (31.9%) (odds ratio, 0.12; 95% confidence interval, 0.02-	The cost of implementing DOT in this setting is low; no additional staff was required to administer this therapy	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
								0.62; $\chi^2=7.44$; $P<.001$).		
Non-EU/EEA PRL	Wohl, 2003 [80] USA Longitudinal study	6 of 74 NCDOC facilities September 1999 – April 2000	DOT: patients visit medication window at specified times and swallow medication in sight of nurse or officer SAT: self-administered Protease inhibitors always DOT, other medications DOT or SAT (according to preference of clinician) Medications dispensed to patient (SAT) or staff (DOT) in 30-day allotments; pill bottles returned at end 30-day period and refilled	n=31 HIV+ inmates on ART (consecutive sample) Adults with documented HIV infection, no expected release during 4 study months, receiving ≥ 3 ART of which ≥ 1 administered via DOT, and having received ART for ≥ 3 months prior to study start DOT vs SAT - 58% (18/31) all ART agents via DOT - 42% (13/31) one ART agent via DOT	NR	Median electronic monitoring caps adherence: - Overall: 86% (>90% in 32% of subjects) - 92% (range 0-100) in SAT vs. 82% (range 16-100) in DOT (p=0.46) Median pill count adherence: - Overall: 90% - 90% (range 43-100) in SAT vs. 89% (range 25-100) in DOT (p=0.82) Median self-reported adherence: - Overall: 100% - 100% (range 92-100) in SAT vs. 100% (range 52-100) in DOT (p=0.32) ¹⁰ (n/N NR)	NR	NR	Among 13 subjects who received only 1 of their medications by DOT (41.9%) - No adherence difference between DOT- and SAT-provided medications irrespective of measurement - On 74% of days that any ART doses were missed, both DOT-based and SAT-provided medications were not taken (n/N NR)	Very low
Intervention: DOT vs. SAT										
Non-EU/EEA PRL	White, 2015 [79] USA Pilot of RCT	3 prison-based HIV clinics covering 11 of the largest 74 North Carolina State prison system facilities	DOT: prison staff observed and recorded each inmate ingest all ART medications; if missed >3 pills, they notify it	n=20 DOT vs. n=23 SAT HIV+ inmates (consecutive sample) Adults with documented HIV infection, on ART,	Viral load: - No difference in the proportion achieving viral suppression between the two study arms at week 24 (p=0.21) or 48 (p=0.48)	Median (IQR) MEMS adherence ¹ - 24 weeks: 99.0% (93.9-100) in DOT vs. 98.3% (96.0-100) in SAT (p=0.82) - 48 weeks: 99.8% (96.3-100) in DOT vs.	NR	45.0% (9/20) of the DOT participants 60.9% (14/23) of the SAT participants participants opted to receive adherence counselling	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
		August 2003 – February 2005	SAT: monthly allotments of all ART medications and signing for each medication bottle; turn in any remaining medication at each monthly refill Protease inhibitors always DOT, other medications DOT or SAT After week 24, optional adherence counselling: 2 motivational interview sessions	no planned inter-prison transfers, Karnofsky score ≥ 70 to measure self-care, expected incarceration ≥ 6 months, available CD4 count and HIV RNA level within 60 days of study entry DOT vs. SAT	CD4 count: - No difference in CD4 count change at 24 weeks ($p=0.69$) and 48 weeks ($p=0.98$) between DOT and SAT	99.9% (85.2-100) in SAT ($p=0.79$) - Odds of achieving >95% adherence DOT vs SAT: OR 0.77 ($p=0.77$) Median (IQR) pill count adherence ⁷ - 24 weeks: 97.1% (95.1-99.3) in DOT vs. 98.5% (95.8-100) in SAT ($p=0.40$) - 48 weeks: 100% (94.8-100) in DOT vs. 99.5% (97.0-100) in SAT ($p=0.84$) - Odds of achieving >95% adherence DOT vs SAT: OR 1.28 ($p=0.75$)		approximately 25 and 26 weeks after randomisation		
Intervention: HIV care with telemedicine vs. usual care										
Non-EU/EEA PRL	Young, 2014 [82] USA Before-after study	IDOC, not further specified July 2009 – June 2010 (pre-telemedicine) & July 2010 – June 2012 (telemedicine)	HIV care: visit every 3-month Pre-telemedicine: on-site management by correctional physician without subspecialty training Telemedicine: encrypted link to dedicated telemedicine suite; each visit with an infectious disease	n=514 pre-telemedicine vs. n=687 telemedicine HIV+ inmates All known HIV+ adults who consented to medical care, with available date from ≥ 2 visits Pre-telemedicine time period vs.	Viral load: - Complete virologic suppression during the first 6 visits telemedicine vs. pre-telemedicine: OR 7.0, 95% CI 5.1–9.8; $p < 0.001$ (when removing all subjects who were suppressed at the first visit: OR 10.5, 95% CI 6.9–16.1; $p < 0.001$; when controlling for total number of clinic visits: OR 4.2, 95% CI 2.5–7.0; $p < 0.001$)	NR	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
			physician, infectious disease-trained pharmacist, a case manager and correctional nurse	telemedicine time period	CD4 count – Mean CD4 count higher in telemedicine group vs. pre-telemedicine group (p=0.032)					
Intervention: pharmacist-run HIV medication management model										
Non-EU/EEA PRL	Bingham, 2012 [83] USA Longitudinal study	BOP facilities December 2004 – December 2009	Provision of ART by a multidisciplinary healthcare team including HIV clinical pharmacist consultant Patients' care included consultation on treatment initiation, medication appropriateness/interaction review, medication regimen complexity, adverse reactions, resistance review, opportunistic infection treatment, comorbid conditions	n=135 HIV+ inmates on ART NR No comparator	Viral load: - From April 2004 to December 2009, the overall percentage of patients with undetectable viral loads (<48 copies/ml) increased from 32% to 66% CD4 count – At December 2009, 76% of patients receiving ART achieved CD4 counts of ≥200 cells/mm ³ All n/N NR	At December 2009, 73% of patients receiving ART were taking ≥90% of the prescribed doses (n/N NR) ¹¹	NR	NR	NR	Very low
Intervention: monthly nurse evaluation										

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to care post release	Other outcomes of interest	Other sub-group considerations	Level of evidence
EU/EAA GL	Martino, 2010 [84] Spain Longitudinal study	Penitentiary center Puerto III (Cadiz) November 2008 – July 2009	Programmed monthly nurse visit including a structured interview	n=54 inmates NR No comparator	Mean CD4 count pre-intervention 460.2 vs. 464.1 cells/mm ³ post-intervention Mean HIV RNA pre-intervention 8340.57 vs. 4040.31 copies/ml post-intervention	NR	NR	NR	NR	Conference abstract

AIDS: autoimmune deficiency syndrome, ART: antiretroviral therapy, BOP: Bureau of Prisons, CI: confidence interval, CTDOC: Connecticut Department of Corrections, DOT: directly observed therapy, ER: emergency room, GL: grey literature, IDOC: Illinois Department of Corrections, IQR: interquartile range, NCDCC: North Carolina Department of Corrections, NNRTI: non-nucleoside reverse-transcriptase inhibitor, NR: not reported, NRTI: nucleoside reverse-transcriptase inhibitor, ns: not significant, OR: odds ratio, PI: protease inhibitor, PRL: peer-reviewed literature, RCT: randomized controlled trial, RNA: ribonucleic acid, SAT: self-administered therapy, SD: standard deviation, USA: United States of America

¹ Self-reported adherence as 'very good' (proportion indicates $\geq 95\%$ adherence)

² Self-reported adherence according to number of pills not ingested in the last 4 days (proportion indicates $\geq 95\%$ adherence)

³ Self-reported adherence: 4 'no' answers or 1 'yes' answer (1 day) to 4 questions related to previous 5 days 'did you forget to take a pill?', 'did you forget any dose of all the drugs?', 'did you take a tablet or a dose outside the timetable?' and 'did you take any tablet or the doses without realizing that you had to do so with or without meals?'

⁴ Self-reported non-adherence: answering yes to any qualitative question, >2 doses missed in the last week or >2 days without medication in the last 3 months

⁵ Self-reported adherence: 4 'no' answers or 1 'yes' answer (1 day) to 4 questions related to previous 5 days 'did you miss any pill?', 'did you miss any dose of all ART drugs?', 'did you take any pill out of scheduled time?' and 'did you take any pill/all doses without taking into account food requirements?'

⁶ Self-reported adherence: taken $\geq 80\%$ of prescribed doses of medication during 7-day recall period

⁷ Self-reported adherence, not further defined

⁸ Self-reported adherence: taking medications for ≥ 6 days/week, and not missing any doses per day

⁹ A HAART regimen strategy was defined by the type of regimen that was first initiated during the eligible incarceration period, including: a) PI-based regimens with 2 NRTIs and ≥ 1 PI (no NNRTI included); b) NNRTI-based regimens with 2 NRTIs and ≥ 1 NNRTI (no PI included); c) NRTI-only regimens with ≥ 3 NRTIs (no PI or NNRTI included); and d) 3-class regimens (multiple) with ≥ 1 NRTI and 1 NNRTI and 1 PI

¹⁰ Assessed by electronic monitoring caps (eDEM), pill counts of returned medication, self-report (interviews at first clinical appointment after study entry [~ 3 -4 months later]), and medication administration records completed by prison staff who dispensed medications for DOT; Adherence: proportion of prescribed doses taken

¹¹ Adherence not specified

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
HIV treatment in prison – usual care										
EU/EEA PRL	Herraiz, 2008 [68] Spain Longitudinal study	Men's Prison of Barcelona n=75 HIV+ inmates October 2003 – January 2005	Provision of ART	NR	NR	<p><i>Reasons discontinuation/ change treatment (% NR):</i></p> <ul style="list-style-type: none"> - Main reason: forgetting - Less common reasons: side effects, falling asleep, feeling nervous or depressed, having exhausted medication or not taking the medication with you <p><i>Significant correlates of adherence at 6 months:</i></p> <p>Definition 1¹:</p> <ul style="list-style-type: none"> - General self-efficacy (r=0.403, p=0.010), medication management self-efficacy (r=0.379, p=0.016), benefit perception (r=0.330, p=0.043) (all at baseline) - General self-efficacy (r=0.356, p=0.046), medication management self-efficacy (r=0.403, p=0.020), fatigue (r=-0.528, p=0.001), vigour (r=0.427, p=0.007) and viral load (r=0.418, p=0.017) (all at 3 months) <p>Definition 2²:</p> <ul style="list-style-type: none"> - Medication management self-efficacy (r=0.377, p=0.014), vigour (r=0.378, p=0.014), depression (r=0.374, p=0.015) and CD4 level (r=-0.365, p=0.019) (all at baseline) - Fatigue (r=0.377, p=0.015), vigour (r=-0.324, p=0.039) and CD4 level (r=-0.39, p=0.014) (all at 3 months) 	45.3% (34/75) were lost to follow up at six months – no reason provided	60% reported having received limited support from the healthcare staff (n/N NR)	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
EU/EEA PRL	Inés, 2008 [69] Spain Cross-sectional study	Topas Prison n=50 HIV+ inmates March 2001 – January 2002	Provision of ART Drugs were dispensed on a monthly basis to each inmate and medication was self-administered without supervision	NR	NR	- 7.1% discontinued treatment (4/56) (study focuses on 50 inmates who completed 6 months of ART) <i>Significant predictors of good adherence:</i> - Active occupation inside prison (OR 5.56, 95% CI 1.12-27.02; p=0.035) - Absence of HIV-related symptoms (OR 7.81, 95% CI 1.01-62.5; p=0.049) - Good or average acceptance of treatment (OR 10.10, 95% CI 1.23-83.33; p=0.031) - Higher academic background (OR 5.20, 95% CI 1.05–26.31; p=0.044) <i>Significant predictor of non-adherence:</i> - IDU as risk factor for HIV transmission (OR 8.86, 95% CI 1.52–51.77; p=0.015)	3.6% LTFU due to transfer (2/56) (study focuses on 50 inmates who completed 6 months of ART)	NR	NR	Very low
EU/EEA PRL	Orly de Labry Lima, 2007 [70] Spain Longitudinal study	3 prisons (Córdoba, Huelva, Granada) n=281 HIV+ inmates May 2002 – April 2003	Provision of ART	NR	NR	- At the 2 nd visit (6 months), 10.7% (30/281) did not continue taking ART (withdrawal, abandonment or intolerance) - At the 3 rd visit (12 months), 10.3% (29/281) were not on treatment anymore (reasons NR)	- At the 2 nd visit, 23.8% (67/281) were not present (release or transfer) - At the 3 rd visit, 9.2% (17/184) of those at second visit were not present and 0.54% (1/184) did not want to be interviewed	NR	NR	Very low
EU/EEA PRL	Sordo-del-Castillo, 2008 [85] Spain	3 prisons (Córdoba, Huelva, Granada)	Provision of ART	26.2% (153/585) not eligible for ART (no	54.9% (321/585) on ART	2.6% (15/585) discontinued ART due to adverse effects	NR	<i>ART refusers vs. on ART or no ART indication:</i> - more on methadone treatment (p=0.027)	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
	Cross-sectional study	n=585 HIV+ inmates May – July 2004		reason specified) Those with physical/ psychological circumstances excluded from study	16.4% (96/585) refused ART while indicated			<ul style="list-style-type: none"> - more HCV co-infection (p=0.003) - more heroin/cocaine use in prison (p=p=0.040) - more self-perceived health being worse compared to previous year (p<0.001) - more viral load >50,000 copies (p<0.001) - lower mean CD4 count (p<0.001) - proportion with AIDS: those who were not indicated ART having the lowest proportion and those on ART the highest (p<0.001) - proportion previously treated with ART and number of times on ART: those who were not indicated ART having the lowest proportion and those on ART the highest (p<0.001) 		
EU/EEA PRL	Soto Blanco, 2005 [86] Spain Cross-sectional study	3 prisons (Córdoba, Huelva, Granada) n=281 HIV+ inmates receiving ART 2002	Provision of ART	Those with physical/ psychological circumstances excluded from study	NR	<p><i>Main reasons non-adherence</i>³:</p> <ul style="list-style-type: none"> - forgetting: 43.4% (n/N NR) - side effects: 22.4% (n/N NR) <p><i>Factors significantly associated with non-adherence</i>³:</p> <ul style="list-style-type: none"> - having flexible prison officials to open the cell (OR 0.47, 95% CI 0.26-0.84, p=0.01) - good quality of food (OR 5.65, 95% CI 1.93-16.51, p<0.01) 	NR	<p><i>Opinions and beliefs on HIV treatment and care (% yes of n=281)</i>:</p> <ul style="list-style-type: none"> - Prison official flexible in opening cell when medication forgotten: 66.2% - Difficulty in taking medication: 33.2% - Very able to continue with treatment: 83.3% 	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
						<ul style="list-style-type: none"> - being anxious and/or depressed (OR 2.07, 95% CI 1.18-3.66, p=0.01) - having no support outside prison (OR 3.97, 95% CI 1.19-13.23, p=0.02) - having difficulty in taking medication (OR 1.94, 95% CI 1.05-3.57, p=0.03) - being completely or largely unable to continue with treatment (OR 5.37, 95% CI 2.06-13.94, p<0.001) 		<ul style="list-style-type: none"> - Trust in treatment: 86.8% - Trust in doctors: 68.7% - Receive necessary help from doctors: 57.7% - Receive support in prison (professional, other inmates, NGOs/others): 44.4% 		
EU/EEA GL	Prestileo, 2006 [71] Italy Cross-sectional study	7 prisons in eastern Sicily n=144 current or previous HIV+ PWID NR	Provision of ART, Not further specified	68.6% (35/51) HIV-infected inmates received ART	NR	8.5% (3/35) discontinued ART due to prison-related problems (transfer to other institutions and new prescribed drug non available)	NR	NR	NR	Conference abstract
EU/EEA GL	Botana Pazos, 2012 [66] Spain Cross-sectional	1 Penitentiary centre (Madrid VI de Aranjuez) N=102 HIV-infected prisoners NR	Provision of ART, Not further specified	85 (83.3%) received ART	NR	NR	NR	Reasons for not having an HIV RNA<50 copies/ml were: <ul style="list-style-type: none"> - Among the 5.9% (6/102) inmates with HIV RNA >1,000 and ≤10,000 copies/ml: 4 were CDC stage A1 and 1 A2 without ART and 1 NR - Among the 5.9% (6/102) inmates with HIV RNA >10,000 copies/ml: 1.9% (2/102) showed low level of adherence, 1.9% (2/102) refused ART, 1.9% (2/102) had started ART after the study started 	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
HIV treatment in prison – usual care (partly DOT and/or transitional care)										
EU/EEA PRL	Soto Blanco, 2005 [77] Spain Cross-sectional study	2 prisons (Huelva, Granada) n=177 HIV+ inmates on ART 1 July 2000 – 31 August 2000	Provision of ART Freely provided on daily basis in sealed envelopes at prison pharmacy	ART provided to patients with acute HIV syndrome, seroconversion during previous 6 months, clinical symptoms of HIV infection, asymptomatic patients with CD4 cell count <500 cells/mm ³ or viral load ≤10,000 copies/ml ART prescribed to 54.2% (278/513) of HIV-positive inmates	27.0% (75/278) of those prescribed ART refused ART while incarcerated, no reason provided 66.5% (185/278) of those prescribed ART were receiving it (177 participated in the study)	27.0% (18/278) of those prescribed ART discontinued ART while incarcerated <i>Reasons for non-adherence^d (n=18):</i> - side effects: 72.1% - missing pills: 20.9% - other: 7% <i>Significant predictors of non-adherence^e:</i> - poorly capable/incapable to follow the prescribed treatment regimen (OR 5.84, 95% CI 2.27-15) - receiving no visits in a month (OR 2.76, 95% CI 1.22-6.24) - being anxious and/or depressed in the last week (OR 2.40, 95% CI 1.02-5.60)	NR	<i>Opinions and beliefs on HIV treatment and care (% yes of n=177):</i> - Prison official flexible in opening cell when medication forgotten: 31.6% - Difficulty in taking medication: 35% - Very capable to follow treatment schedule: 82.5% - Trust in treatment: 87% - Trust in doctors: 55.9% - Receive necessary help from doctors: 57.7% - Receive support in prison (professional, other inmates, NGOs/others): 43.5%	NR	Very low
Non-EU/EEA PRL	Altice, 2001 [72] USA Cross-sectional study	2 minimum- and 2 maximum-security prisons n=205 HIV+ inmates April – October 1996	Provision of ART Weekly packages or DOT On-site HIV nurse specialist ensures ART regimen is followed, care plan, discharge planning	NR	80.0% (164/205) accepted ART while incarcerated <i>Significant factors of ART acceptance:</i> - increased trust in physician	<i>Significant factors of ART adherence^e:</i> - Having had side effects from ART and having expressed willingness to stop medications if any side effect were to occur (OR 0.09, p<0.0001) - social isolation (OR 0.08, p=0.0005) - complexity of ART regimen (per step from monotherapy to dual nucleoside combination to protease inhibitor-containing combinations OR 0.33, p=0.01)	NR	<i>Opinions on HIV treatment and care:</i> - 82% of females and 65% of males had high level of trust in their current HIV doctor - 55% of females and 72% of males had high level of trust in current HIV nurse - 16% believed that taking medications for HIV was most	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
					(OR 1.08, p=0.0001) - lower with increased mistrust in medication (OR 0.30, p<0.001)			essential for remaining healthy - 83% had high level of trust in HIV medications		
Non-EU/EEA PRL	Kirkland, 2002 [73] USA Longitudinal study	5 prisons April 1998 – March 2000	Provision of ART (old combination treatment) Twice per day under DOT or at dispensing site for medication at specified times twice per day Change of treatment possible due to toxicity, hypersensitivity, or virologic failure	Adult ART-naive with HIV-1 infection (viral load >400 copies/ml, CD4 count ≥50 cells/mm ³ within 14 days before study); no AIDS, various clinical reasons, in another investigational drug study, non-compliant with study schedule	NR	11.1% (12/108) withdrew prematurely for the following reasons (denominator n=108): - virologic failure: 3.6% - adverse events: 3.7% - withdrawal of consent: 1.9% - other: 1.9% The most frequently mentioned reasons for missing doses of the study medication were (n/N NR): - problems with dispensing or confusion (15.0%) - fatigue (13.3%) - illness (12.4%)	5.6% lost to follow-up (6/108)	83.3% (90/108) completed 24 weeks of therapy	NR	Very low
Non-EU/EEA PRL	Meyer, 2014 [75] USA Longitudinal study	CTDOC, an integrated system of 15 male and 1 female facility (pre-trial and sentenced) n=882 HIV+ inmates on ART March 2005 – June 2012	Provision of ART Managed by Infection Control nurse and provided by Infectious Diseases specialists DOT or SAT (based on patient/	Confirmed HIV seropositive, in CTDOC for ≥90 days, prescribed ART, ≥2 sets of laboratory data during incarceration available 90 days apart, pharmacy data available	Type of medication at discharge: - 74.0% SAT - 26.0% DOT Type of medication overall from baseline to release:	NR	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
			provider preference) Transitional case management 30 days before release to 3 months after release; 14 days of medication upon release		- 2.4% continuous SAT - 1.6% change DOT to SAT - 2.5% continuous DOT - 23.5% change SAT to DOT					
Non-EU/EEA PRL	Mostashari, 1998 [76] USA Cross-sectional study	Connecticut's sole correctional facility for women in Niantic n=102 HIV+ female inmates July 1993 – January 1994 & April 1995 – October 1995	Provision of ART Comprehensive care from board-certified infectious disease specialist at regularly scheduled clinic visits Primarily through weekly package dispensation, minority through DOT	CD4 counts <500 cells/µl First offered ART in prison: 67%	74.5% (76/102) accepted ART during current incarceration Respondents were no less likely to accept ART offered in prison than outside (% and p NR) <i>Factors significantly associated with acceptance:</i> - Belief that ART extends life (AOR 3.2, 95% CI 1.2-8.6, p≤0.05)	<i>Factors significantly associated with adherence among current users:</i> - Belief that HIV doctor always understands her (AOR 3.0, 95% CI 1.1-8.5, p≤0.05) - Talks to someone when 'down' (AOR 3.0, 95% CI 1.1-9.4, p≤0.05)	NR	<i>Opinions HIV treatment and care (% yes, denominator NR):</i> * Trust in ART - HIV medications increase survival (efficacy): 71% (72/102) - People I know who took HIV medications were not hurt by taking them (safety): 82% (83/102) * Trust in healthcare system: - Healthcare offered to all inmates is excellent-outstanding: 29% (30/102) - HIV-related healthcare I receive is excellent-outstanding: 55% (53/102) *Relationship with doctor: - The HIV doctor always listens to me: 71% (68/102) - The HIV doctors always understands	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
					- Belief that ART did not harm a friend (AOR 4.3, 95% CI 1.4-12.9, p≤0.01)			what I am saying: 59% (56/102)		
EU/EAA GL	Manzano, 2010 [74] Spain Cross-sectional	Puerto II penitentiary center (Cadiz) n=170 2004 – 2009	Provision of ART, not further specified	73.5% (125/170) received ART	DOT was used in 29.6% (37/125) of ART treated patients - 13.5% (5/37) of DOT receiving patients self-administered ART after some months during the programme	NR	NR	Virological failure occurred in 8.0% (10/125) patients: - 4% (5/125) due to voluntary interruption of ART - 2.4% (3/125) due to low adherence - 1.6% (2/125) due to resistance development	NR	Conference abstract
HIV treatment in prison – usual care (comparison DOT vs SAT)										
Non-EU/EEA PRL	Wohl, 2003 [80] USA Longitudinal study	6 of 74 NCDCC facilities n=31 HIV+ inmates (consecutive sample) - 58% (18/31) all ART agents via DOT - 42% (13/31) one ART agent via DOT	Provision of ART DOT: patients visit medication window at specified times and swallow medication in sight of nurse or officer SAT: self-administered	Adults with documented HIV infection, no expected release during 4 study months, receiving ≥3 ART of which ≥1 administered via DOT, and having received ART for ≥3 months	NR	Of 41 subjects enrolled, 8 (19.5%) discontinued DOT soon after study entry (study focused on 31 inmates with full data)	Of 41 subjects enrolled, 2 (4.9%) transferred from prison during study (study focused on 31 inmates with full data)	68% (n/N NR) would prefer to take medications on their own, rather than provided via DOT 8% (n/N NR) expected that DOT replaced by SAT would lead to an increase in number of missed doses	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
		September 1999 – April 2000	Protease inhibitors always DOT, other medications DOT or SAT (according to preference of clinician) Medications dispensed to patient (SAT) or staff (DOT) in 30-day allotments; pill bottles returned at end 30-day period and refilled	prior to study start						
Intervention: DOT vs SAT										
Non-EU/EEA PRL	White, 2015 [79] USA Pilot of RCT	3 prison-based HIV clinics covering 11 of the largest 74 North Caroline State prison system facilities n=20 DOT vs. n=23 SAT HIV+ inmates (consecutive sample) August 2003 – February 2005	DOT: prison staff observed and recorded each inmate ingest all ART medications; if missed >3 pills, they notify it SAT: monthly allotments of all ART medications and signing for each medication bottle; turn in any remaining medication at each monthly refill	Adults with documented HIV infection, on ART, no planned inter-prison transfers, Karnofsky self-care score ≥ 70 , expected incarceration ≥ 6 months, available CD4 count and HIV RNA level within 60 days of study entry	NR	DOT: - Week 24: 10.0% (2/20) withdrew - Week 48: 6.3% (1/16) discontinued medication, reasons NR SAT: - Week 24 and week 48: 0%	DOT: - Week 24: 10.0% (2/20) transfer - Week 28: 6.3% (1/16) release, 6% (1/16) incomplete data, 6.3% (1/16) study ended SAT: - Week 24: 4.3% (1/23) release, 4.3% (1/23) hospitalised - Week 28: 4.8% (1/21) release, 28.6% (6/21) incomplete data,	45.0% of DOT participants (9/20) and 60.9% of SAT participants (14/23) opted to receive adherence counselling approximately 25 and 26 weeks after randomisation	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Other sub-group considerations	Level of evidence
			Protease inhibitors always DOT, remaining medications DOT or SAT After week 24, optional adherence counselling: 2 motivational interview sessions				14.3% (3/21) study ended			

ART: antiretroviral therapy, CI: confidence interval, DOT: directly observed therapy, GL: grey literature, HCV: hepatitis C virus, HIV: human immunodeficiency virus, NCDoc: North Carolina Department of Corrections, NGO: non-governmental organisation, NR: not reported, OR: odds ratio, PRL: peer-reviewed literature, PWID: People who inject drugs, RCT: randomised controlled trial, RNA: ribonucleic acid, RR: relative risk, SAT: self-administered therapy, USA: United States of America

¹ Self-reported adherence as 'very good' (proportion indicates ≥95% adherence)

² Self-reported adherence according to number of pills not ingested in the last 4 days (proportion indicates ≥95% adherence)

³ Self-reported non-adherence: answering yes to any qualitative question, >2 dopes missed in last week or >2 days without medication in the last 3 months

⁴ Self-reported adherence: 4 'no' answers or 1 'yes' answer (1 day) to 4 questions related to previous 5 days 'did you miss any pill?', 'did you miss any dose of all ART drugs?', 'did you take any pill out of scheduled time?' and 'did you take any pill/all doses without taking into account food requirements?'

⁵ Self-reported adherence: taken ≥80% of prescribed doses of medication during 7-day recall period

Cost-effectiveness

No cost-effectiveness studies were included on HIV care and treatment.

Guidelines

Six guidelines on HIV treatment were included, of which four were specific to prison setting (two supranational and two national guidelines), and the other two were supranational guidelines not specific to prison setting

Summary of guidelines on HIV treatment in prison settings

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	<p>There is evidence that ART is feasible in prison settings. One of the problems of ART is resistance to some of the drugs that can be caused by the interruption of treatment. It is, therefore, most important to avoid any interruption of treatment when individuals are admitted to pre-trial detention centre or prison, when they are transferred from one prison or pre-trial detention centre to another, and when people under treatment are released into the community. In addition, specific attention should be paid to adherence to the treatment.</p> <p>‘Clinical and laboratory follow-up is needed to monitor the response to treatment. The minimum requirement is to monitor the level of CD4. All ART drugs have numerous adverse effects and the treatment requires monitoring for these effects.’</p> <p>Prevention of opportunistic infections</p> <p>Prevention of opportunistic infections is part of the treatment for HIV. In view of the higher risk in prison settings, this component is essential to prevent mortality linked to HIV. Please refer to the WHO website for detailed information.</p>
WHO, 2007 [53]	<p>Providing access to ART for those in need in the context of prisons, particularly in resource-constrained settings, is a challenge, but it is necessary and feasible. Studies have documented that, when prisoners are provided care and access to ART, they respond well. Adherence rates in prisons can be as high or higher than among people in the community, but the gains in health status made during the term of incarceration may be lost unless careful discharge planning and links to community care are undertaken.</p> <p>ART requires clinical and laboratory assessments at baseline and regularly during therapy. Stage of HIV disease, concomitant conditions (TB and pregnancy), concomitant medication use (including traditional therapy), body weight and the patient's readiness for therapy are evaluated at baseline. While on therapy, signs and symptoms of potential drug toxicity, body weight, response to therapy and adherence are assessed and, when clinically indicated, depending on the antiretroviral drug regimen used, laboratory evaluation is performed.</p>
<i>Specific to prison setting – national guidelines</i>	
UK Department of Health, 2011 [55]	<p>All prisoners with HIV will require referral for specialist care. ART is the main type of treatment for HIV.</p> <p>The aim of ART is to stop HIV reproducing and allows the immune system to recover from any damage that HIV might have previously caused.</p>
SIMIT/Ministero della Salute (Italy), 2016 [57]	<p>ART should be offered to every HIV-infected prisoner, independently of CD4 cell count. <u>Early treatment, apart from individual benefit, could result in better linkage to care of the prisoner and the HIV RNA reduction reduces the possibility of HIV transmission during prison stay and after release.</u></p> <ul style="list-style-type: none"> - Offer ART to HIV-infected prisoners according to national and international guidelines - Offer a specific counselling on the efficacy, safety and adherence issues before starting ART - Assure the delivery of ART according to the specialist prescription - <u>Directly Observed Therapy (DOT)</u> - Offer of DAAs treatment for HIV/HCV co-infected prisoners - <u>Monitor adherence to ART</u>

<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	<p>The use of ART for HIV in key populations should follow the same general principles and recommendations as for all adults. HIV treatment adherence can be increased by addressing HIV stigma and discrimination, ensuring the confidentiality of a prisoner's HIV status, and allowing people in prisons and other closed settings access to care and treatment without discrimination by prison officials.</p> <p>ART initiation</p> <ul style="list-style-type: none"> • As a priority ART should be initiated in all individuals with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 counts of ≤ 350 cells/mm³ (strong recommendation, moderate quality of evidence). • ART should be initiated in all individuals with HIV regardless of WHO clinical stage (strong recommendation, moderate quality of evidence) (4). • ART should be initiated in all individuals with HIV, regardless of WHO clinical stage or CD4 count, with priority for the following people (4) : <ul style="list-style-type: none"> – individuals with HIV and active TB disease (strong recommendation, low quality of evidence) ; – individuals co-infected with HIV and HBV with evidence of severe chronic liver disease (strong recommendation, low quality of evidence) ; – partners with HIV in serodiscordant couples, to reduce HIV transmission to uninfected partners (strong recommendation, high quality of evidence) ; – pregnant and breastfeeding women (strong recommendation, moderate quality of evidence) <p><u>All pregnant and breastfeeding women living with HIV should initiate triple antiretrovirals (ARV)</u>, which should be maintained at least for the duration of risk of mother-to-child transmission. Women meeting treatment eligibility criteria should continue ART for life (CD4 <500 cells/mm³) (strong recommendation, moderate quality of evidence).</p> <p>Special consideration should be given to ensuring that pregnant female prisoners have ready access to PMTCT services, as women often face greater barriers to HIV testing, counselling, care, and treatment in prison than outside prison.</p>
European AIDS Clinical Society, 2017 [30]	<p>ART is recommended in all adults with chronic HIV infection, irrespective of CD4 counts</p> <p>ART should always be recommended irrespective of the CD4 count, <u>but the lower the CD4 count, the greater the urgency to start ART immediately.</u></p> <p>Genotypic resistance testing is recommended prior to initiation of ART, ideally at the time of HIV diagnosis; otherwise before initiation of ART.</p> <p>If ART needs to be initiated before genotypic testing results are available, it is recommended to include a drug with high genetic barrier to resistance in the first-line regimen (e.g. a PI/r, PI/c or DTG). Ideally, before starting treatment, the HIV-VL level and CD4-count should be repeated to obtain a baseline to assess subsequent response.</p> <p><u>Use of ART should also be recommended with any CD4-count in order to reduce sexual transmission, risk of AIDS event and mother-to-child transmission of HIV</u> (before third trimester of pregnancy).</p>

Annex 11. Summary tables and guideline summaries – Viral hepatitis treatment

Effectiveness

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
HCV treatment in prison – usual care										
EU/EEA PRL	Strock, 2009 [112] Luxembourg Longitudinal study	Centre Pénitentiaire de Luxembourg January 2003 – December 2006	Provision of pegylated IFN + RBV All HCV+ inmates are offered a specialist consultation (delay after blood tests 2-4 weeks); liver biopsy offered but not mandatory	n=268 HCV+ inmates seen by specialist consultant to evaluate treatment initiation - Positive viral load associated with elevated ALT, expressed in multiples of upper limit of normal or an isolated high viral load or a positive viral load associated with HIV infection - Decision to start therapy finally made in case-by-case discussion between practitioner and inmate No comparator	6 months after end treatment: - SVR: 52.3% (45/86)	65.1% (56/86)	NR	NR	NR	Very low
EU/EEA PRL	De Juan, 2014 [92] Spain Longitudinal study	26 prisons throughout Spain October 2007 – July 2008	Provision of pegylated IFN + RBV	n=431 treated HCV+ inmates who were treatment-naïve. Meeting chronic HCV treatment criteria, following standard clinic practice (not further specified), penalty length ≥2 years and no possibility of being transferred to another institute or any other incident that could alter treatment persistence No comparator	24 weeks after end of treatment: - SVR: 52.0% (224/431)	77.5% (334/431)	NR	NR	NR	Very low
EU/EEA PRL	Marco Mouriño, 2010 [102]	4 prisons in Barcelona	Provision of pegylated IFN + RBV	n=162 HCV+ treated inmates with history of drug use NR	NR	91.4% (148/162)	NR	NR	Treatment completion in those with	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
	Spain Cross-sectional study	January 2003 – December 2007	IFN administered by clinical nurse, RBV delivered to inmate weekly for SAT Treatment coordinated with Internal Medicine Service of a Barcelona hospital	No comparator					history IDU: 88% (n/N NR)	
Non-EU/EEA PRL	Bate, 2010 [89] Australia Longitudinal study	Royal Adelaide Hospital Viral Hepatitis Centre (where inmates are treated) January 1997 – December 2008	Provision of standard IFN (with or without RBV) or pegylated IFN + RBV Patients management was via a shared-care programme between the Royal Adelaide Hospital Viral Hepatitis Centre and the South Australian Prison Health Service	n=79 treated HCV+ inmates To be incarcerated for the entire planned duration of therapy No comparator	6 months after end of treatment: - SVR: 67.1% (53/79)	NR	NR	6.3% re-infected after completion of treatment (5/79; 1 following ETR and 4 following SVR)	NR	Very low
Non-EU/EEA PRL	Farley, 2005 [93] Canada Longitudinal study	10 federal prisons in British Columbia November 2000 – April 2003	Provision of standard IFN + RBV	n=114 HCV+ treated inmates Positive test result for HCV, not taking illicit drugs for ≥6 months	6 months after end of treatment: - SVR: 51.8% (59/114) <i>Significant non-biological predictors of SVR:</i> - Self-reported HCV risk factors ($p < 0.01$ with IDU)	78.7% (63/80)	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
					highest % SVR, followed by non-IDU, and lowest % SVR in those with unknown risk factors)					
Non-EU/EEA PRL	Farley, 2005 [94] Canada Longitudinal study	6 federal prisons in British Columbia March 2001 – October 2002	Provision of standard IFN + RBV Treatment supervised by a Correctional Service Canada Medical Infectious Diseases Consultant; ongoing care delivered by correctional nursing staff	n=90 treated HCV+ inmates Screening for history of psychiatric diseases; standard liver biochemistry, hematology profiles, HCV-RNA with genotyping and, in the majority of cases, liver biopsy No comparator	6 months after end of treatment: - SVR: 47.7% (43/90)	NR	NR	All inmates who completed treatment achieved at least 80% adherence of the doses and duration of IFN + RBV therapy (definition adherence NR)	NR	Very low
Non-EU/EEA PRL	Simonović Babić, 2016 [110] Serbia Longitudinal study	Special Hospital for Prisoners in Belgrade 2007 – 2013	Provision of pegylated IFN + RBV	n=32 treated HCV+ inmates who were IFN-naïve HCV RNA level >100,000 copies/ml, elevated ALT level on ≥2 visits during preceding 6 months, and a liver biopsy performed within 3 years before treatment No comparator	24 weeks after end of treatment: - SVR : 62.5% (20/32)	87.5% (28/32)	NR	NR	NR	Very low
Non-EU/EEA PRL	Boonwaat, 2010 [90] Australia Nested case-control study	Correctional centres in NSW January 1996 – December 2005	Provision of standard IFN (with or without RBV) or pegylated IFN + RBV Hepatitis clinical service - Initiated in 1995; monthly	n=185 treated HCV+ inmates who attended the hepatitis clinics - During 1995–1998 individuals should have had a fibrosis score of ≥1 and current IDUs were ineligible; in May 2001, the exclusion of IDUs was removed - Sentence of ≥6 months	Timing NR: - SVR: 27.6% (51/185)	NR	NR	62.2% (115/185) treatment adherence (definition NR; assuming those without complete follow-up data available have been non-adherent); 100% adherence among	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			clinic held at 1 correctional centre with 1 visiting specialist - By 2005: 12 additional clinics - Clinics supported by public health nurses who were major referral source following screening	No comparator				patients with complete follow up (115/115)		
Non-EU/EEA PRL	Chew, 2009 [91] USA Longitudinal study	Rhode Island Department of Corrections (both jail and prison) October 2000 – April 2004	Provision of pegylated IFN + RBV On-site evaluation and management	n=71 HCV+ inmates who started treatment All patients with detectable virus were potential candidates, although treatment was not generally recommended for earlier stages of disease; patients with addiction history were counselled and referred to addiction treatment programmes and those with psychiatric disorders/depression were referred to on-site psychiatrist for evaluation and clearance and were closely monitored (both groups were eligible under these circumstances); biopsy was recommended but not required to initiate treatment No comparator	6 months after end of treatment: - SVR: 28.2% (20/71)	46.5% (33/71)	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
EU/EAA GL	Marco, 2010 [99] Spain Retro-spective study	Correctional facilities in Catalunya 2002 – 2008	Provision of pegylated IFN+RBV	n=513 inmates with HCV infection NR No comparator	24 weeks after end of treatment: - SVR: 65.9%	NR	NR	NR	NR	Conference abstract
EU/EAA GL	Pallás, 2010 [105] Spain Cross-sectional study	Penitentiary center El Dueso (Cantabria) 2003 – 2010	Provision of pegylated IFN+RBV	n=41 inmates with HCV infection receiving methadone NR No comparator	NR	80.5% (33/41)	NR	NR	Only inmates on methadone were included	Conference abstract
HCV treatment in prison – usual care (fully or partly DOT)										
EU/EEA PRL	Iacomi, 2013 [96] Italy Longitudinal study	5 correctional facilities in Rome January 2008 – December 2009	Provision of pegylated IFN + RBV Administration of IFN via DOT, RBV via SAT Specialist medical consultations in local hospital	n=50 inmates HCV+ at entry who were sent for consultation to National Institute for Infectious Diseases Liver biopsy consistent with chronic hepatitis and fibrosis stage F1/4, alcohol or drug abusers on rehabilitation/ OST No comparator	24 weeks after end treatment: - SVR: 50.0% (25/50)	60.0% (30/50)	NR	NR	Only PWID on rehabilitation/stable OST were included (68% of the participants had history of IDU), IDU was not associated with treatment outcome	Very low
Non-EU/EEA PRL	Allen, 2003 [87] USA Longitudinal study	Rhode Island Department of Corrections (both jail and prison) 1997 – 2001	Provision of standard IFN + RBV Therapy was DOT, with nurses administering all injections and some RBV doses; SAT	n=90 treated HCV+ inmates Sentences of ≥15 months; patients with addiction history strongly encouraged to enrol in prison substance abuse treatment programmes (for some a documented 1-year sobriety period was required);	6 months after end of treatment: - SVR: 28.9% (26/90) 12 months after end of treatment: - SVR: 18.9% (17/90)	45.6% (41/90)	NR	Adherence to treatment >90%	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			RBV dosing was monitored by random spot checks of medication kept by the patient	during course of study the requirement of liver biopsy was lifted, but still recommended No comparator						
Non-EU/EEA PRL	Maru, 2008 [103] USA Longitudinal study	20 facilities of the Connecticut Department of Corrections September 2002 – October 2006	Provision of pegylated IFN + RBV Primary care provider refers eligible inmates to infectious diseases specialist; treatment initiated in conjunction with an infectious disease nurse DOT	n=68 treated HCV+ inmates who were treatment-naïve Referred to infectious diseases specialist if persistently elevated transaminase levels for ≥6 months; eligible for treatment if fulfils criteria ¹ including laboratory testing and liver biopsy (for genotypes 1/4) No comparator	6 months after end of treatment: - SVR: 47.1% (32/68)	69.1% (47/68)	NR	NR	NR	Very low
Non-EU/EEA PRL	Sterling, 2004 [111] USA Longitudinal study	Virginia Department of Corrections March 1998 – October 2000	Provision of standard IFN + RBV Telemedicine, using real-time video conferencing between correctional facilities and Virginia University, was utilised for all treatment visits	n=59 treated HCV+ inmates (out of consecutive sample of evaluated inmates) HCV-RNA positive and negative for HBV surface antigen and HIV antibodies; patients with ≥2 years of incarceration without contraindication for therapy, if they had evidence of histologically significant HCV as defined by a total HAI ≥5 or the presence of any degree of fibrosis (score ≥1); all HCV+ receive liver biopsy;	24 weeks after end of treatment: - SVR: 35.6% (21/59)	98.3% (58/59)	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			DOT (by prison nurses)	patients with anaemia, renal failure, HIV infection or significant co-morbid or psychiatric diseases were not eligible; final decision on receiving therapy was left to the correctional facility No comparator						
HCV treatment in prison – provision of first generation DAAs										
EU/EAA GL	Marco, 2014 [100] Spain Retrospective study	7 correctional institutions in Spain 2013	Provision of Telaprevir + pegylated IFN + RBV	n=24 HCV infected inmates NR No comparator	62.5% (15/24) eRVR (time period NR)	87.5% (21/24)	NR	Virological failure: 9.5% (2/21)	NR	Conference abstract
EU/EAA GL	Marco, 2014 [101] Spain Retrospective study	Correctional facilities in Catalunya January 2013 – June 2014	Provision of Telaprevir or Boceprevir + pegylated IFN + RBV	n=32 HCV infected inmates - n=27 received Telaprevir - n=5 received Boceprevir No comparator	Time period NR: 85.7% (9/11) as treated analysis	NR	NR	NR	NR	Conference abstract
HCV treatment in prison – provision of second generation DAAs										
EU/EAA GL	Touzón-López, 2016 [113] Spain Longitudinal study	5 correctional facilities in Catalunya October 2014 – April 2016	Provision of DAAs	n=207 inmates with HCV - 18 received pegylated IFN +DAA and - 189 DAA without pegylated IFN -58.8% of patients also received RBV NR. No comparator.	12 weeks after end of treatment: - SVR: 91.1% (123/135)	95.5 % (199/207)	NR	5.2% (7/135) failures without SVR at 12 weeks post-treatment	There were more failures in genotype 3 but this difference was not significant	Conference abstract
EU/EAA GL	Jiménez-Galán, 2016 [97] Spain	1 correctional facility in Madrid	Provision of DAAs	n=50 inmates with HCV - 38 (Sofosbuvir+Ledipasvir) - 28 with and 10 without RBV - 7 paritaprevir/ritonavir/ombitasvir/dasabuvir + RBV	12 weeks after end of treatment: - SVR: 92%	NR	NR	Virological failure: 2 (4%) Significant fibrosis reduction in 32 evaluable patients	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
	Longitudinal, retrospective study	February 2015 – June 2016		NR No comparator						
EU/EAA GL	Minguez-Gallego 2016 [104] Spain Longitudinal retrospective study	1 correctional institution (Albocasser, Castellón) 2015 – 2016	Provision of DAAs	n=40 inmates with HCV infection NR No comparator	Time period NR: - SVR: 85.0% (34/40)	90.0% (36/40)	NR	Virological failure: 2 (5%)	HIV/HCV no difference in efficacy (93.7% vs. 95% at on treatment analysis)	Conference abstract
EU/EAA GL	Fernández-González, 2016 [95] Spain Prospective longitudinal study	Spanish correctional facilities NR	Provision of DAAs	n=83 inmates with HCV infection - 92.8% (77/83) received RBV NR No comparator	12 weeks after end of treatment: - SVR: 94.7 % (36/38)	NR	NR	NR	NR	Conference abstract
EU/EAA GL	Pontali, 2017 [106] Italy Prospective longitudinal study	25 Italian correctional facilities May 2015 – October 2016	Provision of DAAs	n=142 inmates with HCV infection - Sofosbuvir/daclatasvir/RBV= 25.4% - Sofosbuvir/ledipasvir/RBV 21.1% - Sofosbuvir/ledipasvir 14.1% NR No comparator	12 weeks after end of treatment: - SVR: 90%	94.4% (134/142)	NR	NR	NR	Conference abstract
EU/EAA GL	Michel, 2017 [114] France Prospective study	Ile de France prisons, October 2016-April 2017	Provision of DAAs	45 patients with HCV infection (38% newly diagnosed, 62% already known to be HCV infected) NR No comparator	NR	69.5% (16/23), of these, 68.7% (11/16) in prison	31.3% (5/16) completed treatment outside of prison	In 30.4% (7/23) treatment still ongoing		Unpublished research report

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
EU/EAA GL	Meroueh, 2017 [115] France Prospective study	Villeneuve Les Maguleon prison 2010-2016	Provision of pegylated IFN + RBV (2010-2013) Provision of DAAs (2014-206)	287 patients with HCV infection After 2016 all HCV infected prisoners regardless of fibrosis No comparator	62% (29/47) in 2010 65% (19/29) in 2011 65% (24/37) in 2012 68% (22/33) in 2013 90% (48/53) in 2014 98% (58/59) in 2015 98% (28/29) in 2016	NR	NR	NR	NR	Unpublished research report
HCV treatment in prison vs. community – usual care										
EU/EEA PRL	Aspinall, 2016 [88] Scotland Matched cohort study	Health Boards with comprehensive data on prison and community treatment initiations 2 June 2009 – 31 May 2012	Provision of pegylated IFN + RBV with or without a protease inhibitor	Inmates and community patients who initiated HCV treatment at NHS clinics in Scotland: n=291 inmates/ n=1137 community patients (part 1); n=200 inmates (part 2) - Part 1: treatment-naïve adults aged ≥20 years infected with GT 1-4, treated with pegylated IFN + RBV with or without a protease inhibitor, initiated treatment after 1 June 2009 and before 1 December 2011 (GT 1 & 4) and 1 June 2012 (GT 2 & 3) - Part 2: inclusion criteria Part 1 & initiated treatment in prisons in Forth Valley, Greater Glasgow and Clyde, or Lothian - Part 1: inmates vs. community patients - Part 2: inmates treated fully in prisons (n=125) vs. inmates transferred but not released (n=37) vs. inmates released during treatment (n=38)	<i>Part 1</i> 24 weeks after end treatment: - SVR in inmates: 60.5% (176/291; 95% CI 55-66%) - SVR in community: 62.9% (715/1137; 95% CI 60-66%) <i>Part 2</i> 24 weeks after end treatment: - SVR in inmates treated in prison: 73.6% (92/125; 95% CI 65-81%) - SVR in transferred inmates: 59.4% (22/37; 95% CI 42-75%) - SVR in released inmates: 44.7% (17/38; 95% CI 29-62%) for those released during treatment <i>Significant non-biological predictors of SVR:</i> <i>Part 1: NR</i> <i>Part 2</i> - Being released from prison during treatment (OR 0.33; 95% CI 0.15-0.71; p<0.01), but not transfer during treatment (p=0.18)	<i>Part 1</i> NR <i>Part 2</i> 73.5% (147/200; 95% CI 67-80%)	NR	<i>Part 1</i> - Achieving SVR not significantly associated with prisoner status at treatment initiation in ITT analysis (OR 0.87, 95% CI 0.67-1.15; p=0.33); nor in PP analysis (OR 1.18, 95% CI 0.76-1.83, p=0.46) - The same findings were observed when stratifying by genotype <i>Part 2</i> NR	NR	Moderate

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
Non-EU/EEA PRL	Rice, 2012 [107] USA Comparative study	University of Wisconsin Hepatology or Infectious Diseases clinic January 2002 – December 2007	Provision of pegylated IFN + RBV	n=234 HCV-infected inmates and n=319 community patients - Incarcerated patients: expected release date after proposed treatment completion data - Patients with genotype 1/4: at least Metavir stage 2 fibrosis on liver biopsy, medically/psychiatrically appropriate for treatment - All medically and psychiatrically appropriate patients with genotypes 2/3 eligible for treatment without a staging biopsy Inmates vs. community patients	- SVR in incarcerated and non-incarcerated patients: 42.9% (97/226) vs. 38.0% (115/303) (p=0.282) (reported for the per-protocol population only) - When stratifying by genotype: SVR for genotype 1 (30.4% vs. 28.2%; p=0.644); SVR for genotypes 2 and 3 virus (61.3% vs. 64.4%; p=0.749)	- Inmates: 75.0% (174/234) - Community patients: 68.6% p=0.124	NR	Incarcerated patients were as likely to be treated for HCV and as likely to achieve an SVR as non-incarcerated patients (25.0% vs. 22.1%; p=0.304)	Incarcerated patients were more likely to be younger at time of treatment initiation (p<0.001), and to have a history of previous alcohol or IDU (p<0.001)	Low
Intervention: DOT vs SAT										
EU/EEA PRL	Saiz de la Hoya, 2014 [109] Spain RCT	Healthcare centres of 25 prisons in Spain July 2006 – April 2007	Provision of pegylated IFN + RBV DOT: RBV given by study nurse on ongoing basis (1 or 3 times/week) SAT: RBV was self-administered	n=109 DOT vs. n=135 SAT treatment-naive HCV+ inmates Adults with child Pugh score of 5, cirrhotic patients should not have hepatocellular carcinoma and should have alpha-fetoprotein level <100 ng/ml; exclusion criteria ² DOT vs. SAT	24 weeks after end of treatment: - Overall SVR: 63.5% (155/244) - SVR in DOT: 60.6% (66/109; 95% CI, 51.17-69.22) - SVR in SAT: 65.9% (89/135, 95% CI, 57.59-73.38) - SVR in DOT vs. SAT: RR 0.918, 95% CI 0.746-1.125 <i>Significant non-biological predictors of SVR:</i> - No HIV co-infection and low viral load (p<0.05)	83.0% (186/224)	NR	Mean proportion administered doses (n/N NR) ³ : - Overall: 97.9% (SD 6.5) - DOT: 97.6% (SD 8.1) - SAT: 98.2% (SD 4.9) - DOT vs. SAT p=0.117 Mean treatment continuance proportion (n/N NR) ⁴ : - Overall: 82.9% (SD 30.5) - DOT: 81.3% (SD 29.6)	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
								- SAT: 84.2% (SD 31.3) - DOT vs. SAT p=0.091		
EU/EEA GL	Saiz de la Hoya, 2010 [108] Spain Prospective, randomised study	3 correctional facilities in Spain July 2006 – September 2008	Provision of pegylated IFN+RBV	n=244 inmates with HCV infection NR DOT-RBV vs. SAT-RBV (both plus DOT pegylated-IFN)	24 weeks after end of treatment: - SVR: 62.2% 58.5% in DOT arm vs 65.9% in SAT arm; p=0.27 No difference in SVR between PWID vs non-injecting inmates; HIV co-infected showed a lower response rate (46.2% vs 66.7%)	79.8%	NR	NR	NR	Conference abstract
Intervention: nurse-led and specialist-supported telemedicine model										
Non-EU/EEA PRL	Lloyd, 2013 [98] Australia Longitudinal study	3 correctional centres January 2009 – December 2010	Provision of therapy, not specified - 3 nurses followed extensive HCV training - Nurses independently triaged inmates, following blood investigations, structured, hepatitis- and IDU-focused history and physical examination, and further investigations (if necessary), taking into	n=108 treated inmates (out of 391 inmates consecutively assessed by nurse) NR No comparator	24 weeks after end of treatment: - SVR: 43.5% (47/108)	69.4% (75/108)	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	SVR in ITT population Significant non-biological predictors of SVR	Treatment completion	Linkage to care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			account comorbidities, motivation, psychosocial supports, and risk of adverse events - Specialist prescribed treatment after consultation with nurse, via a discussion only (A), teleconference (B), or face-to-face assessment (C)							

ALT: alanine aminotransferase, CI: confidence interval, DAA: direct-acting antiviral, DOT: directly observed therapy, eRVR: extended rapid virologic response - HCV RNA not detected at week 4 and 12, ETR: end of treatment response, GL: grey literature, GT: genotype, HCV: hepatitis C virus, HIV: human immunodeficiency virus, IDU: injecting drug use, IFN: interferon, ITT: intention-to-treat, NHS: National Health Service, NSW: New South Wales, OR: odds ratio, OST: opioid substitution therapy, PP: per-protocol, PRL: peer-reviewed literature, RBV: ribavirin, RCT: randomised controlled trial, RR: relative risk, SAT: self-administered therapy, SVR: sustained viral response, USA: United States of America

1 Detectable HCV RNA, persistent elevations in hepatic transaminase levels ≥6 months, not treated with IFN therapy before, no evidence of another aetiology of chronic liver disease, stability of other chronic illnesses, no evidence of decompensated cirrhosis or chronic renal insufficiency, pre-treatment mental health screening with evidence of stable mental health, with findings confirmed by a psychiatrist, sufficiently long prison sentence to obtain liver biopsy (~3 months) and complete treatment while incarcerated (9 months for genotypes 2/3, 15 months for all others), willing to defer any early-release programmes until treatment is fully completed, willing to be transferred to and remain at a correctional facility where 24-h nursing is available, willing to sign a treatment contract regarding adherence with treatment and recommendations by the infectious diseases specialist, HIV-HCV-coinfected patients are eligible for treatment, chemical dependence is assessed but enrolment in a treatment programme not required

2 Patients who had undergone any systemic antiviral, antineoplastic or immunomodulator therapy in the 6 months prior to the 1st dose of study treatment or any investigational therapy in the 6 weeks prior to the 1st dose of study treatment; patients with the following comorbidities: hepatic disease of an etiology other than HCV; positive IgM anti-HAV test; decompensated hepatic disease (Child-Pugh >6); prior transplantation with a current functional graft; high risk of anaemia, coronary disease or cerebrovascular disease that, according to investigator criteria, were unlikely to tolerate an acute hemoglobin reduction (down to 4 g/dL); history of severe cardiac disease, thyroid disorder or abnormalities in thyroid function tests, unless it could be controlled with conventional treatment; and other severe comorbid conditions, such as chronic respiratory disease, immunological disease, severe retinopathy, severe psychiatric disorders or convulsive disorder; pregnant or lactating women, and men whose partner was pregnant; patients with neutropenia (neutrophil count <1500 cells/mm³), thrombocytopenia (platelet count <90,000 cells/mm³), anaemia (hemoglobin concentration <12 g/dL) or serum creatinine level >1.5 times the upper limit of normal; patients with a history of drug use (including alcohol) in the previous year, except those who were already on methadone maintenance programmes

3 Treatment compliance: number of doses that were actually administered divided by the number of doses that were prescribed

4 Treatment continuance: the number of days that the treatment was actually administered divided by the number of days that the treatment was prescribed

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
HCV treatment in prison – usual care									
EU/EEA PRL	Strock, 2009 [112] Luxembourg Longitudinal study	Centre Pénitentiaire de Luxembourg n=268 HCV+ inmates seen by specialist consultant to evaluate treatment initiation January 2003 – December 2006	Provision of pegylated IFN + RBV All HCV+ inmates are offered a specialist consultation (delay after blood tests 2-4 weeks)	<ul style="list-style-type: none"> - Positive viral load associated with elevated ALT, expressed in multiples of upper limit of normal or an isolated high viral load or a positive viral load associated with HIV infection - Decision to start therapy finally made in case-by-case discussion between practitioner and inmate <p>32.1% (86/268) of evaluated HCV+ inmates started treatment</p> <p><i>Reasons not initiating treatment (n=182):</i></p> <ul style="list-style-type: none"> - Negative PCR results: 31.3% - Deceased: 0.5% - Medical contraindication: 3.3% - Spontaneous viral clearance: 2.7% - Mild disease on liver biopsy: 6.0% - Normal transaminases: 15.9% - Released while in work-up: 13.7% - Still in work-up/waiting for biopsy: 6.6% - Refusal of therapy: 8.2% - Wanting to wait until after release: 11.5% <p>In genotype 2/3 group, 50% started therapy vs. 33% with other genotypes (p=0.01)</p>	<p>16.3% (14/86) inmates stopped therapy early</p> <p><i>Reasons discontinuation (n=14):</i></p> <ul style="list-style-type: none"> - non-compliance: 35.7% - non-responding: 21.4% - side-effects: 42.9% 	<p>18.6% (16/86) inmates were released from prison while under therapy</p> <p>6 months after end of treatment:</p> <ul style="list-style-type: none"> - 1.2% (1/86) refused blood test - 31.4% (27/86) lost to follow-up 6 months after the end of therapy 	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
				(due to waiting period for biopsy in non-genotype 2/3; other reasons for not treating were similar in both groups)					
EU/EEA PRL	De Juan, 2011 [116] Spain Cross-sectional study	26 prisons throughout Spain n=195 untreated HCV+ inmates October 2007 – July 2008	Provision of pegylated IFN + RBV	Meeting chronic HCV treatment criteria, following standard clinic practice (not further specified) <i>Reasons not initiating treatment (n=195 for main group reasons*):</i> <ul style="list-style-type: none"> * Medical reasons: 30.8% <ul style="list-style-type: none"> - Immunological status: 35.0% - Psychiatric/ neurological: 28.3% - Other pathology: 21.7% - Mild fibrosis/ low viral load: 8.3% - Drug use: 5.0% - Pregnancy: 1.7% * Patient reasons: 41.0% <ul style="list-style-type: none"> - Lack of motivation/ awareness only: 47.5% - Fear of adverse events only: 18.8% - Former 2 combined: 20.0% - Influence by relatives/ others: 6.3% - Lack of motivation/ awareness + influence by relatives/others: 3.8% - Lack of confidence in health professionals: 2.5% - Other: 1.3% * Prison reasons: 24.6% <ul style="list-style-type: none"> - Impending release/transfer to another centre: 64.6% - Lack of material resources: 2.1% - Delayed diagnostic tests: 33.3% 	NR	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
				* Patient and prison reasons: 3.6%					
EU/EEA PRL	De Juan, 2014 [92] Spain Longitudinal study	26 prisons throughout Spain n=431 treated HCV+ inmates October 2007 – July 2008	Provision of pegylated IFN + RBV	Meeting chronic HCV treatment criteria, following standard clinic practice (not further specified) 68.8% (431/626) started treatment	22.5% (97/431) discontinued treatment - Most treatment discontinuations occurred in the 1 st trimester of treatment (p<0.05) <i>Reasons discontinuation (n=97 for main group reasons*):</i> * Medical reasons: 20.6% - Adverse events: 75.0% - Drug-addiction relapse: 10.0% - Other: 15.0% * Patient reasons: 37.1% - Lack of motivation/awareness only: 41.7% - Fear of adverse events only: 11.1% - Former 2 combined: 41.7% - Influence by relatives/others: 5.6% * Other causes: 42.3% - Release from prison: 85.4% - Transfer to another prison: 14.4% Release from prison was the most frequent cause for treatment discontinuation for all trimesters except the 1 st , during which the main cause was lack of motivation	NR	NR	NR	Very low
EU/EEA PRL	Marco Mouriño, 2010 [102] Spain	4 prisons in Barcelona n=162 HCV+ treated inmates with history of drug use	Provision of pegylated IFN + RBV IFN administered by clinical nurse, RBV	NR	5.4% discontinued treatment (9/168) <i>Reasons discontinuation (n=9):</i> - Voluntary withdrawal: 33.3% - Adverse effects: 33.3% - Lack of response: 33.3%	3.0% was released or transferred during treatments (5/168)	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	Cross-sectional study	January 2003 – December 2007	delivered to inmate weekly for SAT Treatment co-ordinated with Internal Medicine Service of a Barcelona hospital		<i>Predictors discontinuation (including those released/transferred):</i> - IDU in and out of prison: OR 10.39, 95% CI 1.93-55.88, p=0.006				
Non-EU/EEA PRL	Bate, 2010 [89] Australia Longitudinal study	Department of Gastroenterology and Hepatology of the Royal Adelaide Hospital n=86 treated HCV+ inmates January 1997 – December 2008	Provision of standard IFN (with or without RBV) or pegylated IFN + RBV	To be incarcerated for the entire planned duration of therapy	1.3% (1/79) discontinued therapy because of adverse events	5.8% (5/86) LTFU before 6 months after end of treatment	NR	NR	Very low
Non-EU/EEA PRL	Farley, 2005 [93] Canada Longitudinal study	10 federal prisons in British Columbia n=114 HCV+ treated inmates November 2000 – April 2003	Provision of standard IFN + RBV	Positive test result for HCV, not taking illicit drugs for ≥6 months	14.9% (17/114) discontinued therapy - mostly because of side effects or failure to achieve early response	29.8% (34/114) had no treatment outcome data – reasons NR	NR	NR	Very low
Non-EU/EEA PRL	Farley, 2005 [94] Canada Longitudinal study	6 federal prisons in British Columbia n=214 HCV+ inmates evaluated for treatment	Provision of standard IFN + RBV Treatment supervised by a Correctional Service Canada	42.1% (90/214) eligible for treatment <i>Reasons not eligible (n=124):</i> - Undetectable serum HCV-RNA: 19% - Normal serum aminotransferase levels during incarceration follow-up: 8%	18.9% (17/90) discontinued treatment <i>Reasons discontinuation (n=17):</i> - Adverse events: 47.1% - Non-response: 52.9%	14.4% (13/90) of treated patients were lost to follow-up before assessment of SVR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		March 2001 – October 2002	Medical Infectious Diseases Consultant; ongoing care delivered by correctional nursing staff	<ul style="list-style-type: none"> - Inmate preference not to be treated including those awaiting future therapies: 8% - Psychiatric disease: 3% - Comorbid medical conditions: 1.6% - Normal liver biopsy: 0.8% - Released before start of treatment: 4% - No specified reason for non-treatment: 52% (on review, it was thought that the most likely reason was because of unremarkable serum liver enzymes) 					
Non-EU/EEA PRL	Simonović Babić, 2016 [110] Serbia Longitudinal study	Special Hospital for Prisoners in Belgrade n=32 IFN-naive HCV+ inmates who were treated 2007 – 2013	Provision of pegylated IFN + RBV	<p>HCV RNA level >100,000 copies/ml, elevated ALT level on ≥2 visits during preceding 6 months, and a liver biopsy performed within 3 years before treatment</p> <p>42.1% (32/76) of screened inmates started treatment</p> <p><i>Reasons ineligible (n=44):</i></p> <ul style="list-style-type: none"> - Frequent transfer: 27.2% - Normal biopsy finding: 24.9% - Normal ALT level: 22.7% - Patient discharged too early: 6.8% - Non-compliant patient: 2.2% - Uncontrolled psychiatric disease: 2.2% - Refused therapy: 4.4% - Other: 9.0% 	<p>12.5% (4/32) discontinued therapy</p> <p><i>Reasons discontinuation (n=4):</i></p> <ul style="list-style-type: none"> - Tuberculosis relapse: 25.0% - Drug overdose: 25.0% - Gave up on therapy: 25.0% (not further specified) - No early virologic response: 25.0% 	No follow-up data available 24 weeks after end treatment: 15.6% (5/32)	NR	NR	Very low
Non-EU/EEA PRL	Boonwaat, 2010 [90] Australia	Correctional centres in NSW n=185 treated vs. n=186 untreated	Provision of standard IFN (with or without RBV) or pegylated IFN + RBV	<ul style="list-style-type: none"> - During 1995–1998 individuals should have had a fibrosis score of ≥1 and current IDUs were ineligible; in May 2001, the exclusion of IDUs was removed 	NR	38% (70/185) of treated inmates LTFU before assessment of SVR (timing NR)	Compared to treated inmates, untreated inmates were more often IDU in the community	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	Nested case-control study	HCV+ inmates who attended the hepatitis clinics January 1996 – December 2005	Hepatitis clinical service - Initiated in 1995; monthly clinic held at 1 correctional centre with 1 visiting specialist - By 2005: 12 additional clinics - Clinics supported by public health nurses who were major referral source following screening	- Sentence of ≥ 6 months 50.1% (186/371) initiated treatment <i>Reasons not initiating treatment (n=186):</i> - Imminent release from prison: 59.7% - Ineligible according to Pharmaceutical Benefits Scheme: 20.4% - Free of hepatitis C viraemia on follow-up: 12.9% - Patient refusal: 3.8% - Not specified: 3.2%		- all released from prison	(p=0.01), co-infected with HBV (p=0.001), or had either genotype 1/4 or untypeable genotype, and less often had a biopsy performed (p<0.001) or HCV genotyping results available (p<0.001)		
Non-EU/EEA PRL	Chew, 2009 [91] USA Longitudinal study	Rhode Island Department of Corrections (both jail and prison) n=71 HCV+ inmates who started treatment October 2000 – April 2004	Provision of pegylated IFN + RBV On-site evaluation and management	All patients with detectable virus were potential candidates, although treatment was not generally recommended for earlier stages of disease; patients with addiction history referred to addiction treatment programmes and those with psychiatric disorders/depression were closely monitored (both groups were eligible under these circumstances); biopsy was recommended but not required to initiate treatment	43.7% (31/71) discontinued treatment <i>Reasons discontinuation (n=31):</i> - Side effects: 83.9% - Non-responder: 16.1%	- 9.9% (7/71) LTFU before end of treatment - 5.6% (4/71) LTFU between end of treatment and SVR assessment	NR	NR	Very low
EU/EAA GL	Marco, 2010 [99] Spain	4 correctional facilities n=513 inmates with HCV infection	Provision of pegylated IFN + RBV	NR	20.1% (104/513) discontinued treatment <i>Reasons discontinuation (n=104):</i> - Release from prison: 53.8%	NR	NR	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	Retrospective study	2002-2008							
EU/EAA GL	Pallás, 2010 [105] Spain Cross-sectional study	Penitentiary centre El Dueso (Cantabria) n=41 inmates with HCV infection receiving methadone 2003 – 2010	Provision of pegylated IFN+RBV	NR	19.5% (8/41) discontinuations <i>Reason for discontinuation (n=8):</i> - Patient's decision: 37.5%	NR	NR	Only inmates on methadone were included	Conference abstract
HCV treatment in prison – usual care (fully or partly DOT)									
EU/EEA PRL	Iacomi, 2013 [96] Italy Longitudinal study	5 correctional facilities in Rome n=50 inmates HCV+ at entry who were sent for consultation to National Institute for Infectious Diseases and were treated January 2008 – December 2009	Provision of pegylated IFN-α2a + RBV Administration of IFN via DOT, RBV via SAT	Liver biopsy consistent with chronic hepatitis and fibrosis stage F1/4, alcohol or drug abusers should be on rehabilitation/ OST 37.1% (59/159) of HCV+ inmates evaluated at the institute were eligible - 15.3% (9/59) of eligible inmates refused therapy <i>Reasons not initiating treatment (n=100):</i> - length of detention: 69.0% - contraindicated due to psychiatric problems: 14.0% - contraindicated due to substance abuse: 12.0% - Absence of HCV replication: 4.0% - Decompensated cirrhosis: 1.0%	40.0% (20/50) did not complete treatment <i>Reasons discontinuation (n=20):</i> - No response: 75% (9 null and 6 non-responder) - Side effects: 25%	NR	NR	NR	Very low
Non-EU/EEA PRL	Allen, 2003 [87] USA	Rhode Island Department of Corrections (both jail and prison)	Provision of standard IFN + RBV	Sentences of ≥15 months; patients with addiction history strongly encouraged to enrol in prison substance abuse treatment programmes (for	45.6% (41/90) discontinued treatment <i>Reasons discontinuation (n=41)</i>	- 8.9% (8/90) LTFU before treatment completion	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	Longitudinal study	n=90 treated HCV+ inmates 1997 – 2001	Therapy was essentially DOT, with nurses administering all injections and some RBV doses; SAT RBV dosing was monitored by random spot checks of medication kept by the patient	some a documented 1-year sobriety period was required) 25.8% (90/349) of evaluated inmates started therapy <i>Reasons not initiating treatment (n=259):</i> - Duration of sentence criteria: 75.7% - Spontaneous virus clearance: 11.6% - Decision to decline/defer after informed consent discussions: 11.6% - Exclusion by psychiatrist: 1.2%	- Side effects: 26.8% - Death: 2.4% - Non-response: 70.7%	- 5.6% (5/90) LTFU between treatment completion and 6-month SVR assessment - 8.9% (8/90) LTFU between 6- and 12-month SVR assessment			
Non-EU/EEA PRL	Maru, 2008 [103] USA Longitudinal study	20 facilities of the Connecticut Department of Corrections n=68 treated HCV+ inmates who were treatment-naïve September 2002 – October 2006	Provision of pegylated IFN + RBV Primary care provider refers eligible inmates to infectious diseases specialist; treatment initiated in conjunction with an infectious disease nurse DOT	Referred to infectious diseases specialist if persistently elevated transaminase levels for ≥6 months; eligible for treatment if fulfils criteria ¹ (for genotypes 1/4) 49.3% (68/138) evaluated treatment-naïve patients were eligible to receive therapy <i>Reasons not initiating treatment (n=70):</i> - Release too soon: 57.1% - Normal liver function test results: 11.4% - Normal biopsy findings: 10.0% - Patient refused consent/change of facilities: 2.9% - Patient refused consent/other: 7.1% - Hepatic decompensation: 2.9%	30.9% (21/68) discontinued treatment <i>Reasons discontinuation (n=21):</i> - Lack of EVR: 57% - Mental health issues: 14.3% - Adverse effects: 9.5% - Early release/patient discontinuation of treatment/missing chart: 19%	NR	NR	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
				<ul style="list-style-type: none"> - Patient deemed to be non-compliant: 1.4% - Uncontrolled HIV disease: 4.3% - Uncontrolled diabetes: 1.4% - Unclear: 1.4% 					
Non-EU/EEA PRL	Sterling, 2004 [111] USA Longitudinal study	Virginia Department of Corrections n=59 treated HCV+ inmates (out of consecutive sample of evaluated inmates) March 1998 – October 2000	Provision of standard IFN + RBV Telemedicine, using real-time video conferencing between correctional facilities and Virginia University, was utilised for all treatment visits DOT (by prison nurses)	<p>HCV-RNA positive and negative for HBV surface antigen and HIV antibodies; patients with ≥2 years of incarceration without contraindication for therapy, if they had evidence of histologically significant HCV as defined by a total HAI ≥5 or the presence of any degree of fibrosis (score ≥1); all HCV+ receive liver biopsy; patients with anaemia, renal failure, HIV infection or significant co-morbid or psychiatric diseases were not eligible; final decision on receiving therapy was left to the correctional facility</p> <p>- 73.1% (87/119 NR) of consecutive inmates who underwent liver biopsy, were eligible for treatment - 49.6% (59/119) of inmates who underwent liver biopsy received therapy</p>	1.7% (1/59) stopped treatment for unclear reasons	13.6% (8/59) LTFU between completion of treatment and SVR assessment (unclear if some inmates LTFU before completion of treatment)	NR	NR	Very low
HCV treatment in prison – provision of first generation DAA									
EU/EAA GL	Marco, 2014 [100] Spain Retrospective study	7 correctional institutions in Spain n=24 HCV infected inmates	Provision of Telaprevir + pegylated IFN + RBV	NR	12.5% (3/24) discontinuations <i>Reasons discontinuation (n=3):</i> - LTFU after release from prison: 33.3% - Adverse events: 33.3%	NR	NR	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		2013			- Rash (telaprevir only): 33.3%				
EU/EAA GL	Marco, 2014 [101] Spain Retrospective study	Correctional facilities in Catalunya n=32 HCV infected inmates January 2013 – June 2014	Provision of Telaprevir or Boceprevir + pegylated IFN + RBV	NR	21.9% (7/32) discontinuations <i>Reasons discontinuation (n=7):</i> - Lack of virologic response: 28.6% - Adverse events: 28.6% - Release from prison: 28.6% - Unknown (telaprevir only): 14.3%	NR	NR	NR	Conference abstract
HCV treatment in prison – provision of second generation DAA									
EU/EAA GL	Touzòn-López, 2016 [113] Spain Longitudinal study	5 correctional facilities in Catalunya n=207 inmates with HCV October 2014 – April 2016	Provision of DAAs	NR	5.9% (8/135) discontinuations <i>Reasons discontinuation (n=8):</i> - Release from prison: 62.5% - Adverse events: 12.5% - NR: 25.0%	NR	NR	NR	Conference abstract
EU/EAA GL	Jiménez-Galán, 2016 [97] Spain Longitudinal Retrospective Study	1 correctional facility in Madrid n=50 inmates with HCV February 2015 – June 2016	Provision of DAA	NR	Voluntary discontinuation: 2% (1/50)	NR	NR	NR	Conference abstract
EU/EAA GL	Minguez-Gallego, 2016 [104] Spain Longitudinal retrospective Study	1 correctional institution (Albocasser, Castellón) n=40 inmates with HCV infection	Provision of DAAs	NR	NR	10% (4/40) LTFU	NR	NR	Conference abstract

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		2015 – 2016							
EU/EAA GL	Fernández-González, 2016 [95] Spain Prospective longitudinal study	Spanish correctional facilities n=83 inmates with HCV infection NR	Provision of DAAs	NR	2.4% (2/83) discontinuations (reasons NR) No discontinuation due to adverse events	NR	NR	NR	Conference abstract
EU/EAA GL	Pontali, 2017 [106] Italy Prospective longitudinal study	25 Italian correctional facilities n=142 inmates with HCV infection May 2015 – October 2016	Provision of DAAs	NR	5.6% (8/142) patients discontinued <i>Reasons discontinuation (n=8):</i> - Adverse events: 12.5%	NR	NR	NR	Conference abstract
EU/EAA GL	Marco-Mourino, 2016 [117] Spain Prospective longitudinal study	Prisons in Catalunya N=212 inmates with HCV infection October 2014- April 2016	Provision of DAAs	NR	3.8% (8/212) discontinuations <i>Reasons for discontinuation (n=8):</i> -37.5% (3/8) release from prison -25% (2/8) other concomitant diagnosis -12.5% (1/8) patient's decision -12.5% (1/8) adverse events -12.5% (1/8) death	NR	NR	NR	Conference abstract
HCV treatment in prison vs. community – usual care									
EU/EEA PRL	Aspinall, 2016 [88] Scotland Matched cohort study	Health Boards with comprehensive data on prison and community treatment initiations	Provision of pegylated IFN + RBV with or without a protease inhibitor	NR	Part 1 NR Part 2 - 17.5% (35/200) did not complete treatment – no reasons reported - 9.0% (18/200) unknown if completed or not (for the	NR	NR	NR	Moderate

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		Inmates and community patients who initiated HCV treatment at NHS clinics in Scotland: n=291 inmates/ n=1137 community (part 1; treatment-naïve); n=200 inmates (part 2) 2 June 2009 – 31 May 2012			logistic regression, it was assumed that they had not completed treatment) <i>Predictors of completion:</i> - Having cirrhosis (OR 0.16; 95% CI 0.03-0.81; p=0.03) - Being transferred during treatment (OR 0.41; 95% CI 0.17-1.00; p=0.05) - Being released during treatment (OR 0.10; 95% CI 0.04- 0.24; p<0.01)				
Non-EU/EEA PRL	Rice, 2012 [107] USA Comparative study	University of Wisconsin Hepatology or Infectious Diseases clinic n=234 HCV-infected inmates and n=319 community patients January 2002 – December 2007	Provision of pegylated IFN + RBV	- Incarcerated patients: expected release date after proposed treatment completion data - Patients with genotype 1/4: at least Metavir stage 2 fibrosis on liver biopsy, medically/psychiatrically appropriate for treatment - All medically and psychiatrically appropriate patients with genotypes 2/3 eligible for treatment without a staging biopsy - 60.3% (234/388) incarcerated and 61.2% (319/521) non-incarcerated patients started treatment <i>Reasons for not treating HCV-infected inmates (n=154):</i> - Failure to meet DOC requirements: 43.5% (most	NR	NR	NR		Low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
				<p>common reason being expected release date before anticipated treatment completion)</p> <ul style="list-style-type: none"> - Medical: 15.6% - Psychiatric: 3.9% - Medical and psychiatric: 1.3% - Patient declined: 3.2% - Other: 3.2% - Unknown: 29.2% <p><i>Reasons for not treating HCV-infected community members (n=202):</i></p> <ul style="list-style-type: none"> - Medical: 26.2% - Psychiatric: 6.9% - Medical and psychiatric: 4.5% - Substance abuse: 6.9% - Patient declined: 22.8% - Payment issue: 3.5% - Other: 7.9% - Unknown: 28.2% <p>- Significant differences between both groups in the percentage of reasons for not initiating treatment were found for meeting DOC requirements ($p < 0.0001$), medical and psychiatric issues ($p = 0.0007$), active substance use ($p = 0.0004$), and patient declining ($p < 0.0001$)</p>					
Intervention: DOT vs SAT									
EU/EEA PRL	Saiz de la Hoya, 2014 [109] Spain	Healthcare centres of 25 prisons in Spain n=109 DOT vs. n=135 SAT	Provision of pegylated IFN + RBV DOT: RBV given by study	Child Pugh score of 5, cirrhotic patients should not have hepatocellular carcinoma and should have alpha-fetoprotein level <100 ng/ml; exclusion criteria ²	9.4% (21/244) discontinued treatment <i>Reasons discontinuation (n=21):</i> - Treatment failure: 66.7%	4.9% (11/224) lost to follow-up before completion of treatment	NR	NR	Moderate

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	RCT	treatment-naive HCV+ inmates July 2006 – April 2007	nurse on on-going basis (1 or 3 times/week) SAT: RBV was self-administered	No treatment was initiated in 3.3% (4/122) of randomised inmates in original DOT group - LTFU: 25.0% - Voluntary withdrawal: 25.0% - Withdrawal due to assignment to DOT: 50.0% No treatment was initiated in 3.1% (4/130) of randomised inmates in original SAT group - LTFU: 25.0% - Voluntary withdrawal: 50.0% - Delayed biopsy: 25.0% 7.4% (9/122) of inmates who had been randomly allocated to DOT, rejected to follow DOT and followed SAT instead	- Patient decision: 19.0% - Adverse event: 14.3%				
EU/EEA GL	Saiz de la Hoya, 2010 [108] Spain Prospective, randomised study	3 correctional facilities in Spain n=244 inmates with HCV infection July 2006 – September 2008	Provision of pegylated IFN+RBV	NR	<i>Reasons discontinuation:</i> - 2.8% transfer to centre not involved in the study - 9.4% release from prison - 4.5% voluntary decision - 3.6% adverse events	NR	NR	NR	Conference abstract
Intervention: nurse-led and specialist-supported telemedicine model									
Non-EU/EEA PRL	Lloyd, 2013 [98] Australia Longitudinal study	3 correctional centres n=108 treated inmates (out of 391 inmates consecutively seen by nurse)	Provision of therapy, not specified - 3 nurses followed extensive HCV training - Nurses independently	- 55.5% (217/391) completed the nurse-led assessments - 36.1% (141/391) completed the specialist physician review - 27.6% (108/391) initiated treatment <i>Reasons not initiating treatment (n=283):</i> - IDU: 3.2%	12.0% (13/108) discontinued treatment <i>Reasons discontinuation (n=13)</i> - IDU: 7.7% - Adverse events: 61.5% - Non-response: 30.8%	9.3% (10/108) LTFU before treatment completion due to release 13.0% (14/108) LTFU between treatment completion and	- The timelines for completion of each clinical milestone varied widely with a mean of 58 days from enrolment to nurse-led assessment completion (95% CI, 44–72 days); a	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/access	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		January 2009 – December 2010	triaged inmates, following blood investigations, structured, hepatitis- and IDU-focused history and physical examination, and further investigations (if necessary), taking into account comorbidities, motivation, psychosocial supports, and risk of adverse events - Specialist prescribed treatment after consultation with nurse, via a discussion only (A), teleconference (B), or face-to-face assessment (C)	- Transfer: 6.4% - PCR-negative: 11.7% - Released: 33.6% - Refusal of therapy: 31.4% - Adverse events: 2.1% - Treatment non-response: 1.4% - Still in progress towards initiating treatment: 10.2%	9.3% (10/108) treatment not yet completed	SVR assessment due to release 4.6% (5/108) were still in follow-up (no post-treatment outcomes reported)	mean of 67 days from nurse-led assessments to specialist review (95% CI, 51–84 days); and a mean of 54 days from specialist review to treatment initiation (95% CI, 42–65 days) - Longer lead time from assessment to treatment initiation among those patients who needed a consultation with the specialist either via telemedicine or face-to-face (p-value NR)		

CI: confidence interval, DAA: Direct-acting antiviral agents; DOT: directly observed therapy, EVR: early viral response, GL: grey literature, GT: genotype, HCV: hepatitis C virus, IDU: injecting drug use, IFN: interferon, LTFU: lost to follow-up, NHS: National Health Service, OR: odds ratio, OST: opioid substitution therapy, PRL: peer-reviewed literature, RBV: ribavirin, RCT: randomised controlled trial, RR: relative risk, RVR: rapid viral response, SAT: self-administered therapy, SVR: sustained viral response, USA: United States of America

¹ Detectable HCV RNA, persistent elevations in hepatic transaminase levels ≥ 6 months, not treated with IFN therapy before, no evidence of another aetiology of chronic liver disease, stability of other chronic illnesses, no evidence of decompensated cirrhosis or chronic renal insufficiency, pre-treatment mental health screening with evidence of stable mental health, with findings confirmed by a psychiatrist,

sufficiently long prison sentence to obtain liver biopsy (~3 months) and complete treatment while incarcerated (9 months for genotypes 2/3, 15 months for all others), willing to defer any early-release programmes until treatment is fully completed, willing to be transferred to and remain at a correctional facility where 24-h nursing is available, willing to sign a treatment contract regarding adherence with treatment and recommendations by the infectious diseases specialist, HIV-HCV-coinfected patients are eligible for treatment, chemical dependence is assessed but enrolment in a treatment programme not required

² Patients who had undergone any systemic antiviral, antineoplastic or immunomodulator therapy in the 6 months prior to the 1st dose of study treatment or any investigational therapy in the 6 weeks prior to the 1st dose of study treatment; patients with the following comorbidities: hepatic disease of an aetiology other than HCV; positive IgM anti-HAV test; decompensated hepatic disease (Child-Pugh >6); prior transplantation with a current functional graft; high risk of anaemia, coronary disease or cerebrovascular disease that, according to investigator criteria, were unlikely to tolerate an acute haemoglobin reduction (down to 4 g/dL); history of severe cardiac disease, thyroid disorder or abnormalities in thyroid function tests, unless it could be controlled with conventional treatment; and other severe comorbid conditions, such as chronic respiratory disease, immunological disease, severe retinopathy, severe psychiatric disorders or convulsive disorder; pregnant or lactating women, and men whose partner was pregnant; patients with neutropenia (neutrophil count <1500 cells/mm³), thrombocytopenia (platelet count <90,000 cells/mm³), anaemia (haemoglobin concentration <12 g/dL) or serum creatinine level >1.5 times the upper limit of normal; patients with a history of drug use (including alcohol) in the previous year, except those who were already on methadone maintenance programmes.

Cost-effectiveness

Region Source	Reference, country, study design	Prison setting, sample	Perspective, time horizon	Scenarios	Conclusions	Sub-group considerations	Level of evidence
Intervention: no treatment vs. 2 drug therapy vs. 3-drug therapy							
Non-EU/EEA PRL	Liu, 2014 [118] USA Cost-effectiveness study	Correctional facilities in USA n=NR	Societal Lifetime	No treatment vs. 2-drug therapy (pegylated IFN and RBV for 48 weeks) vs. 3-drug therapy with either boceprevir or sofosbuvir (4 weeks of pegylated IFN and RBV followed by 24 weeks of triple therapy)	<i>Short sentences (<1.5 years)</i> - Costs no treatment vs. sofosbuvir 3-drug therapy: \$174,174 vs. \$228,316 - QALY yields no treatment vs. sofosbuvir 3-drug therapy: 13.21 vs. 15.31 QALYs - Sofosbuvir cost \$25,700 per QALY gained compared with no treatment <i>Long sentences (≥1.5 years)</i> - Costs no treatment vs. 2-drug therapy vs. 3-drug therapy with boceprevir vs. with sofosbuvir: \$182,596 vs. \$227,832 vs. \$235,151 vs. \$241,948 - QALY yields no treatment vs. 2-drug therapy vs. 3-drug therapy with boceprevir vs. with sofosbuvir: 13.12 vs. 13.57 vs. 14.43 vs. 15.18 QALYs - Sofosbuvir 3-drug therapy dominated other treatments, costing \$28 800 per QALY gained compared with no treatment Sofosbuvir-based treatment is cost-effective for incarcerated persons. Given the high price of sofosbuvir, affordability is an important consideration	NR	Moderate
Intervention: treatment with or without liver biopsy							
Non-EU/EEA PRL	Sterling, 2005 [119] USA	Virginia DOC n=302 inmates	Virginia DOC Until 24 months after	Treating (IFN and RBV) all patients without a liver biopsy vs.	- Costs to simply treat 100 representative patients without a biopsy: \$1,775,900; cost per SVR: \$35,517 - Costs to treat only those patients with an elevated serum ALT (51% of the cohort): \$905,709; cost per SVR would be unaffected	NR	Low

Region Source	Reference, country, study design	Prison setting, sample	Perspective, time horizon	Scenarios	Conclusions	Sub-group considerations	Level of evidence
	Cost-effectiveness study		end of treatment	<p>Treating (IFN and RBV) only those patients with an elevated ALT without performing a liver biopsy</p> <p>vs.</p> <p>Liver biopsy and examination of liver histology utilised to define which patients had sufficient liver injury from chronic HCV (Knodell score <5 and no fibrosis) to warrant treatment (IFN and RBV)</p>	<p>- Costs to treat 100 inmates after performing liver biopsy (85% of the cohort): \$1,651,200; cost per SVR: \$38,851</p> <p>- Cost savings biopsy-directed strategy: \$124,700 for 100 patients; incremental cost associated with treating all patients: \$3,334 for each additional SVR. Cost savings would increase to \$408,857 when only those with fibrosis were treated (69% of the cohort)</p> <p>- Cost savings ALT-directed strategy: \$870,191 for the 100 patients; incremental cost associated with treating all patients: \$0 for each additional SVR</p> <p>A strategy in which inmates with chronic HCV undergo liver biopsy and only those with a histologically significant liver disease undergo therapy with standard IFN and RBV is cost-effective compared to treating all inmates without a biopsy or elevated ALT</p>		
Non-EU/EEA PRL	Tan, 2008 [120] USA Cost-effectiveness study	US prisons n=NR	US prison healthcare system Lifetime	<p>Prisoners did not undergo a liver biopsy prior to starting treatment (pegylated IFN and RBV)</p> <p>vs.</p> <p>All prisoners underwent a liver biopsy prior to beginning therapy (pegylated IFN and RBV) in order to determine stage of fibrosis</p>	<p><i>First strategy</i></p> <p>- Treatment was cost-effective compared to no treatment in prisoners of all age ranges and genotypes when liver biopsy was not a prerequisite to starting ART (first strategy)</p> <p><i>Second strategy</i></p> <p>- Treatment after pre-treatment biopsy was cost-effective compared to no treatment in prisoners of all age ranges and genotypes with portal fibrosis, bridging fibrosis or compensated cirrhosis (second strategy)</p> <p>Pegylated IFN and RBV combination therapy is cost-effective in the prison population. The strategy with pre-treatment biopsy was the most cost-effective, however not for inmates between 40 and 49 years old with genotype 1 and no fibrosis</p>	<p><i>First strategy</i></p> <p>- In prisoners 40-49 years, treatment saved \$41,321 & increased QALYs by 0.75</p> <p>- In prisoners 50-59 years, treatment saved \$33,445 & increased QALYs by 0.69</p> <p>- In prisoners 60-69 years, treatment saved \$11,637 & increased QALYs by 0.5</p> <p><i>Second strategy</i></p> <p>- Patients with no fibrosis:</p> <ul style="list-style-type: none"> o In prisoners 40-49 years, treatment increased costs by \$300 & increased QALYs by 0.02 o In prisoners 50-59 years, treatment saved \$5,937 & increased QALYs by 0.22 o In prisoners 60-69 years, treatment increased costs by \$1,022 & increased QALYs by 0.15 <p>- Patients with portal fibrosis:</p> <ul style="list-style-type: none"> o In prisoners 40-49 years, treatment saved \$18,516 & increased QALYs by 0.58 	Moderate

Region Source	Reference, country, study design	Prison setting, sample	Perspective, time horizon	Scenarios	Conclusions	Sub-group considerations	Level of evidence
						<ul style="list-style-type: none"> o In prisoners 50-59 years, treatment saved \$25,261 & increased QALYs by 0.70 o In prisoners 60-69 years, treatment saved \$7,714 & increased QALYs by 0.45 -Patients with bridging fibrosis: <ul style="list-style-type: none"> o In prisoners 40-49 years, treatment saved \$102,513 & increased QALYs by 1.60 o In prisoners 50-59 years, treatment saved \$85,454 & increased QALYs by 1.64 o In prisoners 60-69 years, treatment saved \$34,773 & increased QALYs by 0.96 -Patients with compensated cirrhosis: <ul style="list-style-type: none"> o In prisoners 40-49 years, treatment saved \$262,313 and increased QALYs by 4.07 o In prisoners 50-59 years, treatment saved \$155,974 & increased QALYs by 2.91 o In prisoners 60-69 years, treatment saved \$61,542 & increased QALYs by 1.54 - Treatment was not cost-effective compared to no treatment in patients 40-49 years with no fibrosis and genotype 1 - Treatment was cost-effective but not dominant compared to no treatment in patients between 40-49 years with no fibrosis (ICER \$15,000/QALY), and in patients 60-69 years with no fibrosis (ICER \$6,813/QALY) 	

ALT: alanine aminotransferase, DOC: Department of Corrections, IFN: interferon, NR: not reported, PRL: peer-reviewed literature, QALY: quality-adjusted life year, RBV: ribavirin, SVR: sustained viral response, US(A): United States (of America)

Guidelines

Four guidelines on HCV treatment were included, of which three were specific to prison settings (one supranational and two national guidelines), and the other one was a supranational guideline not specific to prison setting

Summary of guidelines on HCV treatment

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	<p>As with HBV, diagnosis and treatment for HCV are expensive and not available in all countries. Assessment for HCV is very similar to assessment for HBV. In addition to assessment of the severity of liver disease, it includes the determination of the genotype of the virus. Both components are critical to treatment decisions. It consists of the following steps:</p> <ul style="list-style-type: none"> • Assess the severity of the liver disease (see HBV); • Investigate other causes of liver disease and coinfection with HBV or with HIV; • Determine HCV genotype (1 to 6) prior to antiviral treatment, as the genotype will determine the treatment; • Vaccinate for hepatitis A-B to prevent co-infection with these hepatitis viruses and protect the liver
<i>Specific to prison setting – national guidelines</i>	
National Hepatitis C Strategy 2011-2014 (Ireland) [121]	<ul style="list-style-type: none"> • The principle that treatment should be available in an equitable manner for all those infected with HCV, irrespective of mode of acquisition, has been firmly agreed by the treatment sub-group and endorsed by the main working group. • Improving access to treatment and supporting patients through treatment will reduce the progression from viral infection to liver damage for many patients. It should also contribute to a reduction in the prevalence of HCV infection, thus reducing the associated clinical and social burden of the disease. • The prevalence of HCV amongst prisoners with a history of injecting drug use is particularly high. Those serving custodial sentences should be offered HCV care in line with best practice models. • Recommendation 33: Develop, implement and evaluate a treatment model appropriate to the prison setting on a national basis.
Technical Group of Italian experts on Hepatitis management (Italy), 2009 [122]	<ul style="list-style-type: none"> • Is advisable that the prison stay could represent a unique occasion to inform about health and hepatitis in particular a population of 'hard-to-reach' subjects when they are outside the prison walls. • Start antiviral therapy only in prisoners with an imprisonment duration that allows the completion of treatment or when the linkage and continuity of care is guaranteed. • Apply Directly Observed Therapy (DOT) strategy as already done for HIV infection • Start or maintain OST with methadone or buprenorphine in active PWID in order to limit Hepatitis transmission and reinfection. • Adopt a multidisciplinary approach including hepatologists, infectious disease specialists, psychiatrists, psychologists, nurses, penitentiary physicians. • Establish a clinical and social link between hospital, general practitioners and penitentiary institutions in order to maintain the linkage to care after release from prison. • Start alcohol abuse cessation programmes. • It is advisable to increase the participation to Hepatitis therapy randomized clinical trials in prison setting.

Other guidelines – supranational guidelines

European Association for the Study of the Liver (EASL), 2016 [34]

Recommendations

- The goal of therapy is to cure HCV infection to prevent hepatic cirrhosis, decompensation of cirrhosis, hepatocellular carcinoma (HCC), severe extrahepatic manifestations and death.
 - The endpoint of therapy is undetectable HCV RNA in blood by a sensitive assay (lower limit of detection ≤ 15 IU/ml) 12 weeks (SVR12) and/or 24 weeks (SVR24) after the end of treatment.
 - Undetectable HCV core antigen 12 weeks (SVR12) and/or 24 weeks (SVR24) after the end of treatment is an alternative endpoint of therapy in patients with detectable HCV core antigen prior to therapy if HCV RNA assays are not available or not affordable.
 - In patients with advanced fibrosis and cirrhosis, HCV eradication reduces the rate of decompensation and will reduce, albeit not abolish, the risk of HCC. In these patients surveillance for HCC should be continued.
 - All treatment-naïve and treatment-experienced patients with compensated or decompensated chronic liver disease due to HCV must be considered for therapy.
 - Treatment should be considered without delay in patients with significant fibrosis or cirrhosis (METAVIR score F2, F3 or F4), including decompensated (Child-Pugh B or C) cirrhosis, in patients with clinically significant extra-hepatic manifestations (e.g. symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma), in patients with HCV recurrence after liver transplantation, and in individuals at risk of transmitting HCV (active injection drug users, men who have sex with men with high-risk sexual practices, women of child-bearing age who wish to get pregnant, haemodialysis patients, incarcerated individuals).
 - Patients with decompensated cirrhosis and an indication for liver transplantation with a MELD score ≥ 18 -20 should be transplanted 6 months, these patients can be treated before transplantation.
 - Treatment is not recommended in patients with limited life expectancy due to non-liver-related comorbidities.
 - National elimination plans require the development of economic partnerships and planning to expedite unrestricted access to treatment.
- In 2016 and onwards, IFN-free regimens are the best options in treatment-naïve and treatment-experienced, DAA-naïve patients with compensated and decompensated liver disease, because of their virological efficacy, ease of use and tolerability. Indications depend on the HCV genotype/subtype, the severity of liver disease, and/or the results of prior therapy. The indications are the same in HCV-mono-infected and HIV-co-infected patients.
- The panel recognises the heterogeneity of per capita incomes and health insurance systems across Europe and in other regions, and therefore the imposition to continue to utilise regimens with pegylated IFN- α and ribavirin, with or without DAAs, such as telaprevir, boceprevir, simeprevir or sofosbuvir. However, the advent of new DAAs implies that these regimens are not recommended in 2016. It is hoped that the publication of up-to-date recommendations will guide reimbursement and discounting of drug costs in order to harmonize treatments across different countries and regions.

Annex 12. Summary tables and guideline summaries – Throughcare

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
Intervention: pre-release individual intervention								
Non-EU/EEA PRL	Bauserman, 2003 [123] USA Longitudinal study	Local jails in Maryland counties, Baltimore city, and in some facilities of the Maryland Department of Corrections July 1996 – May 2000	PCM intervention: - Individual counselling and case management services - Skills-building for personal HIV risk, condom use, substance abuse, transitioning into community - Post-release plans, including referrals - Combined with group educational sessions covering variety of topics - Mandatory and optional modules ¹	n=745 PCM completer inmates Inmates within 6 months of expected release date No comparator	NR	Change from pre- to post-test (time after release NR): - Increase attitude towards condoms ($p<0.001$, $d=0.27$) - Increase self-efficacy to use condoms ($p<0.001$, $d=0.27$) - Increase self-efficacy to reduce IDU risk ($p=0.05$, $d=0.16$) - Decrease self-efficacy to reduce other substances risk ($p<0.001$, $d=0.27$) - Increase safer sex intentions ($p<0.001$, $d=0.15$) - Increase likelihood that you have HIV/AIDS ($p=0.001$, $d=NR$) - Same likelihood that you will get HIV/AIDS ($p=0.54$, $d=NR$)	Some participants showed greater changes than others. Data suggested those who initially scored lowest - and consequently more likely to be at risk - showed the greatest improvements	Very low
Non-EU/EEA PRL	Grinstead, 1999 [126] USA RCT	A large state prison for men October 1994 – July 1996	Intervention: - 30-minute session with trained inmate peer educator - Assess post-release HIV risk and make risk reduction plan; provide referrals - Appointments for follow-up survey, for which they receive reimbursements Control: no intervention, not further specified Access to HIV educational materials and informal consultation with staff for all inmates	n=199 intervention vs. n=205 control inmates Males; within 14 days of release Intervention vs. control	NR	Comparison intervention vs. control at follow-up 2 weeks after release: - Significant difference condom use during first time oral, vaginal or anal sex after release ($p=0.05$) - Non-significant difference drug use since release ($p=ns$) - Non-significant difference IDU since release ($p=ns$) - Non-significant difference sharing needles among IDUs since release ($p=ns$)	NR	Very low
Non-EU/EEA PRL	Wolitski, 2006 [130] USA	8 state prisons in 4 states	EI: - 2 individual sessions before release (60-90 minutes) and 4 sessions at 1, 3, 6 and 12	n=263 EI vs. n=259 SSI Aged 18-29 years; incarcerated ≥ 90 days,	NR	At week 1 and 12 post-release: - No statistically significant differences in any sexual behaviour between SSI and EI groups At week 24 post-release, EI vs. SSI:	Given the low prevalence of IDU in both groups at week 1 (1.8%)	Low

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
	RCT	2001 – 2002	<p>weeks after release (30-60 minutes)</p> <ul style="list-style-type: none"> - 1st in-prison sessions same as SSI session - 2nd in-prison session: community re-entry needs, including referrals - Post-release sessions: review and update of risk-reduction plan - Additional sessions if needed <p>SSI:</p> <ul style="list-style-type: none"> - 60-90 individual session ~2 weeks before release - Based on brief HIV-risk assessment and reduction planning intervention (Project START) - Assessment HIV, hepatitis and STI knowledge and risk behaviour, personal risk-reduction plan, provision of information, skills training and referrals 	<p>scheduled for release within 14-60 days; able to provide informed consent and speak English; willing to provide post-release contact information; released to unrestricted environment in site-specific catchment areas</p> <p>EI vs. SSI</p>		<ul style="list-style-type: none"> - Significantly less unprotected vaginal/anal sex at last sexual intercourse with any partner (adjusted OR 0.48, 95% CI 0.24-0.95) - Significantly less unprotected vaginal/anal sex overall with any partner (adjusted OR 0.40, 95% CI 0.18-0.88) - Significantly less unprotected vaginal/anal sex overall with a main partner (adjusted OR 0.30, 95% CI 0.13-0.71) - No significant difference in unprotected vaginal/anal sex at last sexual intercourse with an at-risk partner and overall with a non-main partner <p>EI at week 24 vs. SSI at week 12 after release (same time elapsed since end of intervention):</p> <ul style="list-style-type: none"> - Significantly less unprotected vaginal/anal sex at last sexual intercourse with any partner (adjusted OR 0.45, 95% CI 0.22-0.91) - Significantly less unprotected vaginal/anal sex overall with any partner (adjusted OR 0.45, 95% CI 0.20-0.98) - Significantly less unprotected vaginal/anal sex overall with a main partner (adjusted OR 0.43, 95% CI 0.19-0.99) - Significantly less unprotected vaginal/anal sex at last sexual intercourse with an at-risk partner (adjusted OR 0.42, 95% CI 0.20-0.90) - No significant difference in unprotected vaginal/anal sex overall with a non-main partner² 	<p>SSI, 0.9% EI), 12 (3.6% SSI, 2.4% EI), and 24 (3.6% SSI, 3.9% EI), no outcome analyses were performed</p>	
Intervention: pre-release group intervention								
Non-EU/EEA	EI-Bassel, 1995 [124]	New York City's Rikers Island Jail	<p>SS:</p> <ul style="list-style-type: none"> - 16 2-hour group sessions twice weekly in prison and 6 group booster sessions monthly in the community - Group size n=10, led by 2 group facilitators³ <p>AI:</p>	<p>n=67 SS vs. n=78 AI inmates</p> <p>Females, aged 18-55 years, convicted and serving a sentence of 3-12 months, who used cocaine, crack or heroin ≥3 times/week during 3</p>	NR	<p>Change from pre-test to 1-month post-release test in the SS group compared to AI group for:</p> <ul style="list-style-type: none"> - Safer sex behaviour: OR 3.83 (p<0.09) - Coping skills: OR 2.83 (p=0.02) - Perceived emotional support: OR 2.71 (p=0.03) 	<p>Study focuses solely on incarcerated women with recent histories of significant drug abuse</p>	Very low

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
			<ul style="list-style-type: none"> - 3 2-hour group sessions - HIV/AIDS information primarily focussed on transmission-related issues and safer sex and drug alternatives 	<p>months before arrest, and are within 10 weeks of scheduled release to New York City boroughs (excluding Staten Island)</p> <p>SS vs. AI</p>		No significant difference between intervention groups in perceived vulnerability to HIV, sexual self-efficacy and AIDS knowledge	Participants who were married or living with their partner were significantly less likely to report improving safer sex behaviour (OR 0.229, p=0.02)	
Non-EU/EEA PRL	Fogel, 2015 [125] USA RCT	2 prisons for women in North Carolina (1 is primary processing facility) September 2010 – November 2011	<p>Power</p> <ul style="list-style-type: none"> - 8 interactive group sessions (1.5 hours) delivered over 4 weeks provided by nurse and social worker⁴ - 1 booster session 1 month after session 8 and prior to release; 3 5-minute booster phone calls after release <p>Control</p> <ul style="list-style-type: none"> - 1 1-h standard-of-care STI education session by prison nurse, including information on STI transmission, sexual abstinence, and condom use - During 1st 3 months of incarceration - Provided to all women, also POWER participants 	<p>n=265 Power vs. n=256 control newly incarcerated inmates</p> <p>Females; 18-60 years; total sentence length ≤12 months; speaking English; able to provide verbal and written consent; planning to live in North Carolina during study; having had/ expecting to have sexual activity with a man; HIV-negative; <6 months left of sentence</p> <p>POWER vs. control</p>	NR	<p>* POWER vs. control at 3 months after release:</p> <ul style="list-style-type: none"> - Significantly more HIV knowledge (p<0.001) - Significantly more health-protective communication (p<0.05) - Significantly fewer motivational barriers to condoms (p<0.05) - Significantly fewer physical spousal abuse (p<0.01) <p>* POWER vs. control 6 months after release:</p> <ul style="list-style-type: none"> - Significantly less unprotected vaginal sex outside of monogamous relationships (adjusted OR 0.57, 95% CI 0.35-0.92) - Significantly more condom use during vaginal intercourse with main male partner (adjusted OR 2.06, 95% CI 1.14-3.72) - Significantly more HIV knowledge (p<0.001) - Significantly fewer motivational barriers to condoms (p<0.05) - Significantly fewer partner and physical effect barriers to condoms (p<0.05) - Significantly more tangible social support (p<0.05) <p>No significant difference in:</p> <ul style="list-style-type: none"> - Both time points in: access barriers to condom use, condom self-efficacy, sexual protective practices barriers, depression, social support, emotional/informational/affectionate support, positive social interaction, social network risk, number of stressors, non-physical spouse abuse, power and attitudes in relationships 	NR	Moderate

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
						<ul style="list-style-type: none"> - 3 months only: condom barriers overall and partner and physical effect barriers to condoms, tangible support - 6 months only: health-protective communication, physical spousal abuse, and (measured only at 6 months) condom use with non-main male partner, partner concurrency, number of male sexual partners, drug use before sexual intercourse, trading sex, incidence of non-viral STIs 		
Non-EU/EEA PRL	Knudsen, 2014 & Leukefeld, 2012 [127,128] USA RCT	4 state prisons March 2007 – December 2008	<p>RRR-HIV:</p> <ul style="list-style-type: none"> - 5 90-minute prison-based group sessions starting ~6 weeks before release - 1 telephone/face-to-face booster session after release - Didactic and interactive skill-building exercises focused on 7 relationship thinking myths⁵ to make healthier and safer decisions about risky sexual behaviour and drug use - Receive also control intervention in session 1 <p>Control:</p> <ul style="list-style-type: none"> - 17-minute HIV/AIDS risk reduction information and awareness video 	<p>n=378 inmates (Knudsen), n=344 inmates (Leukefeld)</p> <ul style="list-style-type: none"> - The 34 inmates without follow-up data are included in the study of Knudsen et al by using imputation) <p>Females; ≥18 years old; being scheduled to appear before the parole board or complete one's sentence within 6 weeks; consenting to participate; reporting at least weekly substance use before incarceration; no past-month psychotic features or having specific parole/probation conditions that would prohibit participation</p> <p>RRR-HIV vs. control</p>	NR	<p>Knudsen et al.:</p> <ul style="list-style-type: none"> - At 90 days follow-up (post-release), women in RRR-HIV reported significantly fewer past-month unprotected sexual behaviours than women assigned to the control condition (p=0.007) <p>Leukefeld et al.:</p> <p>90-day change (pre-release to post-release) RRR-HIV vs. control:</p> <ul style="list-style-type: none"> - Greater increase in overall HIV knowledge of HIV risk behaviours (p=0.024) - Greater increase in self-esteem (p=0.032) - Greater increase sexual relationship power (p=0.018) - Greater increase relationship control (p=0.019) - Greater improvement in specific HIV risk knowledge items: can get HIV through sharing works (p=0.008), female/male condom not used together (p<0.001), women who use drugs do not make healthier choices (p=0.011) - Greater improvement in specific thinking myths: use drugs and make healthy choices regarding protection (p=0.002), unhealthy choices regarding protection when using drugs (p=0.009), know partner safe from HIV by how talks (p=0.014) and how acts (p=0.032), will not get HIV because not at risk (p=0.048) - For non-significant changes, see corresponding evidence table 	<p>Study focuses solely on inmates with at least weekly substance use before incarceration</p> <p>Knudsen et al.: Re-incarceration (p=0.005) during 90 days follow-up and older age (p=0.001) were negatively associated with unprotected sexual behaviours</p>	Low

Region Source	Reference, country, study design	Prison setting, time period	Intervention description	Sample, eligibility, comparator	HIV prevalence /incidence	Other outcomes of interest	Sub-group considerations	Level of evidence
Non-EU/EEA PRL	Magura, 1995 [129] USA Comparative study	New York City's central jail facility for women at Rikers Island 1991 (not further specified)	Health education curriculum: - 4 alternate-day, 1-hr small-group (n=8) educational sessions - Focusing on drug use, sexual behaviour and HIV/AIDS knowledge and risk reduction and how to seek health and social services in the community - Led by counsellor Control: - No health education, not further specified	n=53 educations vs. n=48 control inmates - At start study: women who were detoxified for heroin or were being maintained on methadone in jail, and who were not in drug dependency treatment at arrest - Later in study: eligibility extended to women who were in drug dependency treatment at arrest and female drug users who were not injecting Health education vs. control	NR	None of the following outcomes measured at median 7 months after release were significantly associated with AIDS education in jail ($p>0.05$): - Drug injection - Needle/syringe sharing - Needle/syringe sterilisation - Heroin use - Crack use - Multiple sexual partners - High-risk sexual partners - Condom use - Enrolling or remaining in drug dependency treatment	Study focuses solely on drug users Being in drug dependency treatment at the time of follow-up was associated with reductions in heroin use ($p<0.01$) and drug dealing ($p<0.05$)	Very low

AI: standard AIDS information intervention, AIDS: acquired immunodeficiency syndrome, EI: enhanced intervention, HIV: human immunodeficiency virus, IDU: injecting drug use, NR: not reported, OR: odds ratio, PCM: prevention case management, PRL: peer-reviewed literature, RCT: randomised controlled trial, RRR-HIV: reducing risky relationships for HIV, SS: skills building and social support enhancement intervention, SSI: single-session intervention, STI: sexually transmitted infection, USA: United States of America

¹ The initial PCM curriculum in 1996 included 2 mandatory modules (Personalizing HIV/AIDS Risk and Risk Reduction and Transitioning Into the Community) and 5 optional modules (Condoms and Other Devices, Substance Abuse, Self-Esteem, Relationships, and Employment and Career Goals). In 1998 the Condoms and Substance Abuse modules became mandatory. Additional optional modules have been developed by counsellors to meet client needs, e.g. Personal Responsibility, Coping, Communication, and Decision-Making. Methods for each module include activities such as informational lecturing by counsellors; individual or group discussion, according to the format of particular sessions; practice exercises and role play; and homework activities to be completed between sessions

² Main partner: someone the inmate feels a special emotional attachment or commitment to; at-risk partner: a partner who 1) had ever injected drugs, 2) had ever smoked crack, 3) had ever traded sex for money or drugs, 4) had ever had an STI, 5) currently had other sexual partners, or 6) was HIV seropositive

³ Aims to bolster participants' awareness of HIV/AIDS risk behaviours and their ability to anticipate high-risk situations; to enhance their self-efficacy, problem-solving, and coping skills in high-risk and other life problem situations; to enable participants to assess their social networks, strengthen ties to drug-free support networks, and use supportive individuals in reducing HIV/AIDS risk behaviour and solving life problems; and to help participants gain access to formal and informal help to support their efforts to acquire and sustain protective behaviours

⁴ Session 1: purpose intervention, HIV-STIs facts; Session 2: self-protection/individual strength, signs and symptoms of HIV-STIs; Session 3: substance abuse, HIV-STI prevention practices, partner information, condoms, cleaning drug paraphernalia; Session 4: female sexuality/ roles, sexual decision-making; Session 5: male-female interaction/relationships, identifying triggers to unsafe sex; Session 6: violence, strategies for decreasing risk; Session 7: preparing for the life after release; Session 8: condom negotiation/use, setting goals for oneself, graduation ceremony

⁵ 7 risky relation thinking myths: 1) Fear of rejection: 'Having sex without protection will strengthen my relationship'; 2) Self-worth/self-esteem: 'I only think good things about myself when I am in a relationship, even if it is risky'; 3) Drug use: 'I can use drugs and still make healthy decisions about sex'; 4) Safety: 'I know my partner is safe by the way my partner looks, talks and/or acts'; 5) Trust: 'I've been with this partner for a long time so there's no need to practice safe sex'; 6) Invincibility: 'I will not get HIV because I'm not really at risk'; 7) Strategy/power: 'I have to use sex to get what I want'

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/ access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
Intervention: pre-release individual intervention										
Non-EU/EEA PRL	Bauserman, 2003 [123] USA Longitudinal study	Local jails in Maryland counties, Baltimore city, and in some facilities of the Maryland Department of Corrections n=745 PCM completers July 1996 – May 2000	PCM intervention: - Individual counselling and case management services - Skills-building for personal HIV risk, condom use, substance abuse, transitioning into community, optional - Post-release plans, including referrals - Combined with group educational sessions covering variety of topics - Mandatory and optional modules ¹	Within 6 months of expected release date	NR	Completion rates per mandatory module varied from 21.2% to 95.8% 88% completed ≥2 mandatory modules, but only 39% completed 3 or 4 Participants completed a median of 6 modules and 9 sessions in about 11 hours total	NR	Despite the goal of individualised attention, participants completed more modules and spent more programme time in group sessions	NR	Very low
Non-EU/EEA PRL	Grinstead, 1999 [126] USA RCT	A large state prison for men n=199 intervention vs. n=205 control inmates October 1994 – July 1996	Intervention: - 30-minute session with trained inmate peer educator - Assess post-release HIV risk and make risk reduction plan; provide referrals - Appointments for follow-up survey, when they receive reimbursements Control: no intervention, not further specified Access to HIV educational materials and informal consultation with staff for all inmates	Males; within 14 days of release 97.6% of inmates interviewed at baseline (404/414) were randomised 39.7% (79/199) of those randomised to the intervention group, received the intervention, reasons were: failed to appear for their intervention appointment (not further specified), unable to attend due to institutional lock-downs, or unexpectedly paroled (n/N NR)	Baseline refusal rate 19% (n/N NR)	NR	42.5% (176/414; 47.5% in intervention and 42% in control group – n/N NR)	NR	NR	Very low
Non-EU/EEA	Wolitski, 2006 [130]	8 state prisons in 4 states	EI:	Aged 18-29 years; incarcerated ≥90 days;	94.8% (561/592) of	EI:	Available for follow-up	A total of 91 optional EI	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/ access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
PRL	USA RCT	n=263 EI vs. n=259 SSI 2001 – 2002	<ul style="list-style-type: none"> - 2 individual sessions before release (60-90 minutes) and 4 sessions at 1, 3, 6 and 12 weeks after release (30-60 minutes) - 1st in-prison sessions same as SSI session - 2nd in-prison session: community re-entry needs, including referrals - Post-release sessions: review and update of risk-reduction plan - Additional sessions if needed <p>SSI:</p> <ul style="list-style-type: none"> - 60-90 individual session ~2 weeks before release - Based on brief HIV-risk assessment and reduction planning intervention (Project START) - Assessment HIV, hepatitis and STI knowledge and risk behaviour, personal risk-reduction plan, provision of information, skills training and referrals 	<p>scheduled for release within 14-60 days; able to provide informed consent and speak English; willing to provide post-release contact information; released to unrestricted environment in site-specific catchment areas</p> <p>71.3% (592/830) of men selected for recruitment were screened and eligible</p> <p>88.2% (522/592) of eligible inmates were released to unrestricted environment and therefore included</p>	eligible inmates provided informed consent	<ul style="list-style-type: none"> - 1st pre-release session (=SSI): 98.5% - 2nd pre-release session: 88.6% - Post-release sessions: 79.8%, 65.8%, 65.8% and 74.5% at week 1, 3, 6 and 12 after release - 67% ≥5 of the 6 sessions <p>SSI: 94.2%</p>	<p>after release:</p> <ul style="list-style-type: none"> - Week 1: 87.3% SSI and 84.8% EI - Week 12: 76.4% SSI and 82.1% EI - Week 24: 82.2% SSI and 83.3% EI <p>(p=ns)</p>	sessions were delivered to 49 participants, of whom 61% received 1 additional session		
Intervention: pre-release group intervention										
Non-EU/EEA PRL	El-Bassel, 1995 [124] USA RCT	New York City's Rikers Island Jail n=67 SS vs. n=78 AI NR	<p>SS:</p> <ul style="list-style-type: none"> - 16 2-hour group sessions twice weekly in prison and 6 group booster sessions monthly in the community - Group size n=10, led by 2 group facilitators² <p>AI:</p> <ul style="list-style-type: none"> - 3 2-hour group sessions - HIV/AIDS information primarily focussed on 	NR	NR	<p>SS: 52.2% attended ≥13 sessions, 28.4% 4-12 sessions, 19.4% ≤3 sessions</p> <p>AI: 85.9% attended all sessions</p>	<p>Lost to follow-up from pre-test to post-test:</p> <ul style="list-style-type: none"> - SS: 26.9% (18/67) - AI: 33.3% (26/78) <p>Reasons NR</p>	NR	Study focuses solely on incarcerated women with recent histories of significant drug abuse	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/ access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
			transmission-related issues and safer sex and drug alternatives							
Non-EU/EEA PRL	Fogel, 2015 [125] USA RCT	2 prisons for women in North Carolina (1 is primary processing facility) n=265 POWER vs. n=256 control newly incarcerated inmates September 2010 – November 2011	POWER - 8 interactive group sessions (1.5 hours) delivered over 4 weeks provided by nurse and social worker ³ - 1 booster session 1 month after session 8 and prior to release; 3 5-minute booster phone calls after release Control - 1 1-h standard-of-care STI education session by prison nurse, including information on STI transmission, sexual abstinence, and condom use - During 1 st 3 months of incarceration - Provided to all women, also POWER participants	Females; 18-60 years; total sentence length ≤12 months; speaking English; able to provide verbal and written consent; planning to live in North Carolina during study; having had/ expecting to have sexual activity with a man; HIV-negative; <6 months left of sentence Among 820 screened women: - 12.9% (106/820) were not eligible - 2.0% (16/820) were transferred to non-participating prisons - 0.37% (3/820) initially expressed interest but dropped out prior to randomisation - 0.24% (2/820) were removed at prison's request	21.0% (172/820) of screened women refused to participate	The average number of POWER sessions attended was 5.8; 12.8% (34/265) did not attend any of the intervention sessions	POWER: 67.5% (179/265) and 59.6% (158/265) completed the 3-month and 6-month post-release assessments Control: 60.5% (155/256) 55.5% (142/256) completed the 3- and 6-month post-release assessments	NR	NR	Moderate
Non-EU/EEA PRL	Knudsen, 2014 & Leukefeld, 2012 [127,128] USA RCT	4 state prisons n=378 or 344 inmates March 2007 – December 2008	RRR-HIV: - 5 90-minute prison-based group sessions starting ~6 weeks before release - 1 telephone/face-to-face booster session after release - Didactic and interactive skill-building exercises focused on 7 relationship thinking myths ⁴ to make healthier and safer decisions about risky sexual behaviour and drug use - Receive also control intervention in session 1 Control:	Females; ≥18 years old; being scheduled to appear before the parole board or complete one's sentence within 6 weeks; consenting to participate; reporting at least weekly substance use before incarceration - 20.7% (124/599) of screened women were ineligible - 0.83% (5/599) of screened women discharged before intervention start (4 prison transfer, 1 mental health reasons)	4.3% (26/599) of screened women declined to participate	NR	Available at 3-month follow-up interview: 91.0% (344/378)	NR	Study focuses solely on inmates with at least weekly substance use before incarceration	Low

Region Source	Reference, country, study design	Prison setting, sample, time period	Intervention description	Eligibility/ access	Acceptance	Intervention adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
			- 17-minute HIV/AIDS risk reduction information and awareness video	- 14.9% (66/444) of randomised women were not included in the analyses as they were not released <i>Reasons ineligible (n=124):</i> - Insufficient pre-incarceration drug use: 47.6% - Release-related reasons: 45.2% - NR: 7.3%						
Non-EU/EEA PRL	Magura, 1995 [129] USA Comparative study	New York City's central jail facility for women at Rikers Island n=53 educations vs. n=48 control inmates 1991 (not further specified)	Health education curriculum: - 4 alternate-day, 1-hr small-group (n=8) educational sessions - Focusing on drug use, sexual behaviour and HIV/AIDS knowledge and risk reduction and how to seek health and social services in the community - Led by counsellor Control: - No health education, not further specified	- At start study: women who were detoxified for heroin or were being maintained on methadone in jail, and who were not in drug dependency treatment at arrest - Later in study: eligibility extended to women who were in drug dependency treatment at arrest and female drug users who were not injecting.	NR	NR	Follow-up interviews completed with 51.5% (53/103) of the education group and 44.4% (48/108) of the control group.	NR	Study focuses solely on drug users	Very low

AI: standard AIDS information intervention, AIDS: acquired immunodeficiency syndrome, EI: enhanced intervention, HIV: human immunodeficiency virus, IDU: injecting drug use, PCM: prevention case management, RCT: randomised controlled trial, RRR-HIV: reducing risky relationships for HIV, SS: skills building and social support enhancement intervention, SSI: single-session intervention, STI: sexually transmitted infection, USA: United States of America

¹The initial PCM curriculum in 1996 included 2 mandatory modules (Personalizing HIV/AIDS Risk and Risk Reduction and Transitioning Into the Community) and 5 optional modules (Condoms and Other Devices, Substance Abuse, Self-Esteem, Relationships, and Employment and Career Goals). In 1998 the Condoms and Substance Abuse modules became mandatory. Additional optional modules have been developed by counsellors to meet client needs, e.g. Personal Responsibility, Coping, Communication, and Decision-Making. Methods for each module include activities such as informational lecturing by counsellors; individual or group discussion, according to the format of particular sessions; practice exercises and role play; and homework activities to be completed between sessions

²Aims to bolster participants' awareness of HIV/AIDS risk behaviours and their ability to anticipate high-risk situations; to enhance their self-efficacy, problem-solving, and coping skills in high-risk and other life problem situations; to enable participants to assess their social networks, strengthen ties to drug-free support networks, and use supportive individuals in reducing HIV/AIDS risk behaviour and solving life problems; and to help participants gain access to formal and informal help to support their efforts to acquire and sustain protective behaviours

³ Session 1: purpose intervention, HIV-STIs facts; Session 2: self-protection/individual strength, signs and symptoms of HIV-STIs; Session 3: substance abuse, HIV-STI prevention practices, partner information, condoms, cleaning drug paraphernalia; Session 4: female sexuality/ roles, sexual decision-making; Session 5: male-female interaction/relationships, identifying triggers to unsafe sex; Session 6: violence, strategies for decreasing risk; Session 7: preparing for the life after release; Session 8: condom negotiation/use, setting goals for oneself, graduation ceremony

⁴ 7 risky relation thinking myths: 1) Fear of rejection: 'Having sex without protection will strengthen my relationship'; 2) Self-worth/self-esteem: 'I only think good things about myself when I am in a relationship, even if it is risky'; 3) Drug use: 'I can use drugs and still make healthy decisions about sex'; 4) Safety: 'I know my partner is safe by the way my partner looks, talks and/or acts'; 5) Trust: 'I've been with this partner for a long time so there's no need to practice safe sex'; 6) Invincibility: 'I will not get HIV because I'm not really at risk'; 7) Strategy/power: 'I have to use sex to get what I want'

Cost-effectiveness

No studies were found on cost-effectiveness of interventions to prevent BBVs post-release.

Guidelines

No guidelines were found on interventions to prevent BBVs post-release.

Linkage to care post-release

Effectiveness

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
HIV treatment in prison – Usual care										
Non-EU/EEA	Beckwith, 2014 [131]	Rhode Island Jail	Provision of ART in prison or post release	n=64 newly diagnosed HIV+ inmates	NR	NR	57.8% (37/64) - 12.5% <90 days - 20.3% >90 days - 25.0% after subsequent incarceration	NR	NR	Very low
PRL	USA Longitudinal study	2001 – 2007	On-site care by HIV physicians from community hospital, which serves as primary referral centre after release	All individuals newly diagnosed in study period (no previous HIV diagnosis) No comparator			No significant association between length of incarceration and linkage to care			
Non-EU/EEA	Althoff, 2013 [137]	10 prisons/jails	Post-release follow up of individuals receiving ART during detention and receiving comprehensive jail-based services	N=867 included participants	NR	NR	58% (55/867) had a HIV visit in the first 3-month; 47% (406/867) had a HIV visit in the second 3-month period; 38% had sustained retention in care (two HIV visits in 6-month)	Correlates of sustained retention in care were: being male (p<0.01); having HIV care provider prior to incarceration (p=0.02); receiving pre-release services (e.g. disease management session, discharge planning) and post-release services (e.g. needs assessment)		
PRL	USA Longitudinal study	January 2008-March 2011		6-month follow up period						

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
HIV treatment in prison – Usual care (partly DOT)										
Non-EU/EEA PRL	White, 2001 [135] USA Cross-sectional study	San Francisco City and County Jail January 1997 – 1 April 2000	Provision of ART Seen by the San Francisco Department of Public Health, Jail Health Services, Forensic AIDS Project If already on treatment at entry, efforts made to keep same medication; if not on ART, efforts were made to refer and facilitate follow-up with community-based provider; 3-day supply of medication upon release	n=77 inmates on ART in jail, who were released in first quarter of 1997 Receive care if tested positive for HIV in jail or self-report a previous positive test and outside documentation is available to confirm this test result	NR	NR	68.6% (24/35) of inmates released on ART in jail received prescriptions and a 3-day supply when they left jail; 70.8% (17/24) picked up the prescription and medicine Among those who were re-jailed, 46.3% (25/54) received HIV medications in the community	NR	Among those re-jailed, patients who had a pre-incarceration primary health care provider in the community were more likely to receive ART in the community before their re-arrest (63.2%, 12/19) compared with those who did not (37.1%, 13/35)	Very low
HIV treatment - Different interventions										
Non-EU/EEA PRL	Grinstead Reznick, 2013 [134] USA RCT	California jail and 2 prisons NR	Ecosystem-focused (family, friends, drug/sex partners, service providers) intervention ¹ Individually focused intervention ² Both interventions include a 45-minute HIV education session, 2 pre-release and up to 16 post-release sessions in 4 months after release, ART, and medication supply upon release	n=76 ecosystem vs. n=75 individual intervention HIV+ inmates Adults within 21-90 days of release, speaking English or Spanish, able to name ≥1 adult in local area to participate in intervention, willing to be contacted after release Ecosystem vs. individual intervention	NR	NR	* 4-month post-release (92% retention): - Both groups: decrease taking anti-HIV medications and lower adherence ³ (p<0.01 ecosystem, p<0.05 individual) - Ecosystem less likely to be taking anti-HIV medications (OR NR, p<0.01) and to be adherent (OR NR, p<0.05) * 8-month (89% retention) and 12-month (76% retention) post-release: no significant differences in groups and between groups (p>0.05)	No significant difference between both groups on sexual behaviour after release (p>0.05) When pooling both intervention groups significant declines of any unprotected sex (including serodiscordant sex) was observed across the study period post-release	NR	Moderate

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
							<p>* Averaging across post-release periods: - Both groups: decrease taking anti-HIV medications and lower adherence (both $p < 0.05$) -The percentage of participants taking anti-HIV medications increased across the post-release period (OR=1.81, 95% CI 1.16-2.81, $p = 0.0089$) to approximate pre-release levels - Ecosystem group less likely to be taking anti-HIV medications (OR=0.20, 95% CI 0.05-0.80, $p=0.0236$) and to be adherent (OR=0.35, 95% CI 0.13-0.95, $p=0.0408$)</p>			
Non-EU/EEA PRL	Jacob Arriola, 2007 [132] USA Comparative study	Jails and prisons in 5 states May 2001 – April 2004	Corrections Demonstration Project: - Individual/group HIV prevention & disease management education, individual counselling, and discharge planning - Collaboration with community providers - Personal support by dedicated staff at the gate or soon after release - Management programme starts ~6 months before release (baseline) -Follow up six months post release	n=226 HIV+ inmates Receiving case management services that started inside the facility and continued after release Being met by a case manager upon release (i.e. at the gate) vs. not being met by a case manager at the gate (although protocol is that a case manager meets inmate soon after release, only 46%	NR	NR	NR	Those being met at the gate were since release significantly more participating in drug/alcohol treatment (OR 1.99, 95% CI 1.12-3.55, $p < 0.01$) and significantly less engaging in sex exchange (OR .014, 95% CI 0.03-0.71, $p < 0.05$)	Significant increase in participating in drug or alcohol treatment ($p=0.00$ 33.6% vs 60.2%); and significant decrease in reported use of street drug ($p=0.01$, 43.8% vs. 31.4%) and engaging in sex exchange ($p=0.00$, 65.9% vs. 6.2%) at 6-month follow up	Very low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			Treatment NR	(104/226) were met at the gate by a case manager)						
Non-EU/EEA PRL	MacGowan, 2015 [133] USA RCT	California 2 prisons and 5 jails July 2008 – July 2009	POST: individual-level educational and skills-building intervention (4 sessions in 2 weeks before release, 2 sessions in 2 weeks after release) ⁴ TCM: standard of care (frequency NR) ⁵ Both: treatment NR	n=37 POST+TCM vs. n=36 TCM only HIV+ inmates Adults incarcerated <5 years, scheduled for release to local bay area counties within 60 days and before end July 2009, speaking English POST+TCM vs TCM only	NR	Change in proportion of inmates taking HIV medications at release vs. three months post-release: - POST+TCM: significant increase (OR infinite, p=0.0156) - TCM only: no significant difference (p=0.2266) - POST+TCM vs. TCM: no significant difference (OR 1.52, 95% CI 0.43-5.37, p=0.5115) - Combining both groups: significant increase (OR 5.00, 95% CI 1.54-16.27, p=0.01)	Change in proportion of inmates receiving healthcare at HIV clinic at 3 months pre-incarceration vs. 3 months post-release: - POST+TCM: significant increase (OR infinite, p=0.0156) - TCM only: no significant difference (p=0.2266) - POST+TCM vs. TCM: no significant difference (OR 1.52, 95% CI 0.43-5.37, p=0.5115) - Combining both groups: significant increase (OR 5.00, 95% CI 1.54-16.27, p=0.01)	Change from 3 months pre-incarceration to 3 months post-release not significant between both groups for: - unprotected vaginal sex, (OR 1.85, 95% CI 0.38-8.95, p=0.4432) - unprotected anal sex, (OR 0.77, 95% CI 0.28-2.09, p=0.6016) - IDU, (OR 2.25, 95% CI 0.65-7.76, p=0.2003) - STI diagnosis (OR 0.49, 95% CI 0.02-10.65, p=0.6477)	Combining the two groups, a statistically significant change in IDU (39.0% at baseline vs. 23.7% at follow-up; OR 0.18, 95% CI 0.04-0.79, p=0.0225)	Low
Non-EU/EEA PRL	Springer, 2012 [138] USA Comparative study –	Connecticut Department of Correction 2004-2009	94 PWID among participants enrolled in the CONNECT study [144] eligible for OST offered retention on buprenorphine (BPN)	94 subjects: 50 (53%) selected BPN; 44 (47%) selected no BPN BPN vs no BPN	At 6-month post-release BPN had AOR 5.37 (p=0.03) of achieving viral			No difference in viral suppression level with DOT vs SAT or with methadone		Low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
	nested in RCT		for 6-month after release Participants received ART via DOT or SAT depending on parent study arm		suppression (<50 copies/ml)					
Non-EU/EEA PRL	Wohl, 2011 [136] USA RCT	North Carolina State Prison system NR	BCM: intensive case management intervention from 3 months before release to 6 months after release SOC: 3 pre-release sessions from 3-6 months pre-release ART, 30-day supply upon release	n=52 BCM vs. n=52 SOC HIV+ inmates (consecutive sample) Adults not expected to be release during 4 months following study entry, receiving ≥3 antiretrovirals (≥1 using DOT) for ≥3 months prior to study entry, prison within 2h drive from the release counties BCM vs. SOC	NR	NR	No significant difference between both groups in: - % medical care access ≥once (p=0.2) - Median time to clinic access (p=0.8) - Mean number clinic visits (p>0.05) - Rate of hospitalisations, ER or UCC visits (p=ns)	NR	No significant difference between groups in ever receiving outpatient care for substance abuse (p=0.48)	Low
Opioid Substitution Treatment in prison										
Non-EU/EEA PRL	Kinlock, 2009 [139] USA RCT	One Baltimore pre-release facility for male prisoners September 2003 and June 2005	Provision services to PWID pre-release: 1.Counselling and recommendation to enrol in a community OST programme 2.Counselling and passive referral to OST community programme 3.Counselling and induction on OST before release with active referral to community OST programme	n=204 individuals randomised to: 1.n=70 2.n=70 3.n=71 1 vs 2 vs 3	NR	-Group 1: 0% were on OST at 12-month -Group 2: 17.3% were on OST at 12-month -Group 3: 36.7% were on OST at 12-month Pairwise comparison	-Group 1:25% enrolled in care; -Group 2: 53.6% enrolled in care; -Group 3: 70.4% enrolled in care; Pairwise comparison all significant (p<0.01)	Positive urine test for opioid at 12-month post-release: -Group 1: 65.6% -Group 2: 48.7% -Group 3: 25% Group 3 significantly less as compared to Group 1 & 2. No difference between Group 1 & 2	NR	Low

Region Source	Reference, country, study design	Prison setting, time period	Description model of care	Sample, eligibility, comparator	Viral load, CD4 count	Treatment adherence	Linkage to HIV care post release	Other outcomes of interest	Sub-group considerations	Level of evidence
			12-month follow-up			all significant (p<0.01)				
Non-EU/EEA PRL	Gordon, 2017 [140] USA RCT	Two Baltimore pre-release prisons (one for men; one for women) September 2008 and July 2012; follow-up completed in 2014.	Study design was a 2 In-Prison Treatment: Buprenorphine (BPN) Treatment: vs. Counselling Only 12-month follow up	Adult pre-release prisoners who were heroin-dependent during the year prior to incarceration were eligible, N=211.		Participants in the in-prison BPN group had a higher mean number of days of community buprenorphine treatment vs participants who initiated medication after release (P=0.005).	Participants in the in-prison BPN group were significantly more likely (p=0.012) of enrolling into community OST programmes (47.5% vs. 33.7%).	No statistically significant difference for days of heroin use and crime, and opioid and cocaine positive urine screening test results (all Ps>0.14)	No statistically significant gender effects (all Ps>0.18).	Low
Non-EU/EEA PRL	McKenzie, 2013 [141] USA RCT	Rhode Island Department of Corrections October 2006 - February 2009	3 study arms include Arm 1—initiation of OST pre-release with referral post-release and short-term payment of treatment costs; Arm 2—referral to OST programme upon release with provision of short-term financial assistance; Arm 3—referral to OST programme upon release without financial assistance.	90 participants randomised to Arms 1-3 Arm 1 vs Arm 2 vs Arm 3			Participants on OST prior to release were significantly more likely to enter treatment postrelease (P < .001); Among participants who enrolled in community OST, those who received OST in prison did so within fewer days (P = .03).	Participants on OST prior to release reported less heroin use (P = .008), other opiate use (P = .09), and injection drug use (P = .06) at 6 months		Very Low

AIDS: autoimmune deficiency syndrome, ART: antiretroviral therapy, BCM: Bridging Case Management, BOP: Bureau of Prisons, CI: confidence interval, DOT: directly observed therapy, ER: emergency room, IDOC: Illinois Department of Corrections, IQR: interquartile range, NR: not reported, ns: not significant, OR: odds ratio, POST: Positive Transitions, PRL: peer-reviewed literature, RCT: randomised controlled trial, SAT: self-administered therapy, SD: standard deviation, SOC: standard of care, TCM: transitional case management, UCC: urgent care centre, USA: United States of America

¹ 3 core activities: 1) assessing membership, functional patterns, and roles in participant's ecosystems, including his family, friends, sexual and drug using partners, service providers; 2) connecting with participant's ecosystems through joint meetings and other communication; and 3) restructuring interactions and roles through direct interventions, and 3 phases: 1) initiation during which the counsellor built the therapeutic alliance and mapped the participant's ecosystem, and initial joining in which the counsellor established his or her role in the participant's ecosystem; 2) treatment in which the restructuring interventions were conducted through both individual and group counselling sessions and newly acquired interaction patterns within ecosystems were reinforced; and 3) termination in which treatment sessions

tapered off and ended. Throughout treatment and at the termination of treatment, counsellors offered facilitated referrals as needed

² The participant established goals and objectives in the initial session and worked with the counsellor to achieve and modify the goals as the intervention progressed. Intervention techniques included motivational interviewing, facilitated referral and goal setting (based on Project START intervention)

³ Adherent to HIV medication: those who either did not require HIV medications or who reported taking all prescribed doses in 3-day recall

⁴ The first 4 sessions covered the topics: (1) health conditions, medications, skills-building on communicating effectively with providers, assistance with enrolment in AIDS drug assistance programmes, (2) sexual risk reduction, (3) substance use and mental health, and (4) planning for transition and access to HIV or other health care provider, HIV medication adherence, and public services after release. Each participant set goals and developed an individual action plan to meet during the first 3 months after release. Pre-release sessions included client-centred discussions of motivations, barriers, facilitators, risks, and repercussions of risk behaviour. The 2 post-release intervention sessions included discussions of achievement and barriers to reaching individuals goals. These sessions focused on any challenges in achieving goals, including determining appropriate health care and prevention services, problem solving to overcome challenges, and discussions about potential repercussions of risk behaviour and any desired changes to individual sex and drug use action plan

⁵ The TCM programme provided referrals to community-based medical and social services, including assistance with medical appointments, enrolment into AIDS Drug Assistance Programme, housing placement, substance abuse treatment, hepatitis testing and vaccination, and provision of food and transportation vouchers (taxi vouchers for 1st visit after release when lack of transportation was reported as barrier to accessing services)

Acceptability/barriers

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
HIV treatment in prison – Usual care										
Non-EU/EEA	Beckwith, 2014 [131]	Rhode Island Jail	Provision of ART; ART provided on-site by HIV physicians	9.4% (6/64) started ART during current incarceration	NR	NR	NR	NR	NR	Very low
PRL	USA Longitudinal study	n=64 newly diagnosed HIV+ inmates 2001 – 2007		<i>Significant factors of starting ART:</i> - incarcerated for >60 days more likely to start ART (30.0%) than incarcerated ≤60 days (0.0%) (p<0.001)						
HIV treatment in prison – Usual care (partly DOT and/or transitional care)										
Non-EU/EEA	White, 2001 [135]	San Francisco City and County Jail	Provision of ART	National guidelines, not further specified	- 58.4% (45/77) were on ART in jail	NR	NR	Those who were not given a prescription at the time of release (n=11) were either released to residential drug treatment programmes that provided	NR	Very low
PRL	USA Cross-sectional study	n=77 inmates on ART in jail, who were released in first quarter of 1997	Seen by the San Francisco Department of Public Health, Jail Health Services, Forensic AIDS Project If already on treatment at entry,	According to guidelines available during the study period, ART was indicated for 70.1% (54/77) of inmates	Of 54 eligible ART inmates: - 14.8% (8/54) refused therapy, reasons NR					

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
		January 1997 – 1 April 2000	efforts made to keep same medication; if not already under care, efforts were made to refer and facilitate follow-up with community-based provider; 3-day supply of medication upon release	of whom 72.2% (39/54) were on ART in jail; 5.6% (3/54) scheduled for release before therapy could be started - 7.4% (4/54) unknown An additional 6 inmates who did not fit the criteria, were on ART, probably therapy started before jail				medications or were released precipitously from court before notice could be given to the jail medical personnel		
Different interventions										
Non-EU/EEA PRL	Grinstead Reznick, 2013 [134] USA RCT	California jail and 2 prisons n=76 ecosystem vs. n=75 individual intervention NR	Ecosystem-focused (family, friends, drug/sex partners, service providers) intervention ¹ Individually focused intervention ² Both interventions include a 45-minute HIV education session, 2 pre-release and up to 16 post-release sessions in 4 months after release, HAART (not further specified), and medication supply upon release	NR	NR	Similar median (SD) level of exposure to assigned intervention (p=ns): 9.5 (5.0) sessions in ecosystem vs. 9.9 (5.2) sessions in individually focussed intervention	92.1% (139/151), 89.4% (135/151) and 85.4% (129/151) completed the 4-month, 8-month, and 12-month assessment post-release, respectively (p=ns ecosystem vs. individual), reasons for non-completion NR	Ecosystem group: 28% had no ecosystem members attend a session with them, 34% only a service provider, 24% both family and service provider, and 11% only family members, NR of remaining 3% (n/N NR)	NR	Moderate
Non-EU/EEA PRL	Jacob Arriola, 2007 [132] USA	Jails and prisons in 5 states n=226 HIV+ inmates	Corrections Demonstration Project: - Individual/ group HIV prevention & disease management	NR	NR	NR	34.9% (226/647) of eligible inmates completing the baseline interview had no	Intervention protocol indicate that a case manager meets the inmate soon after release, only	NR	Very low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
	Comparative study	May 2001 – April 2004	education, individual counselling, and discharge planning - Collaboration with community providers - Starts in jail shortly after intake, in prison ~6 months before release Treatment NR				follow-up data – reasons were a range of logistical constraints (e.g. released unexpectedly, released, transferred to another facility), and lost to follow-up (% NR)	46.0% (104/226) were met at the gate by a case manager		
Non-EU/EEA PRL	MacGowan, 2015 [133] USA RCT	California 2 prisons and 5 jails n=37 POST+TCM vs. n=36 TCM only July 2008 – July 2009	POST: individual-level educational and skills-building intervention (4 sessions in 2 weeks before release, 2 sessions in 2 weeks after release) ³ TCM: standard of care (frequency NR) ⁴ Both: treatment NR	NR	NR	15.6% (5/32) did not complete all 6 POST+TCM intervention sessions, reasons for non-completion NR	25.0% (9/36) TCM only and 13.5% (5/37) POST+TCM LTFU before post-release assessments, reasons NR	During the 6th intervention session (~2 weeks post-release), POST+TCM participants reported achieving 19 (34%) of the personal goals they had set overall; sexual risk behaviours (36% of goals), drug-related risk behaviours (45% of goals), health care at HIV clinic (27% of goals), adherence to HIV medication (27% of goals), and use of HIV prevention resources (36% of goals)	NR	Low
Non-EU/EEA PRL	Wohl, 2011 [136] USA RCT	North Carolina State Prison system n=52 BCM vs. n=52 SOC NR	BCM: intensive case management intervention from 3 months before release to 6 months after release	NR	NR	NR	17.3% (9/52) BCM and 11.5% (6/52) SOC LTFU before post-release assessment	NR	NR	Low

Region Source	Reference, country, study design	Prison setting, sample, time period	Description model of care	Eligibility/ access	Acceptance	Treatment discontinuation/ non-adherence	Attrition	Other outcomes of interest	Sub-group considerations	Level of evidence
			SOC: 3 pre-release sessions from 3-6 months pre-release ART, 30-day supply upon release				27.9% (12/43) BCM and 39.1% (18/46) SOC did not complete 48-week post-release visit, main reasons LTFU and release			

ART: antiretroviral therapy, BCM: Bridging Case Management, CI: confidence interval, DOT: directly observed therapy, HCV: hepatitis C virus, HIV: human immunodeficiency virus, LTFU: lost to follow-up, NCDCC: North Carolina Department of Corrections, NGO: non-governmental organisation, NR: not reported, ns: not significant, OR: odds ratio, POST: Positive Transitions, PRL: peer-reviewed literature, RCT: randomised controlled trial, RNA: ribonucleic acid, RR: relative risk, SAT: self-administered therapy, SD: standard deviation, SOC: standard of care, TCM: transitional case management, USA: United States of America

¹ 3 core activities: 1) assessing membership, functional patterns, and roles in participant's ecosystems, including his family, friends, sexual and drug using partners, service providers; 2) connecting with participant's ecosystems through joint meetings and other communication; and 3) restructuring interactions and roles through direct interventions, and 3 phases: 1) initiation during which the counsellor built the therapeutic alliance and mapped the participant's ecosystem, and initial joining in which the counsellor established his or her role in the participant's ecosystem; 2) treatment in which the restructuring interventions were conducted through both individual and group counselling sessions and newly acquired interaction patterns within ecosystems were reinforced; and 3) termination in which treatment sessions tapered off and ended. Throughout treatment and at the termination of treatment, counsellors offered facilitated referrals as needed

² The participant established goals and objectives in the initial session and worked with the counsellor to achieve and modify the goals as the intervention progressed. Intervention techniques included motivational interviewing, facilitated referral and goal setting (based on Project START intervention)

³ The first 4 sessions covered the topics: (1) health conditions, medications, skills-building on communicating effectively with providers, assistance with enrolment in AIDS drug assistance programmes, (2) sexual risk reduction, (3) substance use and mental health, and (4) planning for transition and access to HIV or other health care provider, HIV medication adherence, and public services after release. Each participant set goals and developed an individual action plan to meet during the first 3 months after release. Pre-release sessions included client-centred discussions of motivations, barriers, facilitators, risks, and repercussions of risk behaviour. The 2 post-release intervention sessions included discussions of achievement and barriers to reaching individuals goals. These sessions focused on any challenges in achieving goals, including determining appropriate health care and prevention services, problem solving to overcome challenges, and discussions about potential repercussions of risk behaviour and any desired changes to individual sex and drug use action plan

⁴ The TCM programme provided referrals to community-based medical and social services, including assistance with medical appointments, enrolment into AIDS Drug Assistance Programme, housing placement, substance abuse treatment, hepatitis testing and vaccination, and provision of food and transportation vouchers (taxi vouchers for 1st visit after release when lack of transportation was reported as barrier to accessing services)

Cost-effectiveness

No studies were found on cost-effectiveness of interventions to increase linkage to care post-release.

Guidelines

Five guidelines that reported on throughcare were included, of which four were specific to the prison setting (two supranational and two national guidelines) and one was a supranational not specific to prison settings.

Summary of guidelines on throughcare (linkage to care post-release)

Guideline	
<i>Specific to prison setting – supranational guidelines</i>	
WHO, 2014 [7]	For both HIV and hepatitis C, continuity of treatment is essential to ensure the best outcomes and prevent the development of resistance. Health programmes in prisons should, therefore, work in close collaboration with the HIV programme in the community to ensure that treatment is not interrupted when people enter and leave prison. It is also important to organise this continuity when prisoners are transferred from one prison to another within the police/justice system. Before an individual is released from prison, links should be established with a service that will continue treatment. Sometimes it is difficult for ex-prisoners to go to these services. This situation should be identified in advance and remedies or support should be provided to ensure that contact will be established. The continuity of treatment is best when community services can provide support to a prisoner in prison and after release and accompany his/her re-entry into the community. Before release, prisoners undergoing treatment should be provided with a stock of medications for one month and a complete copy of their medical files, including the results of all tests conducted during incarceration. When a prisoner is transferred between prisons, health professionals should ensure that the medical file follows the prisoner.
WHO, 2007 [53]	Adherence rates in prisons can be as high or higher than among people in the community, but the gains in health status made during the term of incarceration may be lost unless careful discharge planning and links to community care are undertaken. Ensuring continuity of care from the community to the prison and back to the community as well as continuity of care within the prison system is a fundamental component of successful efforts to scale up treatment. Sustainable HIV treatment programmes in prisons, integrated into countries' general HIV treatment programmes or at least linked to them, are needed. One serious problem of ART is that any interruption of treatment can lead to resistance to at least some of the drugs used. Health staff should try to ensure compliance. In addition, other measures are needed to ensure that interruption of treatment does not occur.
<i>Specific to prison setting – national guidelines</i>	
SIMIT/ Ministero della Salute (Italy), 2016 [57]	Assure the linkage of HIV infected prisoners to the local Infectious Diseases (ID) division and arrange a calendar of weekly visits. <ul style="list-style-type: none"> - In order to assure continuity of care, at least 7 days of ART treatment should be given to the prisoner upon release. - Transfer of medication (if not available) to the prison of destination if the prisoner is transferred. - In order to guarantee continuity of care (50% of prisoners do not show up at the specialist visit after release) the referral ID specialist must be involved in outpatients' networks present in the community.
SAMHSA, 2017 [142]	Guideline 5: Anticipate that the periods following release (the first hours, days, and weeks) are critical and identify appropriate interventions as part of transition planning practices for individuals with mental health and co-occurring substance use disorders leaving correctional settings. Guideline 6: Develop policies and practices that facilitate continuity of care through the implementation of strategies that promote direct linkages (i.e. warm hand-offs) for post-release treatment and supervision agencies.
<i>Other guidelines – supranational guidelines</i>	
WHO, 2016 [58]	If they are being transferred, people in prisons and other closed settings should be given a supply of ART to last until health care can be established at the new prison location or, if they are being released, until linkage can be made to community-based HIV care.

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