



**UNODC**

United Nations Office on Drugs and Crime



# Systematic Literature Review on Stimulant use and HIV (B)

Part 5/5

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Treatment and Prevention of HIV, HCV  
&HBV among Stimulant Drugs Users

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This report is part of a series of five documents:

**A. Stimulant use: HIV risk and transmission**

1. Systematic Literature Review on HIV and Stimulant use: Methodology and summary of the findings of
2. Systematic Literature Review on HIV and Stimulant use: ATS and HIV Risk and Transmission
3. Systematic Literature Review on HIV and Stimulant use: Cocaine use and HIV Risk and Transmission
4. Systematic Literature Review on HIV and Stimulant use: NPS and HIV Risk and Transmission

**B. Prevention of HIV, HCV & HBV and treatment**

5. Systematic Literature Review on HIV and Stimulant use: Treatment and Prevention of HIV, HCV & HBV and treatment

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## Background

While the focus in HIV prevention among people who use drugs has concentrated on injection of opiate users, reports indicate that there are also HIV-related risks attached to other forms of drug use and to injection of other drugs including stimulant: cocaine and ATS. In particular, there seems to be a nexus between stimulant drugs and HIV transmission. The use of crack cocaine has been associated with sexual transmission of HIV, including in Brazil and the Caribbean, often mediated through sex work or other forms of transactional sex. Also, there have been reports of amphetamine type stimulants and its association with HIV, particularly in South-East Asia. Injection of ATS, new psychoactive substances (NPS) and cocaine has been reported a possible main contributor to HIV incidence among people who inject drugs in some regions such as in Eastern Europe

Areas of particular concern:

- Recent HIV increase in Eastern Europe possible link with stimulant use
- Use of crack-cocaine in Latin America and possible link with HIV prevalence
- ATS and NPS increase use in SE Asia and possible link with HIV prevalence (UNODC report, 2013).

Identify specific groups at risk:

- Environmental factors: geographic distribution
- Individual factors: gender, age, health
- Behavioural factors: exchange of sex for drugs or money, MSM

In addition, in its June 2009 session, the UNAIDS Programme Coordinating Board (PCB) called upon “Member States, civil society organizations and UNAIDS to increase attention on certain groups of non-injecting drug users, especially those who use crack cocaine and amphetamine type stimulants, who have been found to have increased risk of contracting HIV through high-risk sexual practices...”. The UNAIDS Fast Track strategy for 2020 and 2030 [http://www.unaids.org/en/resources/documents/2014/JC2686\\_WAD2014](http://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014) report requires a most focused response including for people who use drugs.

## Objectives

This reviewed assessed the scientific and grey literature on effective interventions for prevention, treatment and care of HIV, HCV & HBV among people who use stimulant drugs, particularly crack, cocaine and ATS (injecting and non-injecting use).

## Method

### Eligibility Criteria

#### Including Criteria

The primary criterion of the search was 'stimulant use' and 'HIV, HCV & HBV risk and transmission'. The PICOS elements are detailed below:

<i>Population</i>	<ul style="list-style-type: none"><li>- Well-defined group of injecting or non-injecting stimulant users (use within the last 12 months). Stimulants (cocaine, crack-cocaine, amphetamine-type substances or new psychoactive substances) should be the primary drug of use for at least 50% of the sample.</li></ul>
<i>Interventions</i>	<ul style="list-style-type: none"><li>- Interventions aimed at prevention or treatment of HIV, HCV &amp; HBV among stimulant users. Interventions can be behavioural, biomedical, antiretroviral therapy or educational.</li></ul>
<i>Comparison</i>	<ul style="list-style-type: none"><li>- For intervention comparisons: head to head, treatment as usual or waiting list.</li></ul>
<i>Outcomes</i>	<ul style="list-style-type: none"><li>- Biomarkers of HIV, HCV and HBV status (viral load, counts, prevalence and incidence measures).</li><li>- Sexual behaviour: risk sexual behaviour, number of sexual partners, condom use, safe sex, men who have sex with men and providing sex in exchange for money or drugs.</li><li>- Drug use and unsafe injecting practices.</li></ul>
<i>Study Design</i>	<ul style="list-style-type: none"><li>- Intervention studies including randomised controlled trials, clinical trials, pre and post intervention studies.</li></ul>

#### Excluding Criteria

General reviews, commentaries, letters, editorials, books and book chapters were excluded. Animal studies and studies focused on genetics, drug pharmacology, drug interactions, genotype comparisons, brain and cognitive functions were beyond of the scope of this review. Studies were also excluded if the drug of abuse (injected or not) was not specified, if the sample was formed primarily by opioid users or users of drugs other than stimulants. Studies were also excluded if infection status was self-reported (and other outcomes of interest were not measured) and if the sample size was less than 30 (with exception of studies on NPS).

### Search Methods

#### Electronic Searches

Searches were focus on peer-reviewed journals, other scientific publications (e.g. scientific monographs). MEDLINE, EMBASE, PsycInfo, Global Health, HMC Health Management Information Consortium, the Cochrane Data Base, CINAHL, Scopus were searched from 2004 up to April 2015.

Details of the search strategies with results are listed in appendix. All searches included non-English language literature.

The searches were conducted using Medical Subject Headings (MeSH terms) and also free-text terms. The main terms used in the searches were the following: stimulant, crack-cocaine, amphetamine, ecstasy, crystal methamphetamine, new psychoactive substances, methylphenidate, non-injecting drug users, injecting drug users, smokers, human immunodeficiency virus, HIV viral hepatitis, hepatitis C, HCV, hepatitis B, HBV, sexually transmitted diseases, transmission, risk behaviour, condom use, multiple sexual partners, providing sex in exchange for money or drugs, men who have sex with men, sex workers, SW, Homosexuality (Male), sexual behaviour, needle sharing. The full list of index terms used (including synonyms, broad and specific terms) is available in appendix.

#### *Grey Literature Search*

Reference lists of articles and reviews were searched. Reference lists of all selected articles were scrutinized for further references. Grey literature (technical reports, conference papers, unpublished thesis) were searched.

#### *Consultation with Experts and Users Groups*

Experts (lead authors of important studies) were contacted and asked about their knowledge of other studies, published or unpublished, relevant to this review. Other key informants from the community and researchers were also be contacted via UNODC contacts.

#### *Data Extraction and Analysis*

##### *Study selection*

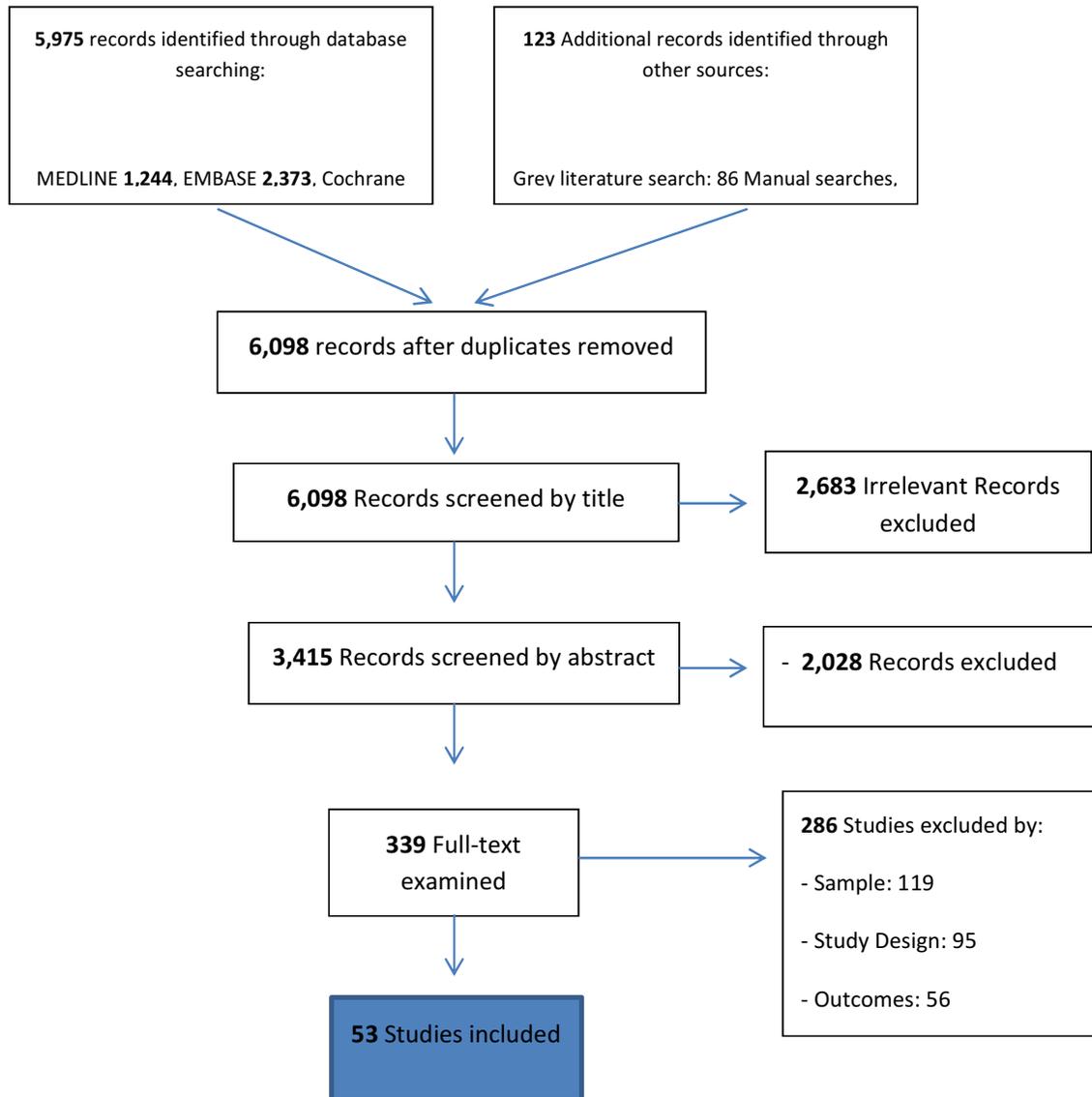
Studies retrieved were assessed for inclusion on the basis of the title and abstract. Those clearly not related to the primary criteria (HIV, HCV, HBV among stimulant users) were excluded. The remaining studies were assessed in more detail against the inclusion and exclusion criteria for the review. Full-text articles were assessed for the studies meeting eligibility criteria.

##### *Data Extraction and Management*

Data was extracted in a standardised format for the studies that satisfy inclusion criteria. Data was be extracted by author, year, location, study design, outcomes (primary and secondary), sample size, population, age, gender, key findings, follow-up points, intervention, control, randomisation.

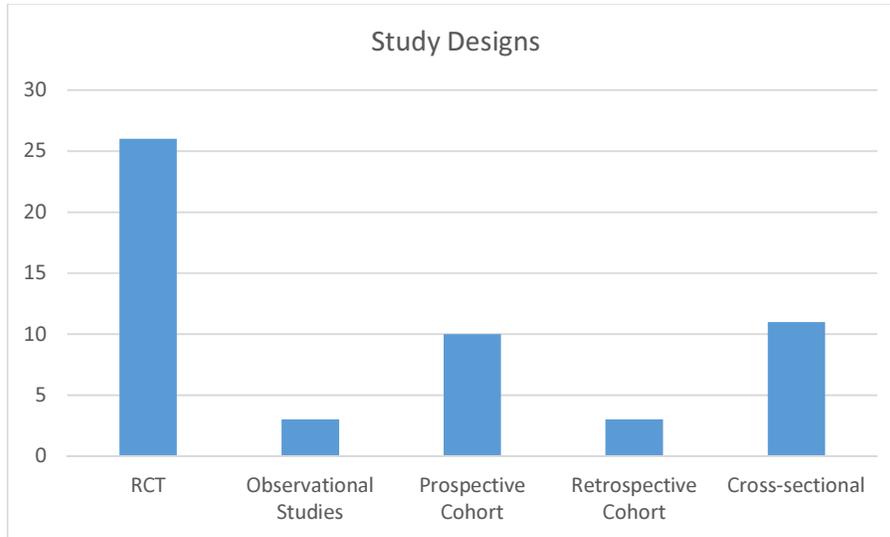
## Results

Out of 339 full-texts examined, a total of 53 studies on treatment and prevention of HIV, HCV and HBV among stimulant users were included in the present review.



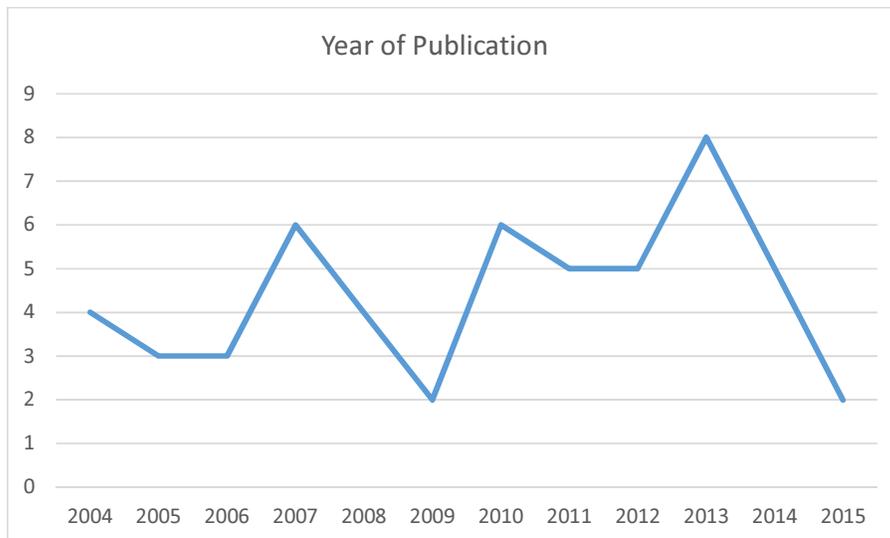
## 1. Design

The figure below shows the study designs of the 53 publications included in this review:



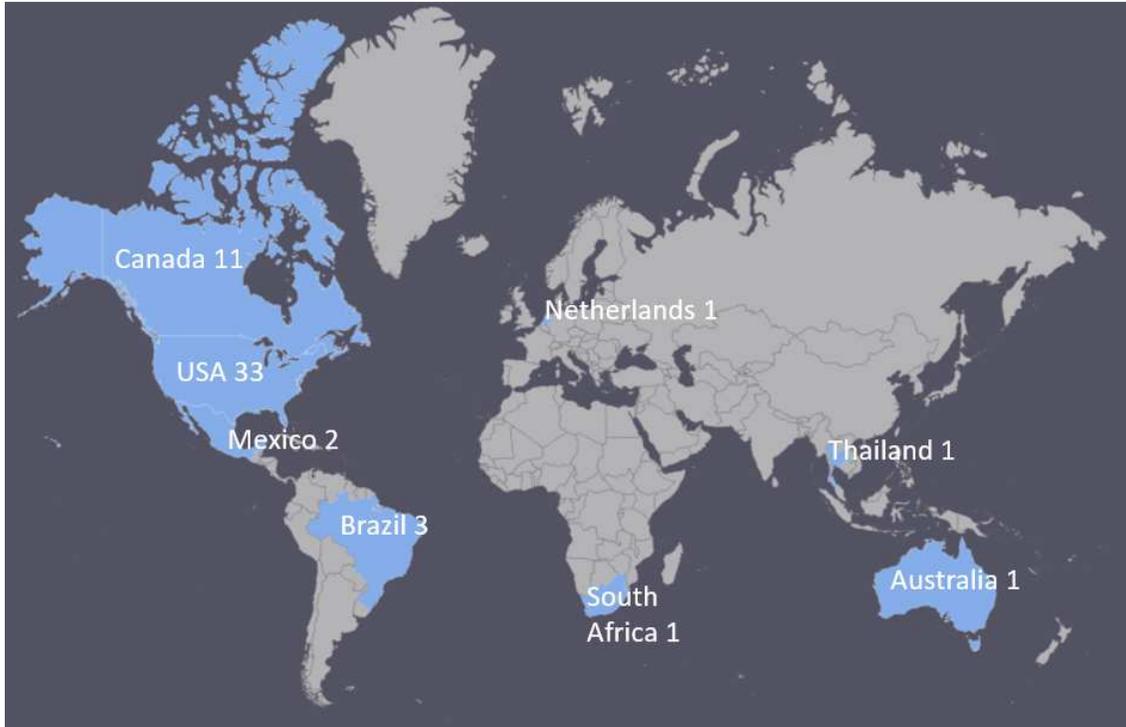
## 2. Year

The figure below shows in which year the studies were published:



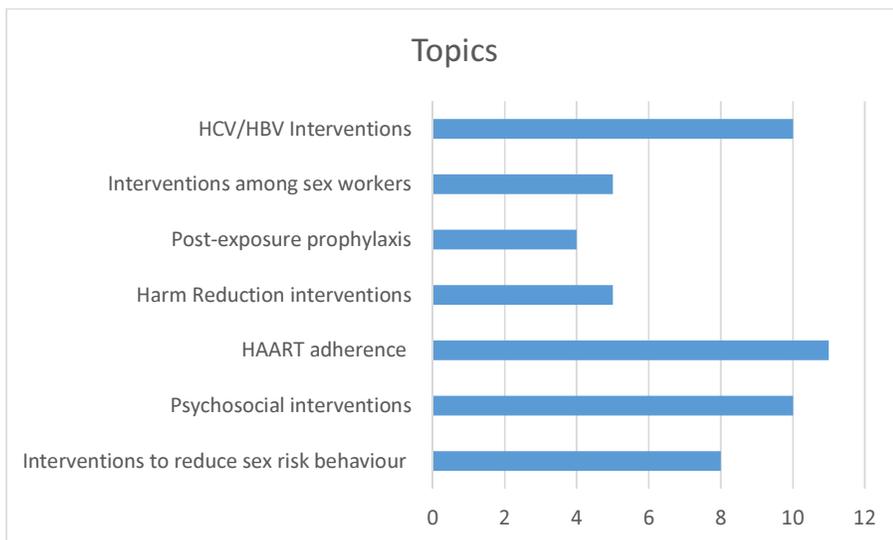
### 3. Country

The figure below shows in which countries the studies took place:



### 4. Topics

The studies were divided into categories or topics in order to analyse the evidence in more detail. The figure below shows the number of studies in each topic explored in this review.



#### 4.1. Interventions to reduce sex risk behaviour

Study	Country	Design	Sample	Interventions	Outcomes/Follow-up	Relevant findings
1. Williams, M., et al. (2012)  "An assessment of brief group interventions to increase condom use by heterosexual crack smokers living with HIV infection."	USA	RCT	347 heterosexual African American crack cocaine users living with HIV infection	Positive choices intervention (PCI) x standard intervention (SI),	Outcomes: condom use and intention to use condoms and to change condom use attitudes and beliefs	Results were similar across groups. The proportion of those assigned to the PCI reporting sex with a paid partner significantly decreased, while the proportion disclosing their sero-status to their partners increased. There were no significant differences on these measures in the SI group. The measure of situational self-efficacy significantly increased in the PCI group, but not the SI group. Results also showed significant time-by-time effects. Mean condom use, intention to use condoms, attitudes, and condom use self-efficacy beliefs showed significant difference between three and nine months. However, there was no clear pattern of change.
			Drug: Crack-cocaine		Follow-up: 3 and 9 months	
2. Wechsberg, W. M., et al. (2010)  "Sustainability of intervention effects of an evidence-based HIV prevention intervention for African American women who smoke crack cocaine."	USA	RCT	455 out-of-treatment African American women in central North Carolina	3 woman-focused HIV intervention: the woman-focused intervention, a modified NIDA intervention, and a delayed-treatment control condition	HIV risk behaviour	The analyses revealed two distinct groups at STFU: women who either eliminated or greatly reduced their risk behaviours (low-risk class) and women who retained high levels of risk across multiple risk domains (high-risk class). At STFU, women in the woman-focused intervention were more likely to be in the low HIV risk group than the women in control conditions, but this effect was not statistically significant at LTFU. However, low-risk participants at STFU were less likely to be retained at LTFU, and this retention rate was lowest among women in the woman-focused intervention. Short-term intervention effects were not observed over 4 years later, possibly due to differential retention across conditions.
			Drug: Crack-cocaine		Follow-up: mean 4.4 years	

<p>3. Wechsberg, W. M., et al. (2004)</p> <p>"Efficacy of a woman-focused intervention to reduce HIV risk and increase self-sufficiency among African American crack abusers."</p>	USA	RCT	620 African American women who use crack	Revised National Institute on Drug Abuse standard intervention, and a control group	Risk behaviour, employment, and housing status	All groups significantly reduced crack use and high-risk sex at each follow-up, <b>but only woman-focused intervention participants consistently improved employment and housing status.</b> Compared with control subjects at 6 months, woman-focused intervention participants were least likely to engage in unprotected sex; revised standard intervention women reported greatest reductions in crack use. Conclusions. <b>A woman-focused intervention can successfully reduce risk and facilitate employment and housing and may effectively reduce the frequency of unprotected sex in the longer term.</b>
<p>4. Rotheram-Borus, M. J., et al. (2010).</p> <p>"Reducing HIV risks among active injection drug and crack users: the safety counts program."</p>	USA	Quasi experimental cross-over design, (sites were randomised)	Injection drug users (IDU) and crack users in two neighbourhoods	Safety Counts program (a CDC-diffused intervention) compared to Voluntary HIV Counseling and Testing	HIV risk, drug use and risky drug injection	<b>Drug users in the Safety Counts program reported significantly greater reductions in risky sex, crack and hard drug use, and risky drug injection.</b> The more sessions of Safety Counts attended, the greater were the reductions in risky acts. Safety Counts is an effective intervention for IDU and crack users.
<p>5. Pechansky, F., et al. (2007)</p> <p>"Using thought mapping and structured stories to decrease HIV risk behaviours among cocaine</p>	Brazil	RCT	119 Brazilian cocaine users	Standard or a standard plus "thought mapping" intervention	Changes in AIDS knowledge and risk behaviours	Significant increases in AIDS knowledge and condom use were observed in the experimental group, as well as significant changes in the sub scores for sexual and drug risks. The experimental intervention was less successful in decreasing mean days of cocaine use when compared to the standard. Conclusion: Although not robust, the findings nevertheless suggest that components of the experimental thought-mapping model might be useful in combination with other approaches
			Drug: Crack-cocaine		Follow-up: 3 and 6 months	
			Drug: Crack-cocaine		Follow-up: 5-9 months	
			Drug: cocaine		Follow-up: 2-8 weeks	

injectors and crack smokers in the South of Brazil"						
6. Mausbach, B. T., et al. (2007).  "Efficacy of a behavioural intervention for increasing safer sex behaviours in HIV-negative, heterosexual methamphetamine users: Results from the fast-lane study."	USA	RCT	451 HIV-negative, heterosexual methamphetamine users	(a) a safer sex behavioural intervention (Fast-Lane [FL]), (b) the FL intervention with boosters (FL + B), or (c) a time-equivalent diet-and-exercise attention-control (D&E) condition.	Safer sex behaviours	Compared to those in the D&E condition, <b>participants in the FL + B condition (p = .019) and FL condition (p = .020) significantly increased their engagement in protected sex acts over the active intervention phase.</b> Also, compared to the D&E condition, those in the FL condition demonstrated a significant decrease in unprotected sex (p = .005) and an increase in percent protected sex (p = .001) during the active intervention. Finally, relative to D&E participants, FL participants demonstrated significant improvements in self-efficacy for negotiating safer sex (p = .011), and change in self-efficacy mediated the efficacy of the FL condition for increasing safer sex behaviours (p = .033). Conclusions: These results suggest that our behavioural intervention was successful in terms of reducing high-risk sexual behaviours in the context of ongoing methamphetamine use among HIV-negative heterosexuals. Reductions in high-risk sexual behaviour were likely because of the impact of the intervention on participants' self-efficacy for negotiating safer sex.
			Drug: MA		Follow-up: over an 18-month period	
7. Mausbach, B. T., et al. (2007).  "Efficacy of a behavioural intervention for increasing safer sex behaviours in HIV-positive MSM methamphetamine users: Results from the EDGE study."	USA	RCT	341 HIV-positive, methamphetamine-using MSM	<b>Sex behavioural intervention (EDGE)</b> or a time-equivalent diet-and-exercise attention-control condition	safer sex behaviours	Participants in the EDGE intervention engaged in significantly more protected sex acts at the 8-month (p = 0.034) and 12-month assessment (p = 0.007). By 12-months post-baseline, a greater percentage of protected sex acts was observed for EDGE (25.8%) vs. control participants (18.7%) (p = 0.038). There was a significant time-by-intervention interaction (p = 0.018) for self-efficacy for condom use, suggesting that EDGE participants' self-efficacy demonstrated a greater increase over time compared to control participants. Conclusions: <b>These results suggest that it is possible to reduce high risk sexual behaviours in the context of ongoing methamphetamine use among HIV-infected MSM.</b>
			Drug: MA		Follow-up: over a 12-month period	

8. Herrmann, E. S., et al. (2013).  "Characterizing and improving HIV/AIDS knowledge among cocaine-dependent outpatients using modified materials."	USA	Cross over RCT	90 cocaine-dependent outpatients	HIV/AIDS educational intervention or control condition (a sham intervention).	HIV/AIDS knowledge	Scores on both pre-tests were lower than those observed in historical controls ( $p < .001$ ). Scores on knowledge tests increased from baseline after participants completed the educational intervention ( $p < .001$ ), but not after the sham intervention ( $p > .05$ ). Scores at follow-up remained higher than baseline scores ( $p < .001$ ). Conclusions: Modifying response formats to include a "don't know" option likely increases identification of baseline knowledge deficits. This brief intervention is effective at increasing HIV/AIDS knowledge among cocaine-dependent outpatients.
			Drug: cocaine		Follow-up: immediate post-intervention analyses then 9 weeks after	

#### 4.2. Psychosocial Interventions

Study	Country	Design	Sample	Interventions	Outcomes/Follow-up	Relevant findings
1. Baker, A., et al. (2005).  "Brief cognitive behavioural interventions for regular amphetamine users: A step in the right direction"	Australia	RCT	214 regular amphetamine users	brief interventions consisting of motivational interviewing and cognitive-behaviour therapy (CBT) compared to control condition	Amphetamine use, HIV risk-taking, crime, social functioning and health	There were no intervention effects on HIV risk-taking
2. Menza, T. W., et al. (2010).  "Contingency management to reduce methamphetamine use and sexual risk among men who have sex with men: a randomized controlled trial."	USA	RCT	127 MSM	12-week a CM intervention (n = 70) or referral to community resources (n = 57)	Methamphetamine use and sexual risk	Comparing consecutive study visits, non-concordant UAI declined significantly in both study arms. During the intervention, CM and control participants were comparably likely to provide urine samples containing methamphetamine (adjusted relative risk [aRR] = 1.09; 95%CI: 0.71, 1.56) and to report non-concordant UAI (aRR = 0.80; 95%CI: 0.47, 1.35). However, during post-intervention follow-up, CM participants were somewhat more likely to provide urine samples containing methamphetamine than control participants (aRR = 1.21; 95%CI: 0.95, 1.54, P = 0.11). Compared to control participants, CM participants were significantly more likely to report weekly or more frequent methamphetamine use and use of more than eight quarters of methamphetamine during the intervention and post-intervention periods. While it is possible to enrol and retain MSM who use methamphetamine in a trial of CM conducted outside drug treatment, our data suggest that CM is not likely to have a large, sustained effect on methamphetamine use.
					Follow up: 24 weeks	

<p>3. Rawson, R. A., et al. (2008).</p> <p>"Methamphetamine dependence and human immunodeficiency virus risk behaviour."</p>	<p>USA</p>	<p>Secondary analysis of an RCT</p>	<p>784 methamphetamine-dependent users</p>	<p>standardized psychosocial protocol (Matrix model) or treatment-as-usual</p>	<p>HIV-related risk behaviour, including injection and unsafe sexual practices</p> <p>Follow-up: 6, 12, and 36 month</p>	<p>Results indicated that HIV risk behaviours substantially decreased over time. Treatment factors (retention and completion) and frequency of MA use were both positively associated with increased reduction of HIV risk behaviours. The findings suggested that treatment of MA dependence is promising for reducing behaviours that have been shown to transmit HIV.</p>
<p>4. Reback, C. J. and S. Shoptaw (2014)</p> <p>"Development of an evidence-based, gay-specific cognitive behavioural therapy intervention for methamphetamine-abusing gay and bisexual men."</p>	<p>USA</p>	<p>CT</p>	<p>methamphetamine-abusing gay and bisexual men</p>	<p>Gay-specific, cognitive behavioural therapy (GCBT) combined with a low-cost contingency management (CM; [GCBT. +. CM]) intervention</p>	<p>methamphetamine use and sexual risk behaviours</p>	<p>Effect sizes for primary outcomes were compared using meta-analysis. Comparisons of effect sizes at end of treatment showed the modified GCBT. +. CM produced significantly fewer consecutive weeks of methamphetamine abstinence (- 0.44, CI: - 0.79, - 0.09) and fewer male sexual partners (- 0.36, CI: - 0.71, - 0.02) than the first trial of GCBT, and more days of methamphetamine use (0.35, CI: 0.02, 0.68) than the second trial of GCBT. At 26-week follow-up, the modified GCBT. +. CM produced greater effects in reducing the number of male sexual partners (- 0.54, CI: - 0.89, - 0.19; - 0.51, CI: - 0.84, - 0.18). The original GCBT produced more and mostly short-term beneficial drug use outcomes, though sexual behaviour changes consistently favoured the modified GCBT. +. CM. On balance, most benefits are retained with the modified GCBT. +. CM intervention.</p>

<p>5. Sherman, S. G., et al. (2009)</p> <p>"Evaluation of a peer network intervention trial among young methamphetamine users in Chiang Mai, Thailand."</p>	Thailand	RCT	983 young methamphetamine users	compare the efficacy of a peer educator, network-oriented intervention with a best practice, life-skills curriculum. Both conditions consisted of seven, 2h, small group sessions	<p>methamphetamine and HIV risk behaviours and incident sexually transmitted infections (STIs)</p> <p>Follow-up occurred at 3-, 6-, 9-, and 12 months.</p>	<p>Over time, participants in both conditions showed a significant and dramatic decline in self-reported methamphetamine use (99% at baseline vs. 53% at 12 months, <math>p &lt; 0.0001</math>) and significant increase in consistent condom use (32% baseline vs. 44% at 12 months, <math>p &lt; 0.0001</math>). Incident STIs were common, with no differences between arms. Chlamydia had the highest incidence rate, 9.85/100 person years and HIV had a low incidence rate of 0.71/100 person years. Among young Thais, peer educator, network-oriented intervention was associated with reductions in methamphetamine use, increases in condom use, and reductions in incident STIs over 12 months. Parallel reductions with the life-skills condition. Small group interventions are an effective means of reducing methamphetamine use and sexual risk among Thai youth.</p>
<p>6. Shoptaw, S., et al. (2005).</p> <p>"Behavioural treatment approaches for methamphetamine</p>	USA	RCT	162 Methamphetamine-dependent gay and bisexual men (GBM)	Four treatment conditions for 16 weeks: standard cognitive behavioural therapy (CBT, $n = 40$ ), contingency management (CM, $n = 42$ ), combined cognitive behavioural therapy and contingency	methamphetamine use and sexual risk behaviours among	<p>Statistically significant differences in retention (<math>F(3,158) = 3.78</math>, <math>p &lt; .02</math>), in longest period of consecutive urine samples negative for methamphetamine metabolites (<math>F(3,158) = 11.80</math>, <math>p &lt; .001</math>), and in the Treatment Effectiveness Score were observed by condition during treatment (<math>F(3,158) = 7.35</math>, <math>p &lt; .001</math>) with post hoc analyses showing the CM and CBT + CM conditions to perform better than standard CBT. GEE modeling results showed GCBT significantly reduced unprotected receptive anal intercourse (URAI) during the first 4 weeks</p>

e dependence and HIV-related sexual risk behaviours among urban gay and bisexual men."				management (CBT + CM, n = 40), and a culturally tailored cognitive behavioural therapy (GCBT, n = 40).	Follow-up: 6 and 12 months	of treatment ( $X^2 = 6.75, p < .01$ ). During treatment between-group differences disappeared at follow-up with overall reductions in outcomes sustained to 1-year. Conclusions: Among high-risk methamphetamine-dependent GBM, drug abuse treatments produced significant reductions in methamphetamine use and sexual risk behaviours. Drug abuse treatments merit consideration as a primary HIV prevention strategy for this population.
7. Parsons, J. T., et al. (2014).  "A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men."	USA	RCT	143 non-treatment-seeking HIV-negative young gay and bisexual men	test a brief motivational interviewing (MI) compared with a content-matched education condition,	sexual risk behaviours/UAI  Follow-up: every 3 months for 1 year	Regardless of condition, participants reported significant reductions in UAI and substance use over time. However, YGBM in the MI condition were 18% less likely to use drugs and 24% less likely to engage in UAI than YGBM in the education condition. Conclusions: The results support the utility of MI, compared with a content-matched education condition, to significantly reduce both UAI and drug use among YGBM.
8. Shoptaw, S., et al. (2008).  "Outcomes using two tailored behavioural treatments for substance abuse in urban gay and bisexual men."	USA	RCT	128 stimulant-abusing gay and bisexual	16 weeks of a gay-specific cognitive-behavioural therapy (GCBT, n = 64) or to a gay-specific social support therapy (GSST; n = 64)	retention, substance use, or HIV-related sexual risk behaviours  follow-up evaluations at 17, 26, and 52 weeks	No overall statistically significant differences were observed between conditions along retention, substance use, or HIV-related sexual risk behaviours. All participants showed a minimum of twofold reductions in substance use and concomitant sexual risk behaviours from baseline to 52-week evaluations. Among methamphetamine-using participants, the GCBT condition showed significant effects over GSST for reducing and sustaining reductions of methamphetamine. Findings replicate prior work and indicate that GCBT produces reliable, significant, and sustained reductions in stimulant use and sexual risk behaviours, particularly in methamphetamine-abusing gay and bisexual men.

<p>9. McDonell, M. G., et al. (2013).</p> <p>"Randomized controlled trial of contingency management for stimulant use in community mental health patients with serious mental illness."</p>	USA	RCT	176 outpatients with serious mental illness and stimulant dependence	3 months of contingency management plus treatment as usual or treatment as usual with reinforcement for study participation only	<p>Stimulant use psychiatric symptoms, HIV risk behaviour, and inpatient service utilization.</p> <p>Follow-up: 3 months</p>	<p>Although participants in the contingency management condition were significantly less likely to complete the treatment period than those assigned to the control condition (42% compared with 65%), they were 2.4 times (95% CI=1.9-3.0) more likely to submit a stimulant-negative urine test during treatment. Compared with participants in the control condition, they had significantly lower levels of alcohol use, injection drug use, and psychiatric symptoms and were one-fifth as likely as those assigned to the control condition to be admitted for psychiatric hospitalization during treatment. They also reported significantly fewer days of stimulant drug use during the 3-month follow-up.</p> <p><b>No group differences were observed in HIV-risk associated sexual behaviour. Participants assigned to the contingent group were 3.3 times (CI=1.8-5.9, p&lt;0.05) less likely to report engaging in injection drug use, relative to non-contingent participants, during treatment. Groups were not different during follow-up.</b></p>
<p>10. McDonell, M. G., et al. (2013).</p> <p>"Randomized controlled trial of contingency management for stimulant use in community mental health patients with serious mental illness."</p>	USA	RCT	176 stimulant-dependent patients with serious mental illness	3 months of contingency management for stimulant abstinence plus treatment as usual or treatment as usual with reinforcement for study participation only	<p>abstinence from stimulant drug (primary),</p> <p>reductions in use of other substances, psychiatric symptoms, HIV risk behaviour, and inpatient service utilization (secondary)</p> <p>Follow-up: 3 months</p>	<p>Although participants in the contingency management condition were significantly less likely to complete the treatment period than those assigned to the control condition (42% compared with 65%), they were 2.4 times (95% CI=1.9-3.0) more likely to submit a stimulant-negative urine test during treatment. Compared with participants in the control condition, they had significantly lower levels of alcohol use, injection drug use, and psychiatric symptoms and were one-fifth as likely as those assigned to the control condition to be admitted for psychiatric hospitalization during treatment. They also reported significantly fewer days of stimulant drug use during the 3-month follow-up. Conclusions: When added to treatment as usual, contingency management is associated with large reductions in stimulant, injection drug, and alcohol use. Reductions in psychiatric symptoms and hospitalizations are important secondary benefits.</p>

### 4.3. HAART Adherence

Study	Country	Design	Sample	Objectives	Relevant findings
1. Sharpe, T. T., et al. (2004)	USA	prospective, observational study: interview data was analyzed of HIV-infected women > 18 years of age reported to 12 health departments between July 1997 and December 2000	1655 HIV-infected women	To ascertain if Black women reported crack use more than other HIV-infected women and to examine the relationship between crack use and antiretroviral treatment (ART) adherence among Black women.	<p><b>"Crack cocaine use and adherence to antiretroviral treatment among HIV-infected black women."</b></p> <p>In multivariate analysis, crack users and users of other drugs were less likely than non-users to take their ART medicines exactly as prescribed (odds ratio [OR] = 0.37; 95% confidence interval [CI] = 0.24-0.56), OR = 0.47; 95% CI = 0.36-0.68), respectively. HIV-infected Black women substance users, especially crack cocaine users, may require sustained treatment and counseling to help them reduce substance use and adhere to ART.</p>
2. Ingersoll, K. S., et al. (2011)	USA	Pilot RCT  The interventions included 6 sessions of Motivational Interviewing plus feedback and skills building (MI+), or Video information plus debriefing (Video+) over 8 weeks. Primary outcomes were adherence by 14-day timeline follow-back and Addiction Severity Index (ASI) Drug Composite Scores at 3 and 6 months.	Participants were 54 adults with crack cocaine use and HIV with <90% HAART adherence. Most participants were African-American (82%) heterosexual (59%), and crack cocaine dependent (92%).	This pilot randomized clinical trial tested the feasibility and efficacy of 2 interventions based on the Information-Motivation-Behavioural Skill model to improve HAART adherence and reduce crack cocaine problems.	<p><b>"A pilot randomized clinical trial of two medication adherence and drug use interventions for HIV+ crack cocaine users."</b></p> <p>Significant increases in adherence and reductions in ASI Drug Composite Scores occurred in both conditions by 3 months and were maintained at 6 months, representing medium effect sizes. No between group differences were observed. No VL changes were observed in either group. Treatment credibility, retention, and satisfaction were high and not different by condition. Conclusions: A counseling and a video intervention both improved adherence and drug problems durably among people with crack cocaine use and poor adherence in this pilot study. The interventions should be tested further among drug users with poor adherence. Video interventions may be feasible and scalable for people with HIV and drug use.</p>
3. Doshi, R. K., et al. (2012).	USA	Cross-sectional	350 hospitalized HIV-infected crack cocaine users recruited for Project HOPE (Hospital Visit Is an Opportunity for Prevention	To assess antiretroviral utilization among hospitalized HIV-	<p><b>"Correlates of antiretroviral utilization among hospitalized HIV-infected crack cocaine users."</b></p> <p>Reporting &gt;2 visits to outpatient HIV care in the past 6 months (AOR 7.55, 95% CI 3.80-14.99), drug or alcohol</p>

			and Engagement with HIV-Positive Crack Users) in Atlanta and Miami who were eligible for ART (reported any lifetime use of ART or CD4 <350 cells/mul).	infected crack cocaine users	treatment in the past 6 months (AOR 2.29, 95% CI 1.06-4.94), and study site being Miami (AOR 2.99, 95% CI 1.56-5.73) were associated with ART use. Current homelessness (AOR 0.41, 95% CI 0.20-0.84) and CD4 <200 cells/mul (AOR 0.29, 95% CI 0.15-0.55) were negatively associated with ART use. Among those taking ART, 60% had an HIV-1 viral load <400 copies/ml; this represented 9% of the eligible population. For HIV-infected crack cocaine users, structural factors may be as important as individual and interpersonal factors in facilitating ART utilization. Few HIV(+) crack cocaine users had viral suppression, but among those on ART, viral suppression was achievable.
4. Atkinson, J. S., et al. (2008).	USA	exploratory path model	130 African-American HIV-positive crack cocaine users on highly active antiretroviral therapy (ART).	This study developed an exploratory path model of schedule adherence	<p><b>"Associations among correlates of schedule adherence to antiretroviral therapy (ART): A path analysis of a sample of crack cocaine using sexually active African-Americans with HIV infection."</b></p> <p>This study developed an exploratory path model of schedule adherence using data from a sample 130 African-American HIV-positive crack cocaine users on highly active antiretroviral therapy (ART). This model was based on the Transactional Model of Stress and Coping developed by Lazarus and Folkman. Following the theory, the effects of psychological distress on schedule adherence were mediated by patients' relationship with their doctor and optimism towards antiretroviral treatment. Adherence was also associated with patients' self-efficacy regarding their medical regimen which, in turn, was associated with their social support.</p>
5. Batista, J. L., et al. (2014).	Brazil	cross-sectional	people living with HIV/AIDS (PLWHA) who attended two referral centers in the city of Recife, in Northeastern Brazil, between June 2007 and October 2009	This study aimed to estimate the prevalence of self-reported irregular use of antiretroviral therapy and the factors associated with such an irregularity in PLWHA.	<p><b>"Association between smoking, crack cocaine abuse and the discontinuation of combination antiretroviral therapy in Recife, Pernambuco, Brazil."</b></p> <p>The prevalence of PLWHA who reported irregular use of combination antiretroviral therapy (cART) was 25.7%. In the final multivariate model, the irregular use of cART was associated with the following variables: being aged less than 40 years (OR = 1.66, 95%-CI: 1.29-2.13), current smokers (OR = 1.76, 95%-CI: 1.31-2.37) or former smokers (OR = 1.43, 95%-CI: 1.05-1.95), and crack cocaine users (OR</p>

					= 2.79, 95%-CI: 1.24-6.32). Special measures should be directed towards each of the following groups: individuals aged less than 40 years, smokers, former smokers and crack cocaine users. Measures for giving up smoking and crack cocaine should be incorporated into HIV-control programs in order to promote greater adherence to antiretroviral drugs and thus improve the quality of life and prolong life expectancy.
6. Crisp, B. R., et al. (2004).	USA	Cross-sectional	African-American crack cocaine smokers	This study sought to obtain baseline information on the adherence to antiretroviral medications by members of this important risk population in Houston, Texas.	<p><b>"Medication compliance and satisfaction with treatment for HIV disease in a sample of African-American crack cocaine smokers."</b></p> <p>It was found that for only 5 of a range of 16 antiviral medications was there a significant correlation between levels of compliance reported by respondents and their beliefs as to how effective these medications are. Medication compliance was also found not to be associated with frequency of crack cocaine use in the month prior to interview. Furthermore, irrespective of both gender and their reported extent of medication compliance, the respondents tended to report positive relationships with their treating physician, with higher levels of satisfaction reported by women. These results suggest that the majority of African-American crack cocaine users are able to comply with HIV treatment regimes, with more than half (53%) claiming full compliance for one or more medications, and a further one third (31%) claiming compliance more than half the time. Moreover, these findings suggest that they will continue to take antiretroviral medications even if they have doubts about the effectiveness of these medications.</p>
7. Carrico, A. W., et al. (2007).	USA	Randomized behavioural prevention trial and provided baseline blood samples to measure T-helper (CD4+) counts and HIV viral load.	A total of 858 HIV-positive participants self-reporting risk of transmitting HIV	The present study examined the associations among affect regulation, substance use, non-adherence to anti-retroviral therapy (ART), and immune status in a diverse	<p><b>"Affect regulation, stimulant use, and viral load among HIV-positive persons on anti-retroviral therapy."</b></p> <p>Among individuals on ART, regular stimulant users had a five-fold (0.70 log<sub>10</sub>) higher HIV viral load than those who denied regular stimulant use. The association between regular stimulant use and elevated HIV viral load remained after accounting for demographics, differences in CD4+ counts, and polysubstance use. In the final model, 1 unit increase in affect regulation (decreased severity of</p>

				sample of HIV-positive persons.	depressive symptoms as well as enhanced positive states of mind) was associated with a 23% decrease in the likelihood of reporting regular stimulant use and 15% decrease in the likelihood of being classified as non-adherent to ART. Regular stimulant users, in turn, were more than twice as likely to be non-adherent to ART. Even after accounting for the effects of non-adherence and CD4+ counts, regular stimulant use was independently associated with 50% higher HIV viral load. CONCLUSIONS: Increased mental health treatment as well as more intensive referrals to substance abuse treatment or 12-step self-help groups may be crucial to assist stimulant users with more effectively managing treatment for HIV/AIDS
8. Altice, F. L., et al. (2007).	USA	RCT  Patients randomized to receive DAART received supervised therapy 5 days per week from workers in a mobile health care van. The primary outcome, using an intention-to-treat approach, was the proportion of patients achieving either a reduction in HIV-1 RNA level of $>1.0 \log_{10}$ copies/mL or an HIV-1 RNA level $<400$ copies/mL at 6 months. Secondary outcomes included the mean change from baseline in HIV-1 RNA level and CD4 <sup>+</sup> T lymphocyte count.	Of the 141 patients who met the entry criteria, 88 were randomized to receive DAART, and 53 were randomized to receive self-administered therapy; 74 (84%) of 88 of the patients randomized to receive DAART accepted the intervention. Of the 74 patients who initiated DAART, 51 (69%) completed the full 6-month intervention.	The biological outcomes of a 6-month community intervention of DAART were compared with those of self-administered therapy among HIV-infected drug users.	<b>"Superiority of directly administered antiretroviral therapy over self-administered therapy among HIV-infected drug users: A prospective, randomized, controlled trial."</b>  At the end of 6 months, a significantly greater proportion of the DAART group achieved the primary outcome (70.5% vs. 54.7; P = .02). Additionally, compared with patients receiving self-administered therapy, patients receiving DAART demonstrated a significantly greater mean reduction in HIV-1 RNA level ( $-1.16 \log_{10}$ copies/mL vs. $-0.29 \log_{10}$ copies/mL; P = .03) and mean increase in CD4 <sup>+</sup> T lymphocyte count ( $+58.8$ cells/ $\mu$ L vs. $-24.0$ cells/ $\mu$ L; P = .002). Conclusions. This randomized, controlled trial was, to our knowledge, the first to demonstrate the effectiveness of DAART at improving 6-month virologic outcomes among drug users. These results suggest that DAART should be more widely available in HIV treatment programs that target drug users who have poor adherence to treatment. © 2007 by the Infectious Diseases Society of America. All rights reserved.

9. Smit, C., et al. (2006).	Netherlands	Prospective cohort study	HIV-infected DU who commenced HAART (n = 67) were matched with those not starting HAART (n = 130) on CD4 cell counts, duration of cohort participation, age and calendar year of visit. Immunological and virological responses of the HAART-treated DU were compared with the HAART-treated homosexual men from the same cohort (n = 212).	To study sexual risk and injecting behaviour among HIV-infected drug users (DU) receiving highly active antiretroviral therapy (HAART).	<p><b>"Highly active antiretroviral therapy (HAART) among HIV-infected drug users: A prospective cohort study of sexual risk and injecting behaviour."</b></p> <p>Non-HAART users reported more episodes of injecting than HAART users. In both groups injecting declined over time with no effect of HAART initiation. Before HAART initiation an increase in sexual risk behaviour was observed among those who had been assigned to receive HAART; their sexual risk behaviour declined thereafter. No change in sexual risk behaviour was found among non-HAART users. Relative to homosexual men, DU had a similar initial therapeutic response, but DU started HAART at lower CD4 cell counts and higher viral load levels. Conclusion: DU who are treated with HAART are not increasing their risk behaviour, and their early response to HAART is similar to homosexual men. However, before the treated DU received HAART they were seen to inject less often than those not treated with HAART. This suggests that selection of potential HAART starters is based on limited drug use. Although the DU who commence HAART are a selected group, our results show that HIV-infected DU can be treated effectively.</p>
10. Kuyper, L., et al. (2011).	Canada	Cohort	380 ART-naive individuals, 171 (45.0%) were female, and the median follow-up duration was 60. months (IQR = 18-113).	To evaluate whether ART initiation was associated with changes in syringe lending patterns among a long-term prospective cohort of HIV-positive IDU	<p><b>"Does initiation of HIV antiretroviral therapy influence patterns of syringe lending among injection drug users?"</b></p> <p>Between May 1996 and April 2008, 260 (68.4%) participants initiated ART. In a generalized linear mixed-effects model which compared each individual's likelihood of sharing syringes prior to and following the initiation of ART, syringe lending was not significantly associated with ART initiation in unadjusted (odds ratio = 0.72, 95% CI: 0.38-1.36) or adjusted (odds ratio = 0.78, 95% CI: 0.42-1.45) analyses. Concerns regarding increased injection risk behaviours following the initiation of ART were not observed in this setting.</p>
11. Shoptaw, S., et al. (2012).	USA	Cohort	HIV-positive and HIV-negative men in the Multicenter AIDS Cohort Study	To examine associations between stimulant use (methamphetamine	<p><b>"Cumulative exposure to stimulants and immune function outcomes among HIV-positive and HIV-negative men in the Multicenter AIDS Cohort Study."</b></p>

				<p>and cocaine) and other substances (nicotine, marijuana, alcohol and inhaled nitrites) with immune function biomarkers among HIV-seropositive (HIV) men taking highly active antiretroviral therapy (ART) and HIV-seronegative (HIV2) men in the Multicenter AIDS Cohort Study.</p>	<p>Among HIV men, cumulative adherence to ART (4.07, 95% confidence interval [CI]: 3.52, 4.71, per 10 years of adherent ART use), and recent cohort enrolment (1.38; 95% CI: 1.24, 1.55) were multiplicatively associated with increase in CD4+/CD8+ ratios. Cumulative use of methamphetamine (0.93; 95% CI: 0.88, 0.98, per 10 use-years), cocaine (0.93; 95% CI: 0.89, 0.96, per 10 use-years) and cumulative medical visits (0.99; 95% CI: 0.98, 0.99, per 10 visit-years), each showed small negative associations with CD4+/CD8+ ratios. Among HIV2 men, cumulative medical visits (0.996; 95% CI: 0.993, 0.999), cumulative number of male sexual partners (0.999; 95% CI: 0.998, 0.9998, per 10 partner-years) and cigarette pack-years (1.10; 95% CI: 1.02, 1.18, per 10 pack-years) were associated with CD4+/CD8+ ratios over the same period. ART adherence is associated with a positive immune function independent of stimulant use, underscoring the influence of ART on immune health for HIV men who engage in stimulant use.</p>
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#### 4.4. Harm Reduction Interventions

Study	Country	Design	Sample	Objectives	Relevant findings
1. Morissette, C., et al. (2007).	Canada	Cross-sectional	275 IDUs were recruited from syringe exchange programs in Montreal, Canada in 2004-2005.	To identify factors associated with using sterile drug injection equipment by injection drug users (IDUs).	<p><b>"Minimal uptake of sterile drug preparation equipment in a predominantly cocaine injecting population: implications for HIV and hepatitis C prevention."</b></p> <p>Sterile syringes, containers, filters, and water were used for at least half of injecting episodes by 95%, 23%, 23%, and 75% of subjects, respectively. In multivariate analysis, users of sterile syringes had higher odds of being older and injecting alone, and were less likely to report problems obtaining sterile syringes and requiring or providing help with injecting. Using sterile filters was associated with having at least high school education, injecting heroin, and injecting alone. In addition to the factors associated with filters, users of sterile containers were more likely to be HCV-negative and older. Using sterile water was associated with daily injecting and being HCV-negative. Improving the uptake of sterile drug preparation equipment among IDUs could be aided by considering drug-specific risks, such as drug of choice and injecting context, while reinforcing existing messages on safer injecting. The association between sterile equipment use and HCV-negative status may be representative of an established subgroup of safer injectors who have remained free of infection because of consistent safe injecting practices.</p>
2. Medd, E. A., et al. (2011)	Canada	Cohort	250 street-recruited active crack smokers in Ottawa,	To examine the impact of the availability of safer inhalation materials through Ottawa's SIP on the use of recommended and non-recommended smoking materials. The Ottawa Safe Inhalation Program (SIP) provides harm reduction services to people who inhale drugs to reduce the risk of HIV and HCV infection.	<p><b>"Use of makeshift pipes to smoke crack declines following the distribution of safer inhalation supplies in Ottawa."</b></p> <p>Comparing pre-implementation data with 11-month post-implementation data, the reported use of non-recommended smoking materials declined significantly (<math>p &lt; 0.001</math>), including the use of metal pipes (40 to 11%), car antennae (7 to 1%), pop cans (42 to 15%) and inhalers (44 to 17%). In addition, the use of the recommended glass stems to smoke crack increased from 89 to 93% over the course of the evaluation (<math>p = 0.09</math>). These data demonstrate the utility of a program that distributes safer crack-smoking resources in reducing the use of makeshift devices to smoke crack which are associated with HIV- and HCV-related risk behaviours and practices.</p>
3. Leonard, L., et al. (2008).	Canada	Cross-sectional	Active, street-recruited IDUs who also smoked crack consented to personal interviews and provided saliva	This study aims to evaluate the impact of this initiative on a variety of HCV- and HIV-related risk practices.	<p><b>"I inject less as I have easier access to pipes". Injecting, and sharing of crack-smoking materials, decline as safer crack-smoking resources are distributed."</b></p> <p>Following implementation of the initiative, a significant decrease in injecting was observed. Pre-implementation, 96 percent of IDUs reported injecting in the month prior to the</p>

			samples for HCV and HIV testing at four time points: 6-months pre-implementation (N = 112), 1-month (N = 114), 6-months (N = 157) and 12-months (N = 167) post-implementation.		interview compared with 84 percent in the 1-month, and 78 percent in the 6- and 12-month post-implementation interviews ( $p < .01$ ). Conversely, approximately one-quarter of participants at both the 6- and 12-month post-implementation evaluation points reported that they were smoking crack more frequently since the availability of clean equipment-25 and 29 percent, respectively. In addition to a shift to a less harmful method of drug ingestion, HCV- and HIV-related risks associated with this method were reduced. Among crack-smoking IDUs sharing pipes, the proportion sharing "every time" declined from 37 percent in the 6-month pre-implementation stage, to 31 percent in the 1-month, 12 percent in the 6-month and 13 percent in the 12-month post-implementation stages ( $p < .01$ ). Since distributing safer crack-smoking materials by a NEP contributes to transition to safer methods of drug ingestion and significantly reduces disease-related risk practices, other NEPs should adopt this practice.
4. Moniruzzaman, A., et al. (2010).	Canada	Cohort	133 Aboriginal young who reported using injection drugs	To identify factors associated with using Vancouver's Safe Injection Site (SIS) among young Aboriginal people who use injection drugs over a five-year study period.	<p><b>"The cedar project: longitudinal analysis of accessing Vancouver's safe injection site among young aboriginal people who use injection drugs"</b></p> <p>A total of participants were eligible for inclusion in this analysis, and they contributed 276 observations over the study period. Among them, 95 (71%) had used the SIS; 61% of which were female. In univariate analysis participants who had used the SIS were more likely to inject cocaine, speedballs and opiates daily or more in the previous six months, to have ever been incarcerated, to have ever been paid for sex, to be HCV positive, and less likely to have ever attempted suicide or to be in a relationship in the last six months. In multivariable analysis, SIS users were less likely to have ever attempted suicide (AOR: 0.39, 95%CI: 0.20-0.78) or to be in a relationship in the last six months (AOR: 0.46, 95%CI: 0.24-0.89), and were more likely to inject opiates daily in the last six months (AOR: 2.5, 95%CI: 1.1-5.63) and to have ever been incarcerated (AOR: 2.00, 95%CI: 0.97-4.12). Conclusions: Vancouver's SIS is an important source for harm reduction among young Aboriginal people who use injection drugs. Expanding access to these young people and bringing this strategy to northern communities in British Columbia should be considered.</p>
5. Reddon, H., et al. (2011).	Canada	Cross-sectional	395 HIV-positive injection drug users (IDUs)	The objective of this study was to examine supervised injecting facility (SIF) use among a cohort of 395 HIV-positive injection drug users (IDUs) in Vancouver, Canada.	<p><b>"Use of North America's first medically supervised safer injecting facility among HIV-positive injection drug users"</b></p> <p>The correlates of SIF use were identified using generalized estimating equation analyses. In multivariate analyses, frequent SIF use was associated with homelessness (adjusted odds ratio [AOR] = 1.90), daily heroin injection (AOR = 1.56), and daily cocaine injection (AOR = 1.59). The reasons given for not using the SIF included a preference for injecting at home and already having a safe place to inject. The SIF services most commonly used were needle exchange and nursing services. The SIF appears to have attracted a high-risk subpopulation of HIV-positive IDUs; this coverage perhaps could be extended with the addition of HIV-specific services such as disease monitoring and the provision of antiretroviral therapy.</p>

#### 4.5. Post-exposure prophylaxis

Study	Country	Design	Sample	Objectives	Relevant Findings
1. Landovitz, R. J., et al. (2012).	USA	single-arm, open label pilot study Participants were followed over 3 months for infectious/biologic, behavioural, and drug use outcomes	Methamphetamine-using men who have sex with men. Those who reported a recent high-risk sexual or injection drug exposure to an HIV-infected or serostatus unknown source were initiated on tenofovir/emtricitabine (Truvada)-based PEP.	To demonstrate the safety, feasibility, and acceptability of PEP combined with the drug abstinence intervention of contingency management (CM) in methamphetamine-using MSM. HIV-uninfected MSM reporting recent methamphetamine use were recruited to a CM intervention	<b>"A novel combination HIV prevention strategy: Post-exposure prophylaxis with contingency management for substance abuse treatment among methamphetamine-using men who have sex with men.</b>  Fifty-three participants enrolled in the study; 35 participants (66%) initiated PEP after a high-risk exposure. The median time from exposure to medication administration was 37.8h (range 12.5-68.0h). Twenty-five (71.4%) PEP initiators successfully completed the treatment course. Median medication adherence was 96% (IQR 57-100%), and medication was generally well tolerated. Methamphetamine abstinence during CM treatment increased PEP adherence (2% [95% CI +1-+3%]) per clean urine toxicology sample provided), and increased the odds of PEP course completion (OR 117, 95% CI 1.04-1.31). One incident of HIV seroconversion was observed in a participant who did not complete PEP treatment, and reported multiple subsequent exposures. Findings demonstrate that PEP, when combined with CM, is safe, feasible, and acceptable as an HIV prevention strategy in methamphetamine-using MSM.
2. Landovitz, R. J., et al. (2014).	USA	a prospective, randomized controlled trial of CM with PEP among SU MSM at a single site in Los Angeles, California.	140 MSM individuals were enrolled and randomized to CM (n=70) or a non-contingent control behavioural intervention (n=70)	To assess if contingency Management Facilitates PEP Completion Among Stimulant-Using MSM	<b>"Contingency Management Facilitates PEP Completion Among Stimulant-Using MSM."</b>  45 participants (32%) initiated PEP after a high-risk sexual exposure during the study period, with a mean exposure-to-PEP time of 35.2 hours. 29 of the 45 had evaluable adherence data. PEP course completion was significantly greater in the CM arm compared to the NC arm (AOR 7.2, 95% CI 1.1-47.9), and there was a trend towards improved medication adherence by self-report in the CM arm (AOR 4.33, 95% CI 0.76-21.86). CM participants had a greater probability of stimulant-free urine specimens vs. NC participants (IRR 1.57, 95% CI 1.12-2.22), and a trend towards reduced episodes of UAI (IRR 0.34 [95% CI 0.11-1.08]). One HIV seroconversion was observed in the context of repeat exposures, and is unlikely to represent PEP failure. Conclusions: In a randomized, controlled trial of SU MSM, CM facilitated the use of PEP by increasing rates of course completion, and suggesting a trend toward improved adherence. Reductions in sexual risk afforded by the CM intervention are a prime example of HIV prevention synergy. Despite small numbers of individuals initiating PEP, findings suggest that CM may be a useful support mechanism for the use of PEP, and potentially other biomedical prophylactic strategies in stimulant-using MSM.
3. Oldenburg, C. E., et al. (2015).	USA	Retrospective cohort study	1130 prescriptions among 788 MSM	To assess post-exposure prophylaxis use and recurrent exposure to HIV among men who have sex with men who use crystal methamphetamine	<b>"Post-exposure prophylaxis use and recurrent exposure to HIV among men who have sex with men who use crystal methamphetamine."</b>

					Compared to those who had not used CM, MSM PEP users who used CM more frequently returned for repeat PEP (aOR 5.13, 95% CI 2.82 to 9.34) and were significantly more likely to seroconvert over the follow-up period (aHR 3.61, 95% CI 1.51 to 8.60). MSM who used CM had increased odds of unprotected anal intercourse as the source of exposure (aOR 2.12, 95% CI 1.16 to 3.87) and knowing that their partner was HIV infected (aOR 2.27, 95% CI 1.42 to 3.64). Conclusions: While MSM who use CM may have challenges accessing ART in general, these data highlight the fact that those who were able to access PEP subsequently remained at increased risk of HIV seroconversion. Counseling and/or substance use interventions during the PEP course should be considered for CM-using MSM.
4. Donnell, D., et al. (2010).	USA	Cross-sectional	4,295 MSM we assessed perceptions and use of nPEP over 4 years in six cities across the United States	To assess perceptions and use of nPEP	<p><b>"Use of non-occupational post-exposure prophylaxis does not lead to an increase in high risk sex behaviours in men who have sex with men participating in the EXPLORE trial."</b></p> <p>Overall, 1.9% of MSM reported use of nPEP prior to enrolment, and 6.3% at least once during the trial. Awareness of nPEP was reported by 47.5%, with higher awareness in two sites with funded nPEP programs. Three seroconversions occurred in the 384 visits where nPEP courses were reported, with no effect of nPEP on risk of HIV acquisition in this cohort (hazard ratio = 0.91, 95% confidence interval [0.29, 2.86]). NPEP users were a riskier group: increased odds of nPEP use were observed in association with multiple partners and unprotected receptive and insertive anal sex with HIV infected partners and partners with unknown HIV status. NPEP use was also associated with use of illicit drugs (injection drugs, crack cocaine, hallucinogens, and amphetamines). Importantly, willingness to use nPEP after high risk sex was associated with lower odds of high risk sex. After an episode of nPEP use, nPEP users remained more likely to report high risk sex than those in this cohort who had not previously used nPEP. However, within the subset of people who had previously reported high risk sex, previous nPEP use was not associated with higher odds of high risk sex, thus allaying fears that availability of nPEP would lead to an increase in high risk sex.</p>

#### 4.6. Interventions among Sex Workers

Author, Year	Country	Design	Sample	Objectives	Relevant findings
1. Gaines, T. L., et al. (2015).	Mexico	Cohort	FSW-IDUs	To examine the prevalence and correlates of short-term sex work cessation among female sex workers who inject drugs (FSW-IDUs) and determined whether injection drug use was independently associated with cessation.	<p><b>"Short-term cessation of sex work and injection drug use: Evidence from a recurrent event survival analysis."</b></p> <p>Overall, 55% of participants stopped sex work at least once during follow-up. Controlling for other characteristics and intervention assignment, injection drug use was inversely associated with short-term sex work cessation in both cities. In Ciudad Juarez, women receiving drug treatment during follow-up had a 2-fold increase in the hazard of stopping sex work. In both cities, income from sources other than sex work, police interactions and healthcare access were independently and significantly associated with shorter-term cessation. Conclusions: Short-term sex work cessation was significantly affected by injection drug use. Expanded drug treatment and counseling coupled with supportive services such as relapse prevention, job training, and provision of alternate employment opportunities may promote longer-term cessation among women motivated to leave the sex industry.</p>
2. Shannon, K., et al. (2005).	Canada	Cross-sectional	150 women	To evaluate the needs of women engaged in survival sex work and to assess utilization and acceptance of HAART	<p><b>"Access and utilization of HIV treatment and services among women sex workers in Vancouver's Downtown Eastside."</b></p> <p>High rates of cocaine injection, heroin injection, and smoke-able crack cocaine use reflect the vulnerable and chaotic nature of this population. Although preliminary findings suggest an overall high uptake of health and social services, there was limited attention to HIV care with only 9% of the women on HAART. Self-reported barriers to accessing treatment were largely attributed to misinformation and misconceptions about treatment. Given the acceptability of accessing HAART through community interventions and women specific services, this study highlights the potential to reach this highly marginalized group and provides valuable baseline information on a population that has remained largely outside consistent HIV care.</p>
3. Sherman, S. G., et al. (2006).	USA	Observational intervention study (pre and 3 months post testing)	50 illicit drug-using women who were involved in prostitution	To examine the efficacy of an economic empowerment and HIV prevention intervention targeting illicit drug-using women who were involved in prostitution in Baltimore, Maryland	<p><b>The evaluation of the JEWEL project: An innovative economic enhancement and HIV prevention intervention study targeting drug using women involved in prostitution."</b></p> <p>Participants were 62.0% African American, 5.0% were currently employed, and the median age was 39 years old (Inter Quartile Range [IQR]: 34-45). Women attended an average of six (IQR: 4.5-6.0) sessions. The women sold over \$7,000 worth of jewellery in eleven sales. In comparing self-reported risk behaviours pre and 3-month post intervention participation, we found significant reductions in: receiving drugs or money for sex (100% versus 71.0%, <math>p &lt; 0.0005</math>); the median number of sex trade partners per month (9 versus 3, <math>p = 0.02</math>); daily drug use (76.0% vs. 55.0%, <math>p = 0.003</math>); the amount of money spent on drugs daily (US\$52.57 versus US\$46.71, <math>p = 0.01</math>); and daily crack use (27.3% versus 13.1.0%, <math>p = 0.014</math>). In the presence of other variables in a multivariate linear model, income from the jewellery sale was associated with a reduction in the number of sex trade partners at follow-up. The pilot indicated</p>

					effectiveness of a novel, HIV prevention, economic enhancement intervention upon HIV sexual risk behaviours and drug utilization patterns.
4. Strathdee, S. A., et al. (2013).	Mexico	RCT: randomized factorial trial comparing four brief, single-session conditions combining either an interactive or didactic version of a sexual risk intervention to promote safer sex in the context of drug use, and an injection risk intervention to reduce sharing of needles/injection paraphernalia.	584 FSW-IDUs >18 years reporting sharing injection equipment and unprotected sex with clients within the last month	To evaluate brief combination interventions to simultaneously reduce sexual and injection risks among female sex workers who inject drugs (FSW-IDUs) in Tijuana and Ciudad Juarez.	<p><b>"Reductions in HIV/STI incidence and sharing of injection equipment among female sex workers who inject drugs: results from a randomized controlled trial."</b></p> <p>After 12 months, HIV/STI incidence decreased &gt;50% in the interactive vs. didactic sex intervention (Tijuana: AdjRR:0.38,95% CI:0.16-0.89; Juarez: AdjRR:0.44,95% CI:0.19-0.99). In Juarez, women receiving interactive vs. didactic injection risk interventions decreased receptive needle-sharing by 85% vs. 71%, respectively (p = 0.04); in Tijuana, receptive needle sharing declined by 95%, but was similar in active versus didactic groups. Tijuana women reported significant increases in access to syringes and condoms, but Juarez women did not. INTERPRETATION: After 12 months in both cities, the interactive sexual risk intervention significantly reduced HIV/STI incidence. Expanding free access to sterile syringes coupled with brief, didactic education on safer injection was necessary and sufficient for achieving robust, sustained injection risk reductions in Tijuana. In the absence of expanding syringe access in Juarez, the injection risk intervention achieved significant, albeit more modest reductions, suggesting that community-level interventions incorporating harm reduction are more powerful than individual-level interventions.</p>
5. Wechsberg, W. M., et al. (2006).	South Africa	RCT: randomly assigned to a modified Standard HIV intervention or to a Woman-Focused HIV prevention intervention	93 women who reported recent substance use and sex trading	To describe an HIV prevention intervention designed in the US that was adapted and implemented in South Africa.	<p><b>"Substance use, sexual risk, and violence: HIV prevention intervention with sex workers in Pretoria."</b></p> <p>Participants reported high rates of sexual risk and violence at baseline. At follow-up, findings showed decreases in the proportion of women reporting unprotected sex and the daily use of alcohol and cocaine. Daily alcohol and cocaine use decreased more for women receiving the Woman-Focused intervention. Although violence continued to be a problem, at follow-up Woman-Focused participants reported being victimized less often than women receiving the Standard intervention. This study demonstrates the feasibility of implementing cross-cultural behavioural HIV prevention interventions, and supports the need for future studies of women's contextual issues and the effectiveness of targeted Interventions.</p>

#### 4.7. Interventions to Prevent HCV and HBV

Author, Year	Country	Design	Sample	Objectives	Relevant findings
1. Charlebois, A., et al. (2012).	Canada	retrospective cohort study	129 persons from marginalized populations with high rates of crack cocaine use and mental health comorbidities	To identify the factors associated with antiviral treatment uptake.	<p><b>"Factors associated with HCV antiviral treatment uptake among participants of a community-based HCV programme for marginalized patients."</b></p> <p>Group participation improved access to health care. While 19% had previously seen an HCV specialist prior to group initiation, 59% saw an HCV specialist during the group. Half of the participants were nonimmune to hepatitis A or B at baseline, and 80% of these patients received immunization through the programme. The programme treated 24 patients with PEGylated interferon and ribavirin and achieved a sustained virologic response (SVR) rate of 91% for genotype 2 or 3 and 54% for genotype 1. Stable housing was independently associated with initiation of treatment, and there was a non-significant trend towards lower rates of treatment initiation among women. SVR rates for those who had used crack or injection drugs in the month prior to joining the programme did not differ significantly from those who had abstained.</p>
2. Dieperink, E., et al. (2013).	USA	retrospective cohort study	Patients with stimulant use were compared to patients with no drug use, other drug users and an unknown drug use group	To determine the impact of stimulant use on antiviral treatment for chronic hepatitis C patients in an integrated hepatitis clinic	<p><b>"The effect of stimulant use on antiviral treatment in an integrated hepatitis clinic."</b></p> <p>Over 15% of hepatitis C patients presenting to the clinic were using stimulants. Stimulant users had higher BDI and AUDIT-C scores. They were more likely to be followed by a co-located mental health clinician than other groups and were just as likely to initiate and finish antiviral therapy. Recent stimulant use is common in hepatitis C patients presenting to a hepatitis clinic. Stimulant users were more depressed and used alcohol to a greater degree than nonusers but were as likely to start antiviral therapy. An integrated mental health/medical care approach appears to be effective in addressing this difficult-to-treat population.</p>
3. Hilsden, R. J., et al. (2013).	Canada	RCT: open-label, parallel group trial of immediate vs delayed treatment with peg-IFN alfa-2a plus RBV. The primary end point was sustained virologic response (SVR).	66 participants (immediate treatment, n = 48; delayed treatment, n = 18). with recent injection drug and/or crack cocaine use (prior 3 months).	To investigate the efficacy and safety of directly observed PEGylated interferon (peg-IFN) alfa-2a plus self-administered ribavirin (RBV) for the treatment of hepatitis C virus (HCV) among people with active drug use.	<p><b>"Directly observed PEGylated interferon plus self-administered ribavirin for the treatment of hepatitis C virus infection in people actively using drugs: a randomized controlled trial."</b></p> <p>In a post hoc intent-to-treat analysis of all randomized individuals, the SVR was 65% (95% confidence interval [CI], 49%-78%; 31/48) in those randomized to immediate treatment as compared to 39% (95% CI, 17%-64%; 7/18) in those randomized to delayed treatment (P = .060). Among those who received delayed treatment (12/18), SVR was 58% (7/12). Among 60 participants who received at least 1 dose of study medication, SVR was 63% (95% CI, 50%-75%, n = 38). Recent drug use at baseline (past month) did not impact completion or SVR. Discontinuation due to adverse events occurred in 7%. The HCV reinfection rate was 2.8 per 100 person-years (95% CI, 0.0-14.5 person-years) with 1 reinfection observed among 23 remaining in follow-up post-SVR (median, 1.8 years; range, 0.5-1.8 years). Among people actively using drugs treated with directly observed peg-IFN alfa-2a plus self-administered RBV, SVR is comparable to that seen in clinical trials of non-drug users, and the rate of HCV reinfection is low.</p>

4. Malta, M., et al. (2011).	Brazil	Cross-sectional survey	111 DU with chronic HBV/HCV	To assess Behaviour and major barriers faced by non-injectable drug users with HBV/HCV seeking treatment for hepatitis and drug addiction	<p><b>"Behaviour and major barriers faced by non-injectable drug users with HBV/HCV seeking treatment for hepatitis and drug addiction in Rio de Janeiro, Brazil."</b></p> <p>In the last 6 months, 61.8% of interviewees snorted cocaine, 64.7% at least once a week. Half of the interviewees had a stable partner and 38.3% of those with occasional partners never/almost never using condoms. Addiction treatment seeking was found to be associated with: being white (OR:5.5), high-school degree (OR:8.7), and employment (OR:5.7). Hepatitis treatment seeking was high (80.9%), and access to low-threshold, user-friendly health services was key for treatment seeking behaviours (OR:3.6). Missed opportunities for hepatitis treatment seem to be associated with structural (uneven political/financial support to hepatitis programs) and patient-related barriers (severe addiction and non-adherence). Those most in need were less likely to access treatment, calling for renewed strategies, in order to curb hepatitis among impoverished drug users and their sexual partners.</p>
5. Nyamathi, A., et al. (2013).	USA	Cross-sectional survey (assessed baseline data of a Cohort study)	267 young (18-39 year old) G/B active methamphetamine, cocaine, and crack-using homeless men enrolled in a longitudinal trial.	To assess correlates of knowledge to HIV and HBV infection	<p><b>"Correlates of Hepatitis B Virus and HIV Knowledge Among Gay and Bisexual Homeless Young Adults in Hollywood."</b></p> <p>Regression modelling revealed that previous hepatitis education delivered to G/B men was associated with higher levels of HIV/AIDS and hepatitis knowledge. Moreover, higher HIV/AIDS knowledge was associated with combining sex and drinking alcohol. Associations with hepatitis B knowledge was found among G/B men who were engaging in sex while under the influence of marijuana, who were receiving support from non-drug users, and who had been homeless in the last 4 months. Although being informed about HIV/AIDS and hepatitis did not preclude risky sexual and drug use behaviour, knowledge about the dangers of concurrent sex with substance use is important. As higher levels of knowledge of hepatitis was associated with more moderate drug use, early access to testing and teaching harm reduction strategies remain critical to reduce exposure and infection of HBV and HIV in this population.</p>
6. Ompad, D. C., et al. (2004).	USA	Cohort	1117 street-recruited drug users were enrolled at one of two neighbourhood locations between 2000 and 2004 and completed risk behaviour questionnaires and HBV testing. Free HBV vaccination was offered.	Correlates of vaccine acceptance and completion in two ongoing prospective studies of young injecting and non-injecting drug users in New York City.	<p><b>"Acceptance and completion of hepatitis B vaccination among drug users in New York City."</b></p> <p>Hepatitis B (HBV) vaccination rates remain low among drug users. Among 1117 participants, 26.1% (275) had a previous HBV infection, 57.9% (610) were susceptible to HBV, and 16.0% (169) had serological evidence of previous vaccination. Of the 610 participants susceptible to HBV, 466 (76.4%) returned for their results and were offered vaccination; 53.9% (251) received at least one dose of the vaccine (acceptors). Correlates of vaccine acceptance included older age, public assistance as main income source, and being recruited in the Bronx. Daily crack users were significantly less likely to initiate the vaccine series. Among 240 vaccine acceptors, 98 (40.8%) completed all three doses. Daily injectors, Hispanics, and those recruited in Harlem were less likely to complete the vaccination series. HBV vaccination acceptance among drug users seems likely in programmes that are convenient and offer remuneration; however, extended efforts are needed to improve series completion.</p>

7. Stein, M. D., et al. (2009).	USA	RCT (24 months)	277 participants	To test whether a four-session motivational intervention would reduce hepatitis C virus (HCV) seroincidence among injection and non-injection drug users compared to an assessment-only condition,	<p><b>"A Trial to reduce hepatitis C seroincidence in drug users."</b></p> <p>Of the 15 (5.4%) individuals who seroconverted, all reported injecting drugs either at baseline or during follow-up. Seroconversion rates did not differ significantly by treatment assignment (<math>p = .79</math>). The annual HCV incident rate was 8.20 (95% confidence interval [CI] = 4.76-14.13) for injectors and 0.74 (95% CI = 0.19-2.98) for non-injectors per 100 person-years. Significantly fewer participants in the intervention group initiated injection drug use behaviours (<math>p = .009</math>). This intervention was no more effective at reducing HCV seroconversion than assessment alone but did decrease injection initiation.</p>
8. Stitzer, M. L., et al. (2010).	USA	RCT : Participants met staff weekly for 24 weeks and receive 7 injections containing either the Hepatitis B vaccine or a placebo. All participants received \$10 at each weekly visit.	26 cocaine users involved in a 6-month hepatitis B vaccination series	To examine effects of prize-based incentives on retention and medication adherence	<p><b>"Drug users' adherence to a 6-month vaccination protocol: Effects of motivational incentives."</b></p> <p>Those randomly assigned to the incentive program received additional monetary payments on an escalating schedule for attendance at weekly monitoring and vaccination visits. Group attendance diverged after study week 8 with attendance better sustained in the incentive than control group (group by time interaction, <math>p = .035</math>). Overall percent of weekly sessions attended was 82% for incentive versus 64% for control (<math>p = .139</math>). Receiving all scheduled injections were 77% of incentive versus 46% of control participants (<math>p = .107</math>). A significantly larger percentage (74% versus 51%; <math>p = .016</math>) of injections were received by incentive versus control participants on the originally scheduled day. Results suggest that monetary incentives can successfully motivate drug users to attend sessions regularly and to receive injected medications in a more reliable and timely manner than may be seen under usual care procedures. Thus, incentives may be useful for addressing adherence and allowing participants to reap the full benefits of newly developed medications.</p>
9. Artenie, A. A., et al. (2014).	Canada	A prospective cohort study, HEPCO, was carried out among PWIDs	160 participants	This study aimed to assess the effect of visiting a PCP on HCV incidence among PWIDs attending syringe	<p><b>"Visiting a primary care physician among persons who inject drugs attending syringe exchange programs: Coupling strategies to optimize HCV prevention."</b></p> <p>35% reported visiting a PCP at baseline. 64 seroconverted to HCV (incidence rate: 23.1/100 person-years, [18.0-29.3]). Visiting a PCP was independently associated with a decreased risk of HCV infection (Adjusted Hazard Ratio [AHR] = 0.51, [0.27-0.97]). Other independent predictors of HCV incidence included prescription opioid injection (AHR = 3.07, [1.82-5.16]) and cocaine injection (AHR = 4.19, [1.95-9.02]). Conclusions: Among PWIDs reporting high levels of poly-substance drug use who attend SEPs, visiting a PCP was found to reduce HCV transmission. However, a minority of</p>

				exchange programs (SEP).	participants reported visits to a PCP. These findings underscore the importance of enhancing access to PCP among highly vulnerable PWIDs, as part of a comprehensive HCV prevention approach. (Table Presented).
10. Artenie, A. A., et al. (2013).	Canada	Cohort	268 participants	The purpose of this study was to identify factors that enable or impede access to PCPs among active PWIDs	<p><b>"Primary healthcare access among HCV-negative persons who inject drugs: A missed opportunity for counseling, testing and treatment?"</b></p> <p>Thirty-two percent visited a PCP in the preceding six months. In a multivariate regression model adjusting for age, male gender (Adjusted Odds Ratio (AOR) = 0.426, [0.232-0.927]), and cocaine injection (AOR) = 0.470, [0.265-0.835]) were negatively associated with access to a PCP. Conversely, a monthly income below 1,000\$ (AOR) = 1.871, [1.040-3.364]), attending food banks (AOR) = 2.455, [1.362-4.425]), and reporting contacts with street nurses (AOR) = 3.143, [1.173-8.420]) were positively linked with PCP access. Conclusion: As reported by other groups, findings from this study indicate that male PWIDs and those who report injection cocaine are less likely to access PCPs. Further, results suggest that community-based outreach services may play an important role in linking PWIDs to PCPs.</p>

## Summary of the Findings

There is no single intervention that will effectively prevent or contain HIV epidemics associated with drug use (Ball, Weiler, Beg, & Doupe, 2005). But comprehensive package of interventions to prevent HIV, HCV and HBV infection among stimulant users are needed. This include developing and implementing specific intervention to reduce sex risk behaviour,

### 1. Interventions to reduce sex risk behaviour

Prevention of sexual transmission by implementing structural interventions within the communities is one ways in which infectious diseases can be controlled. A comprehensive review among PWID in resource-rich and resource-constrained countries found a moderate effect of interventions in reducing the sexual risk behaviour (Jarlais & Semaan). The present review identified several studies testing specific interventions to reduce sex risk behaviour among stimulant users. These include interventions to increase condom use, decrease sexual risk behaviour, increase self-sufficiency, uptake voluntary HIV testing and counselling and increase of HIV knowledge. Only randomized control studies were included in this section.

#### *Cocaine-crack cocaine users*

Rotheram-Borus et al. (2010) assessed 'the safety counts program' which was a programme specifically designed to reducing HIV risks among active injection drug and crack users. The study used a quasi-experimental cross-over design where sites were randomized. (Rotheram-Borus, Rhodes, Desmond, & Weiss, 2010). The Program was compared to voluntary HIV counseling and testing. The study found that the 'Safety Counts Program' was an effective intervention to be used among PWID and crack users. The Program reported significant greater reductions in risky sex, crack and hard drug use, and risky drug injection. And also reported a dose-response relationship: the more sessions of Safety Counts attended, the greater were the reductions in risky acts.

Pechansky et al. (2007) used thought mapping and structured stories to decrease HIV risk behaviours among cocaine injectors and crack smokers in the South of Brazil (Pechansky et al., 2007). The study randomized 119 Brazilian cocaine users to either standard or a standard plus "thought mapping" intervention. Changes in AIDS knowledge and risk behaviours. The effect of the thought mapping were not strong as it was less successful in decreasing mean days of cocaine use. But the authors suggest that components of the experimental thought-mapping model might be useful, as Thought Mapping condition showed significant increases in AIDS knowledge and condom use.

Herrmann et al. (2013) conducted a Cross over RCT to test improvement in HIV/AIDS knowledge among cocaine-dependent outpatients using modified materials. The study randomized 90 cocaine-dependent outpatients to an HIV/AIDS educational intervention or to a control condition. The brief intervention proved effective at increasing HIV/AIDS knowledge among cocaine-dependent outpatients when compared to the control intervention.

#### *African American crack cocaine users*

A study among 347 heterosexual African American crack cocaine users living with HIV infection were randomised to either positive choices intervention (PCI) or standard intervention (SI) found similar effects across groups (Williams et al., 2012).

Wechsberg et al. (2010) assessed three HIV intervention among 455 out-of-treatment African American women who smoke crack cocaine in central North Carolina (Wechsberg et al., 2010). The

interventions were: a woman-focused intervention, a modified NIDA intervention, and a delayed-treatment control condition. Women in the woman-focused intervention were more likely to present low levels of HIV risk behaviour at the short term follow-up. However, this difference was not observed at a long term follow-up (4 years after).

#### *Women Focused Interventions*

Wechsberg et al. (2004) assessed the efficacy of a woman-focused intervention to reduce HIV risk and increase self-sufficiency among 620 African American crack abusers (compared to a control group intervention) (Wechsberg, Lam, Zule, & Bobashev, 2004). All groups significantly reduced crack use and high-risk sex at each follow-up, but only woman-focused intervention participants consistently improved employment and housing status. The study concluded that a woman-focused intervention can successfully reduce risk and facilitate employment and housing and may effectively reduce the frequency of unprotected sex in the longer term. A study among 347 heterosexual African American crack cocaine users living with HIV infection were randomised to either positive choices intervention (PCI) or standard intervention (SI) found similar effects across groups (Williams et al., 2012).

Wechsberg et al. (2010) assessed three HIV intervention among 455 out-of-treatment African American women who smoke crack cocaine in central North Carolina (Wechsberg et al., 2010). The interventions were: a woman-focused intervention, a modified NIDA intervention, and a delayed-treatment control condition. Women in the woman-focused intervention were more likely to present low levels of HIV risk behaviour at the short term follow-up. However, this difference was not observed at a long term follow-up (4 years after).

#### *Methamphetamine Users*

Mausbach et al. (2007) tested the efficacy of a behavioural intervention for increasing safer sex behaviours in HIV-negative, heterosexual methamphetamine users (Mausbach, Semple, Strathdee, Zians, & Patterson, 2007a). The study randomized 451 HIV-negative, heterosexual methamphetamine users to (a) a safer sex behavioural intervention (Fast-Lane), (b) the Fast-Lane intervention with boosters, or (c) a time-equivalent diet-and-exercise attention-control condition. The study concluded that behavioural intervention was successful in terms of reducing high-risk sexual behaviours in the context of ongoing methamphetamine use among HIV-negative heterosexuals. The authors argue that reductions in high-risk sexual behaviour were likely because of the impact of the intervention on participants' self-efficacy for negotiating safer sex.

Mausbach et al. (2007) found that it is possible to reduce high risk sexual behaviours in the context of ongoing methamphetamine use among HIV-infected MSM (Mausbach, Semple, Strathdee, Zians, & Patterson, 2007b). The authors reported the results of the EDGE study which aimed to test the efficacy of a behavioural intervention for increasing safer sex behaviours in HIV-positive MSM methamphetamine users. The study randomized 341 HIV-positive, methamphetamine-using MSM to a sex behavioural intervention (EDGE) or a time-equivalent diet-and-exercise attention-control condition safer sex behaviours. Participants in the EDGE intervention engaged in significantly more protected sex acts at follow-ups. The findings also suggest that EDGE participants' self-efficacy demonstrated a greater increase over time compared to control participants.

## 2. Psychosocial Interventions

This section will report on studies which tested psychosocial interventions among stimulant users and which reported on HIV-related outcomes (rates or risk behaviour). The vast majority of the studies included in this sections were conducted in the USA and among methamphetamine users.

### *Contingency Management*

Contingency management is the process of reinforcing behaviour change through positive rewards (normally vouchers, cash or prizes). There is an expectation that the individuals receiving the rewards will increase the frequency of the desired behaviour (decrease drug use or decrease sexual risk behaviours). The present review identified some randomized controlled trials testing contingency management among stimulant users, the majority of them among methamphetamine users.

Menza et al. (2010) assessed contingency management to reduce methamphetamine use and sexual risk among men who have sex with men (Menza et al., 2010). The study randomized 127 MSM to either 12-week a **CM intervention** or to referral to community resources. The study found positive effects on non-concordant UAI declined significantly in both study arms. However, this study did not find a large, sustained effect of CM on methamphetamine use.

Reback and Shoptaw (2014) developed an evidence-based, gay-specific cognitive behavioural therapy intervention for methamphetamine-abusing gay and bisexual men (Reback & Shoptaw, 2014). The Gay-specific, cognitive behavioural therapy (GCBT) was combined with a **low-cost contingency management** and compared to the original GCBT intervention. The findings indicated that the original GCBT produced superior short-term beneficial drug use outcomes. But sexual behaviour changes superior in the GCBT + CM.

Shoptaw et al. (2005) tested behavioural treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviours among urban gay and bisexual men (Shoptaw et al., 2005). The study randomized 162 Methamphetamine-dependent gay and bisexual men to four treatment conditions for 16 weeks: **standard cognitive behavioural therapy** (CBT, n = 40), **contingency management** (CM, n = 42), **combined cognitive behavioural therapy and contingency management** (CBT + CM, n = 40), and a **culturally tailored cognitive behavioural therapy** (GCBT, n = 40). The study found that drug abuse treatments produced significant reductions in methamphetamine use and sexual risk behaviours. Results revealed that CM and CBT + CM conditions to perform better than standard CBT. Results showed GCBT significantly reduced unprotected receptive anal intercourse (URAI) during the first 4 weeks of treatment. During treatment between-group differences disappeared at follow-up with overall reductions in outcomes sustained to 1-year.

McDonnell et al. (2013) conducted an RCT of contingency management for stimulant use in community mental health patients with serious mental illness (McDonnell et al., 2013). The study randomized 176 outpatients with serious mental illness and stimulant dependence to **3 months of contingency management plus usual treatment** or to treatment as usual. Participants in the contingency management condition were significantly less likely to complete the treatment. But they were they were 2.4 times more likely to submit a stimulant-negative urine test during treatment. The CM group also had significantly lower levels of alcohol use, injection drug use, and psychiatric symptoms and were one-fifth as likely as those assigned to the control condition to be admitted for psychiatric hospitalization during treatment. They also reported significantly fewer days of stimulant drug use during the 3-month follow-up. No group differences were observed in HIV-risk associated sexual behaviour. Participants assigned to the contingent group were 3.3 times less likely to report engaging in injection drug use, relative to non-contingent participants, during treatment.

### *Other Psychosocial Interventions*

Other psychosocial interventions, such as Cognitive Behaviour Therapy (CBT), Motivational Interviewing and specific behavioural interventions have also been tested among stimulant users. The present review identified the following studies which reported HIV-related outcomes:

Rawson et al. (2008) conducted a secondary analysis of an RCT which randomised 784 methamphetamine-dependent users to either **standardized psychosocial protocol** or to treatment-as-usual HIV-related risk behaviour (Rawson et al., 2008). Results indicated that HIV risk behaviours substantially decreased over time. Treatment retention and completion and frequency of MA use were both positively associated with increased reduction of HIV risk behaviours.

Sherman et al. (2009) evaluated a peer network intervention trial among young methamphetamine users in Chiang Mai, Thailand (Sherman et al., 2009). The study randomized 983 young methamphetamine users to either a **peer educator, network-oriented intervention** or to 'a best practice, life-skills curriculum'. The study found that a peer educator, network-oriented intervention was associated with reductions in methamphetamine use, increases in condom use, and reductions in incident STIs over 12 months.

Parsons et al. (2014) tested motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men (Parsons, Lelutiu-Weinberger, Botsko, & Golub, 2014). The study randomized 143 non-treatment-seeking HIV-negative young gay and bisexual men to either **brief motivational interviewing (MI)** compared with a content-matched education condition. Participants reported significant reductions in UAI and substance use over time in both conditions. However, participants in the MI condition were 18% less likely to use drugs and 24% less likely to engage in UAI than the participants in the education condition. The study concluded that the results support the utility of MI, compared with a content-matched education condition, to significantly reduce both UAI and drug use among young gay and bisexual men.

Shoptaw, et al. (2008) assessed two tailored behavioural treatments for substance abuse in urban gay and bisexual men (Shoptaw et al., 2008). The study randomized 128 stimulant-abusing gay and bisexual to either a 16 weeks of a **gay-specific cognitive-behavioural therapy** (GCBT, n = 64) or to a gay-specific social support therapy (GSST; n = 64). No overall statistically significant differences were observed between conditions along retention, substance use, or HIV-related sexual risk behaviours. Among methamphetamine-using participants, the GCBT condition showed significant effects over GSST for reducing and sustaining reductions of methamphetamine.

Baker et al. (2005) tested a **brief cognitive behavioural interventions** for regular amphetamine users in Australia (Baker et al., 2005). The study randomized 214 regular amphetamine users to either a brief interventions consisting of motivational interviewing and cognitive-behaviour therapy (CBT) compared to control condition. The study found no intervention effects on HIV risk-taking.

### 3. HAART Adherence

Highly Active Antiretroviral Therapy is a combination of three drugs which suppress viral replication. This treatment became available in the mid-90s and helped decrease the mortality associated with HIV/AIDS. For this treatment to have its full effect, patients need to adhere adequately to the treatment regime. People who use drugs have reduced access to HAART, start treatment late and might have more difficulty adhering to treatment when compared to people who do not use drugs (Frederick L. Altice, Kamarulzaman, Soriano, Schechter, & Friedland). However several studies have supported HAART effectiveness among drug users, demonstrating that they can adhere to treatment and that treatment can be as effective as among people who do not use drugs (Monica Malta, Magnanini, Strathdee, & Bastos, 2008; Wood, Hogg, Lima, & et al., 2008). A recent systematic review of HAART Adherence Interventions for HIV-Infected drug users concluded that more evidence was required on the use of cognitive behavioural therapy, motivational interviewing, peer-driven interventions and the integration of MAT into HIV clinical care (Binford, Kahana, & Altice, 2012). The present review identified the following studies looking at HAART adherence among stimulant users.

#### *Assessing Antiretroviral Utilisation*

Doshi et al. (2012) conducted Project HOPE in Atlanta and Miami where 350 hospitalized HIV-infected crack cocaine users were interviewed to assess antiretroviral utilization (Doshi et al., 2012). The study identified that for HIV-infected crack cocaine users structural factors may be as important as individual and interpersonal factors in facilitating ART utilization. Being homeless was negatively associated with ART use. Few HIV(+) crack cocaine users had viral suppression, but among those on ART, viral suppression was achievable.

Atkinson et al. (2008) explored path model of schedule adherence among 130 African-American HIV-positive crack cocaine users on highly active antiretroviral therapy (Atkinson, Schonnesson, Williams, & Timpson, 2008). The study found that the effects of psychological distress on schedule adherence were mediated by patients' relationship with their doctor and optimism towards antiretroviral treatment. Adherence was also associated with patients' self-efficacy regarding their medical regimen which, in turn, was associated with their social support.

Crisp et al. (2004) conducted a cross-sectional survey among **African-American crack cocaine smokers** to assess medication compliance and satisfaction with treatment for HIV disease (Crisp, Williams, Timpson, & Ross, 2004). The study found that the majority of African-American crack cocaine users are able to comply with HIV treatment regimes, with more than half (53%) claiming full compliance for one or more medications, and a further one third (31%) claiming compliance more than half the time.

Carrico et al. (2007) conducted a study among 858 HIV-positive participants self-reporting risk of transmitting HIV to assess the associations among affect regulation, substance use, non-adherence to anti-retroviral therapy (ART), and immune status (Carrico et al., 2007). **Among individuals on ART, regular stimulant users had a five-fold higher HIV viral load than those who denied regular stimulant use. Regular stimulant users, in turn, were more than twice as likely to be non-adherent to ART. Even after accounting for the effects of non-adherence and CD4+ counts, regular stimulant use was independently associated with 50% higher HIV viral load.**

Shoptaw, et al. (2012) examined associations between stimulant use (methamphetamine and cocaine) and other substances (nicotine, marijuana, alcohol and inhaled nitrites) with immune function biomarkers among HIV-seropositive (HIV) men taking ART and HIV-seronegative men in the Multicenter AIDS Cohort Study (Shoptaw et al., 2012). Among HIV men, cumulative adherence to ART,

and recent cohort enrolment were associated with increase in CD4+/CD8+ ratios. Cumulative use of methamphetamine, and cocaine showed small negative associations with CD4+/CD8+ ratios. The authors concluded that ART adherence is associated with a positive immune function independent of stimulant use.

Smit et al (2006) conducted a prospective cohort study in the Netherlands to assess sexual risk and injecting behaviour among HIV-infected drug users receiving HAART (Smit et al., 2006). The study matched 67 HIV-infected drug users on HAART with 130 drug users not starting HAART. The study found that drug users who were treated with HAART did not increase their risk behaviour, and their early response to HAART is similar to homosexual men. However, before the treated drug users received HAART they were seen to inject less often than those not treated with HAART. This suggests that selection of potential HAART starters might be based on limited drug use. The authors concluded that HIV-infected drug users, although they seem to be a selected group, they can be treated effectively.

Kuyper et al. (2011) evaluated whether ART initiation was associated with changes in syringe lending patterns among a long-term prospective cohort of 380 HIV-positive IDU (Kuyper et al., 2011). Syringe lending was not significantly associated with ART initiation. Concerns regarding increased injection risk behaviours following the initiation of ART were not observed in this setting.

Sharpe et al. (2004) conducted a prospective cohort study among 1655 **HIV-infected women** to ascertain if Black women reported crack use more than other HIV-infected women (Sharpe, Lee, Nakashima, Elam-Evans, & Fleming, 2004). The study found crack users and users of other drugs were less likely than non-users to take their ART medicines exactly as prescribed.

Batista et al. (2014) conducted a cross-sectional survey in Brazil among people living with HIV/AIDS who attended two referral centres in the city of Recife, in Northeastern Brazil (Batista et al., 2014). The study aimed to estimate the prevalence of self-reported irregular use of antiretroviral. A quarter of the sample reported irregular use of combination antiretroviral therapy (cART). Irregular use of cART was associated with crack cocaine users (OR = 2.79, 95%-CI: 1.24-6.32).

### *Improving HAART Adherence*

Ingersoll et al. (2011) conducted a pilot RCT to test the feasibility and efficacy of two interventions based on the **Information-Motivation-Behavioural Skill model to improve HAART adherence and reduce crack cocaine problems** (Ingersoll et al., 2011). Participants were **54 crack cocaine users and HIV-positive** with <90% HAART adherence. The interventions included 6 sessions of Motivational Interviewing plus feedback and skills building, or video information plus debriefing during 8 weeks. The study found significant increases in adherence and reductions in drug use occurred in both conditions by 3 months and were maintained at 6 months. The study concluded that counseling and a video intervention both improved adherence and drug problems durably among people with crack cocaine use and poor adherence in this pilot study.

Altice et al. (2007) conducted an RCT in which patients were randomized to receive received 88 were randomized to receive **directly administered antiretroviral therapy (DAART)** (supervised therapy 5 days per week from workers in a mobile health care van) and 53 were randomized to receive self-administered therapy (F. L. Altice, Maru, Bruce, Springer, & Friedland, 2007). At the end of 6 months, a significantly greater proportion of the DAART group achieved the primary outcome (reduction in HIV-1 RNA level of  $>1.0 \log_{10}$  copies/mL or an HIV-1 RNA level  $<400$  copies/mL). Patients receiving DAART demonstrated a significantly greater mean reduction in HIV-1 RNA level and mean increase in CD4<sup>+</sup> T lymphocyte count.

#### 4. Harm Reduction Interventions

Harm reduction interventions have also been essential in the prevention of HIV transmission, but they have usually been designed and delivered among opioid using populations. The present review identified five Canadian studies assessing harm reduction interventions to prevent HIV, HCV and HBV infection among predominantly stimulant users groups. The studies were on use of safe injection equipment, safe injecting facilities and the effect of crack pipe distribution (on decreasing non-recommended smoking materials and decreasing injecting). Please see a brief description of these studies below:

##### *Use of sterile drug injection equipment*

Morissette et al. (2007) conducted a survey among 275 IDUs in Montreal, a predominantly cocaine injecting population, to identify factors associated with using sterile drug injection equipment (Morissette et al., 2007). Sterile syringes, containers, filters, and water were used for at least half of injecting episodes. Users drug injection equipment were older, more educated, more likely to be HCV-negative and daily injectors.

Moniruzzaman, et al. (2010) followed 133 aboriginal young IDU to identify factors associated with using Vancouver's Safe Injection Site (SIS) over a five-year study period (Moniruzzaman et al., 2010). The study found that over two-thirds of the sample had used the SIS. Participants who had used the SIS were more likely to inject daily or more in the previous six months, to have ever been incarcerated, to have ever been paid for sex, to be HCV positive.

Reddon et al (2011) assessed 395 HIV-positive injection drug users to examine supervised injecting facility (SIF) in Vancouver, Canada (Reddon et al., 2011). The study found that frequent SIF use was associated with homelessness, daily injecting. The reasons given for not using the SIF included a preference for injecting at home and already having a safe place to inject.

##### *Use of safe inhalation materials*

Medd et al (2011) assessed 250 street-recruited active crack smokers in Ottawa to examine the impact of the availability of safer inhalation materials (Medd et al., 2011). The Ottawa Safe Inhalation Program (SIP) provides harm reduction services to people who inhale drugs to reduce the risk of HIV and HCV infection. The study found that comparing pre-implementation, the use of non-recommended smoking materials declined significantly, including the use of metal pipes, car antennae, pop cans and inhalers. In addition, the use of the recommended glass stems to smoke crack increased from 89 to 93% over the course of the evaluation.

Leonard et al (2008) recruited active, street-recruited IDUs who smoked crack to evaluate the impact of safer crack-smoking resources distribution on a variety of HCV- and HIV-related risk practices (Leonard et al., 2008). Following implementation of the initiative, a significant decrease in injecting was observed. Approximately one-quarter of participants at post-implementation evaluation points reported that they were smoking crack more frequently since the availability of clean equipment. In addition to a shift to a less harmful method of drug ingestion, HCV- and HIV-related risks associated with this method were reduced. Among crack-smoking IDUs sharing pipes, the proportion sharing "every time" declined.

## 5. Post-exposure prophylaxis

Post-exposure prophylaxis (PEP) consists of using antiretroviral therapy (ART) in a preventive capacity. Individuals exposed to HIV take 28 days of ART, which should be initiated immediately after exposure to HIV. Medication adherence and completion of the treatment course are also fundamental for PEP effectiveness. The present review identified four American studies on PEP among stimulant user.

Donnell et al (2010) assessed perceptions and use of PEP among 4,295 MSM over 4 years in six cities across the United States (Donnell et al., 2010). Nearly half of the sample were aware of PEP. About 2% of MSM reported use of PEP prior to enrolment in the study, and 6.3% at least once during the study. Three seroconversions occurred in the 384 visits where PEP courses were reported. This study found that PEP users were a riskier group: increased odds of PEP use were observed in association with sexual risk behaviour and illicit drugs. But willingness to use PEP after high risk sex was associated with lower odds of high risk sex. After an episode of PEP use, PEP users remained more likely to report high risk sex than those in this cohort who had not previously used PEP. However, within the subset of people who had previously reported high risk sex, previous PEP use was not associated with higher odds of high risk sex. Therefore, availability of PEP did not lead to an increase in high risk sex.

A recent retrospective study by Oldenburg et al (2015) assessed PEP use and recurrent exposure to HIV among MSM who use crystal methamphetamine (Oldenburg, Jain, Mayer, & Mimiaga, 2015). The authors analysed 1130 PEP prescriptions among 788 MSM and found that compared to those who had not used crystal methamphetamine, MSM PEP users who used crystal more frequently returned for repeat PEP and were significantly more likely to seroconvert over the follow-up period. MSM who used crystal had increased odds of unprotected anal intercourse as the source of exposure and knowing that their partner was HIV infected. The study concluded that counseling and substance use interventions during the PEP course should be considered for MSM who use crystal meth.

Contingency Management can be used to increase PEP adherence and completion. A study published by Landovitz et al (2012) followed 35 methamphetamine- using MSM who initiated PEP after a high-risk exposure (Landovitz et al., 2012). Over two-thirds of PEP initiators completed the treatment course and median medication adherence was 96% (IQR 57-100%) (Landovitz et al., 2012). This study found that Methamphetamine abstinence during CM treatment increased PEP adherence and increased the odds of PEP course completion. The study concluded that PEP, when combined with CM, is safe, feasible, and acceptable as an HIV prevention strategy in methamphetamine-using MSM. These same authors conducted an RCT of CM with PEP among 140 stimulant-using MSM. Individuals were randomized to CM or a non-contingent control behavioural intervention (Landovitz, Fletcher, Shoptaw, & Reback, 2014). About a third of the participants initiated PEP after a high-risk sexual exposure. This study found that CM facilitated the use of PEP by increasing rates of course completion, and suggesting a trend toward improved adherence. Reductions in drug use and sexual risk behaviour were also observed in the CM group.

## 6. Interventions among Sex Workers

Sex workers are particularly vulnerable and at risk of acquiring and transmitting HIV. The present review identified five studies assessing interventions among sex workers who used stimulant drugs. Few studies were identified among this population.

Gaines et al. (2015) used survival analysis to assess the effects of short-term cessation of sex work and injection drug use in Mexico (Gaines et al., 2015). The study found that over half of the sample stopped sex work at least once during follow-up. Injection drug use was inversely associated with short-term sex work cessation and women receiving drug treatment during follow-up had a 2-fold increase in the hazard of stopping sex work. Income from sources other than sex work, police interactions and healthcare access were independently and significantly associated with shorter-term cessation. The study concluded short-term sex work cessation was significantly affected by injection drug use.

Shannon et al. (2005) conducted a cross-sectional survey among 150 women engaged in survival sex work to assess utilization and acceptance of HAART (Shannon, Bright, Duddy, & Tyndall, 2005). The study identified high rates of cocaine injection, heroin injection, and smokeable crack cocaine use, but only 9% of the women were on HAART. Self-reported barriers to accessing treatment were attributed to misinformation and misconceptions about treatment.

Sherman et al. (2006) conducted an intervention study (pre and 3 months post testing) among 50 illicit drug-using women who were involved in prostitution (Sherman, German, Cheng, Marks, & Bailey-Kloche, 2006). The intervention was comprised of six 2-hour sessions that taught HIV prevention risk reduction and the making, marketing and selling of jewellery. The study aimed to examine the efficacy of an economic empowerment and HIV prevention intervention targeting illicit drug-using women who were involved in prostitution. The results showed that in comparing self-reported risk behaviours pre and 3-month post intervention participation, a significant reduction was identified in receiving drugs or money for sex, in the median number of sex trade partners per month, in daily drug use, in the amount of money spent on drugs daily and in daily crack use. Income from the jewellery sale was associated with a reduction in the number of sex trade partners at follow-up.

Strathdee et al. (2013) conducted a randomized factorial trial comparing four brief, single-session conditions combining either an interactive or didactic version of a sexual risk intervention to promote safer sex in the context of drug use, and an injection risk intervention to reduce sharing of needles/injection paraphernalia among 584 FSW-IDUs (Strathdee et al., 2013). After 12 months in both cities, the interactive sexual risk intervention significantly reduced HIV/STI incidence. Expanding free access to sterile syringes coupled with brief, didactic education on safer injection was necessary and sufficient for achieving robust, sustained injection risk reductions in Tijuana. In the absence of expanding syringe access in Juarez, the injection risk intervention achieved significant, albeit more modest reductions, suggesting that community-level interventions incorporating harm reduction are more powerful than individual-level interventions.

Wechsberg et al. (2006) conducted an RCT in South Africa where 93 women who reported recent substance use and sex trading were randomly assigned to a modified Standard HIV intervention or to a Woman-Focused HIV prevention intervention (Wechsberg, Luseno, Lam, Parry, & Morojele, 2006). Participants reported high rates of sexual risk and violence at baseline. At follow-up, findings showed decreases in the proportion of women reporting unprotected sex and the daily use of alcohol and cocaine. Daily alcohol and cocaine use decreased more for women receiving the Woman-Focused intervention.

## 7. Interventions to Prevent HCV and HBV

The present review also includes studies looking at HCV and HBV prevention and treatment.

### *HCV Prevention/Treatment*

Charlebois et al. (2012) identified factors associated with HCV antiviral treatment uptake among 129 for marginalized patients of a community-based HCV programme in Canada (Charlebois, Lee, Cooper, Mason, & Powis, 2012). Most participants had not previously seen an HCV specialist and most of them were nonimmune to hepatitis A or B prior to group initiation. The vast majority (80%) received immunization during the programme. The programme treated 24 patients. Stable housing was independently associated with initiation of treatment. SVR rates for those who had used crack or injection drugs in the month prior to joining the programme did not differ significantly from those who had abstained.

Dieperink et al. (2013) conducted a retrospective cohort study to determine the impact of stimulant use on antiviral treatment for chronic hepatitis C patients in an integrated hepatitis clinic (Dieperink, Knott, Thuras, & Pocha, 2013). Patients with stimulant use were compared to patients with no drug use, other drug users and an unknown drug use group. Over 15% of hepatitis C patients presenting to the clinic were using stimulants. Stimulant users had higher BDI and AUDIT-C scores. They just as likely to initiate and finish antiviral therapy.

Hilsden et al. (2013) conducted an open-label, parallel group trial of immediate vs delayed treatment with peg-IFN alfa-2a plus RBV to investigate the efficacy and safety of directly observed PEGylated interferon (peg-IFN) alfa-2a plus self-administered ribavirin (RBV) for the treatment of hepatitis C virus (HCV) among people with active drug use (Hilsden, Macphail, Grebely, Conway, & Lee, 2013). The SVR was 65% in those randomized to immediate treatment as compared to 39% in those randomized to delayed treatment ( $P = .060$ ). Among those who received delayed treatment (12/18), SVR was 58% (7/12). Among 60 participants who received at least 1 dose of study medication, SVR was 63%. Recent drug use at baseline (past month) did not impact completion or SVR. Discontinuation due to adverse events occurred in 7%. The HCV reinfection rate was 2.8 per 100 person-years (95% CI, 0.0-14.5 person-years) with 1 reinfection observed among 23 remaining in follow-up post-SVR (median, 1.8 years; range, 0.5-1.8 years). The authors concluded that among people actively using drugs treated with directly observed peg-IFN alfa-2a plus self-administered RBV, SVR is comparable to that seen in clinical trials of non-drug users, and the rate of HCV reinfection is low.

Malta et al. (2011) conducted a cross-sectional survey among 111 drug users with chronic HBV/HCV to assess behaviour and major barriers faced by non-injectable drug users with HBV/HCV seeking treatment for hepatitis and drug addiction in Rio de Janeiro, Brazil (M. Malta et al., 2011). In the last 6 months, 61.8% of interviewees snorted cocaine, 64.7% at least once a week. Half of the interviewees had a stable partner and 38.3% of those with occasional partners never/almost never using condoms. Hepatitis treatment seeking was high (80.9%), and access to low-threshold, user-friendly health services was key for treatment seeking behaviours (OR:3.6). Missed opportunities for hepatitis treatment seem to be associated with structural (uneven political/financial support to hepatitis programs) and patient-related barriers (severe addiction and non-adherence). Those most in need were less likely to access treatment, calling for renewed strategies, in order to curb hepatitis among impoverished drug users and their sexual partners.

Stein et al. (2009) test whether a four-session motivational intervention would reduce hepatitis C virus (HCV) seroincidence among 277 injection and non-injection drug users compared to an assessment-only condition (Stein, Herman, & Anderson, 2009). Of the 15 (5.4%) individuals who seroconverted, all reported injecting drugs either at baseline or during follow-up. Seroconversion rates did not differ significantly by treatment assignment. The annual HCV incident rate was 8.20 (95% confidence interval [CI] = 4.76-14.13) for injectors and 0.74 (95% CI = 0.19-2.98) for non-injectors per 100 person-years. Significantly fewer participants in the intervention group initiated injection drug use behaviours ( $p = .009$ ). This intervention was no more effective at reducing HCV seroconversion than assessment alone but did decrease injection initiation.

### *HBV Prevention / Treatment*

Nyamathi, A., et al. (2013) conducted a survey to assess correlates of knowledge to HIV and HBV infection. The study found that previous hepatitis education delivered to G/B men was associated with higher levels of HIV/AIDS and hepatitis knowledge. Higher HIV/AIDS knowledge was associated with combining sex and drinking alcohol. Associations with hepatitis B knowledge was found among G/B men who were engaging in sex while under the influence of marijuana, who were receiving support from non-drug users, and who had been homeless in the last 4 months. Although being informed about HIV/AIDS and hepatitis did not preclude risky sexual and drug use behaviour, knowledge about the dangers of concurrent sex with substance use is important. As higher levels of knowledge of hepatitis was associated with more moderate drug use, early access to testing and teaching harm reduction strategies remain critical to reduce exposure and infection of HBV and HIV in this population.

Ompad et al. (2004) cohort study of 1,117 street-recruited drug users were enrolled at one of two neighbourhood locations in New York City between 2000 and 2004 and completed risk behaviour questionnaires and HBV testing. Free HBV vaccination was offered. The study aimed to assess correlates of vaccine acceptance and completion in two ongoing prospective studies of young injecting and non-injecting drug users in New York City. Hepatitis B (HBV) vaccination rates remain low among drug users. About a quarter of the participants had a previous HBV infection, and over half were susceptible to HBV, and 16.0% had serological evidence of previous vaccination. Of the 610 participants susceptible to HBV, about two thirds returned for their results and were offered vaccination; over half received at least one dose of the vaccine (acceptors). Correlates of vaccine acceptance included older age, public assistance as main income source, and being recruited in the Bronx. Daily crack users were significantly less likely to initiate the vaccine series. Among 240 vaccine acceptors, 98 (40.8%) completed all three doses. Daily injectors, Hispanics, and those recruited in Harlem were less likely to complete the vaccination series. HBV vaccination acceptance among drug users seems likely in programmes that are convenient and offer remuneration; however, extended efforts are needed to improve series completion.

Stitzer, M. L., et al. (2010) conducted an RCT where participants met staff weekly for 24 weeks and receive 7 injections containing either the Hepatitis B vaccine or a placebo. The study aimed to examine effects of prize-based incentives on retention and medication adherence. Those randomly assigned to the incentive program received additional monetary payments on an escalating schedule for attendance at weekly monitoring and vaccination visits. Group attendance diverged after study week 8 with attendance better sustained in the incentive than control group (group by time interaction,  $p = .035$ ). Overall percent of weekly sessions attended was 82% for incentive versus 64% for control ( $p = .139$ ). Receiving all scheduled injections were 77% of incentive versus 46% of control participants ( $p = .107$ ). A significantly larger percentage (74% versus 51%;  $p = .016$ ) of injections were received by incentive versus control participants on the originally scheduled day. Results suggest that monetary incentives can successfully motivate drug users to attend sessions regularly and to receive injected

medications in a more reliable and timely manner than may be seen under usual care procedures. Thus, incentives may be useful for addressing adherence and allowing participants to reap the full benefits of newly developed medications.

Artenie et al. (2014) conducted a prospective cohort study in Canada aimed to assess the effect of visiting a primary care physician (PCP) on HCV incidence among PWIDs attending syringe exchange programs (SEP). 35% reported visiting a PCP at baseline. 64 seroconverted to HCV (incidence rate: 23.1/100 person-years, [18.0-29.3]). Visiting a PCP was independently associated with a decreased risk of HCV infection (Adjusted Hazard Ratio [AHR] = 0.51, [0.27-0.97]). Other independent predictors of HCV incidence included prescription opioid injection and cocaine injection. Among PWIDs reporting high levels of poly-substance drug use who attend SEPs, visiting a PCP was found to reduce HCV transmission. However, a minority of participants reported visits to a PCP. These findings underscore the importance of enhancing access to PCP among highly vulnerable PWIDs, as part of a comprehensive HCV prevention approach.

Artenie et al. (2013) conducted a prospective cohort study in Canada among 268 participants. The purpose of this study was to identify factors that enable or impede access to PCPs among active PWIDs. Thirty-two percent visited a PCP in the preceding six months. In a multivariate regression model adjusting for age, male gender (Adjusted Odds Ratio (AOR) = 0.426, [0.232-0.927]), and cocaine injection (AOR) = 0.470, [0.265-0.835]) were negatively associated with access to a PCP. Conversely, a monthly income below 1,000\$ (AOR) = 1.871, [1.040-3.364]), attending food banks (AOR) = 2.455, [1.362-4.425]), and reporting contacts with street nurses (AOR) = 3.143, [1.173-8.420]) were positively linked with PCP access. Conclusion: As reported by other groups, findings from this study indicate that male PWIDs and those who report injection cocaine are less likely to access PCPs. Further, results suggest that community-based outreach services may play an important role in linking PWIDs to PCPs.

## Appendix 1: List of Index Terms

Broad terms	c or Specific terms
Stimulant?	central nervous system stimulant?, CNS stimulant?, stimulant drug?, central nervous system agent?
Crack-cocaine	cocain, cocaine, crack (drug), crack cocaine, cocaine hydrochloride, base cocaine,
Amphetamine?	amphetamine-type, meta-amphetamine?
Ecstasy	MDMA
Crystal methamphetamine	crystalline methamphetamine, meth, crystal, crystal meth,
New psychoactive substances	synthetic cathinones, cathinones, ketamine, piperazines, phenethylamines, kratom, BZP, methcathinone, 4-methylmethcathinone, mephedrone,
Methylphenidate	Methylamphetamine
Other stimulants	kath, paramethoxyamphetamine, fenetylline, ephedrine, pseudoephedrine, dexamphetamine, dextroamphetamine, mixed amphetamine salts, dextromethamphetamine, lisdexamfetamine, ampakines, phenmetrazine, xanthines, amfepramone, diethylpropion, phentermine, fenfluramine-phentermine, aka fen-phen, phenylpropanolamine
Route of administration	non-injecting drug users, IDUs, injecting drug users, injectors, smokers
Human immunodeficiency virus	HIV, aids associated virus, aids related virus, AIDS virus, Human immunodeficiency virus, Human immunodeficiency virus 1 [+NT], Human immunodeficiency virus 2 [+NT], seroprevalence, HIV Seropositivity
Viral hepatitis	HCV, Hepatitis C virus type 1, Hepatitis C virus 1, Hepatitis C virus, Hepatitis C virus subtype 1a, Hepatitis C virus subtype 1b, HBV, Hepatitis virus B, human hepatitis B virus, hepatitis virus,
Sexually transmitted diseases	sexually transmitted infections, blood-borne viruses, viral disorders, immunologic disorders
Transmission	acquisition, risk, disease transmission, risk behaviour, condom use, multiple sexual partners, providing sex in exchange for money or drugs, men who have sex with men, MSM, sex workers, SW, Homosexuality (Male), sexual behaviour, needle sharing
Association	prevalence, incidence, incidence rate, rate, epidemiological data, epidemiology, correlation, relation, odds ratio, risk factor?, prospective, retrospective, case-report?, cross-sectional, case-control, anecdotal, report?
Treatment	intervention, reduction, patient care, adherence to treatment, compliance to therapy, compliance to treatment, therapy
Prevention	control, primary prevention, prevention study, prevention trial, prevention, disease
Randomized controlled trial	controlled trial, clinical trial, systematic literature review, meta-analysis, randomized, trial, pragmatic clinical trial, pragmatic clinical trials, randomised controlled study, randomised controlled trial, RCT, controlled clinical trial, evidence based medicine

## Appendix 1: Electronic Searches

### MEDLINE SEARCH – Using Map Search to Subject Heading

#	Searches	Results
1	*Central Nervous System Stimulants/	11188
2	limit 1 to humans-	6930
3	Crack-cocaine.mp. or *Cocaine/ or *Crack Cocaine/	16718
4	limit 3 to humans-	8210
5	*Amphetamine-Related Disorders/ or *Amphetamine/ or Amphetamine.mp.	24739
6	limit 5 to humans	9678
7	Ecstasy.mp.	2849
8	limit 7 to humans	2211
9	*Methamphetamine/ or *Substance Abuse, Intravenous/ or Crystal methamphetamine.mp. or *Central Nervous System Stimulants/ or *Amphetamine-Related Disorders/	23810
10	limit 9 to humans	17225
11	*Designer Drugs/ or New psychoactive substances.mp.	784
12	limit 11 to humans	622
13	Methylphenidate.mp. or *Methylphenidate/	6813
14	limit 13 to humans	5359
15	Human immunodeficiency virus.mp. or *HIV/	82275
16	limit 15 to humans	73451
17	*Hepatitis B/ or *Hepatitis C/ or *Hepatitis, Viral, Human/ or *Hepatitis C, Chronic/ or *Hepatitis B, Chronic/	78206
18	limit 17 to humans	76668
19	*Sexually Transmitted Diseases/cl, co, cn, di, dt, ed, ep, et, mo, nu, pc, px, rh, sn, th, tm [Classification, Complications, Congenital, Diagnosis, Drug Therapy, Education, Epidemiology, Etiology, Mortality, Nursing, Prevention & Control, Psychology, Rehabilitation, Statistics & Numerical Data, Therapy, Transmission]	11106
20	limit 19 to humans	10050
21	*Disease Transmission, Infectious/pc, sn [Prevention & Control, Statistics & Numerical Data]	1337
22	limit 21 to humans	1273
23	risk behaviour.mp. or *Risk-Taking/	11648
24	limit 23 to humans	11342
25	*Sexual Behaviour/bl, cl, di, ed, px, sn, th [Blood, Classification, Diagnosis, Education, Psychology, Statistics & Numerical Data, Therapy]	6201
26	limit 25 to humans	5900
27	Needle Sharing/ or *Injections, Intravenous/	3752
28	limit 27 to humans	2266
29	2 or 4 or 6 or 8 or 10 or 12 or 14	36454
30	16 or 18 or 20	156441
31	29 and 30	2400
32	limit 32 to yr="2004 -Current"	1280

## EMBASE SEARCH – Using Map Search to Subject Heading

#	Searches	Results
1	Stimulant?.mp. or central stimulant agent/	31458
2	limit 1 to human	18334
3	Crack-cocaine.mp. or cocaine/	43605
4	limit 3 to human	26043
5	*amphetamine derivative/ or *amphetamine/	13328
6	limit 5 to human	4657
7	Ecstasy.mp. or *amphetamine/ or *cathinone/	15825
8	limit 7 to human	6603
9	methamphetamine dependence/ or *methamphetamine/ or *amphetamine/ or Crystal meth\$.mp.	18545
10	limit 9 to human	6855
11	*psychotropic agent/ or New psychoactive substance?.mp. or *cocaine/	33565
12	limit 11 to human	19904
13	*methylphenidate/ or *central stimulant agent/ or *psychostimulant agent/ or Methylphenidate.mp. or *dexamphetamine/	25509
14	limit 13 to human	17321
15	*substance abuse/ or *intravenous drug abuse/ or *sexually transmitted disease/ or *drug dependence/ or *hepatitis C/ or *drug abuse/ or *addiction/ or *hepatitis B/ or *Human immunodeficiency virus infection/ or non-injecting drug users.mp. or *"drug use"/	338658
16	limit 15 to human	305075
17	*hepatitis B/ or *Human immunodeficiency virus infection/ or *intravenous drug abuse/ or *sexually transmitted disease/ or non-injecting drug users.mp. or *drug dependence/ or *hepatitis C/	268385
18	limit 17 to human	243329
19	2 or 4 or 6 or 8 or 10 or 12 or 14	67658
20	Human immunodeficiency virus.mp. or acquired immune deficiency syndrome/ or *Human immunodeficiency virus/ or *Hepatitis B virus/ or *homosexuality/	410193
21	limit 20 to human	349404
22	Viral hepatitis.mp. or *virus hepatitis/	22583
23	limit 22 to human	18882
24	Sexually transmitted diseases.mp. or *sexually transmitted disease/	24915
25	limit 24 to human	20932
26	sexual behaviour.mp. or *sexual behaviour/	86234
27	limit 26 to human	61253
28	sex workers.mp. or *prostitution/	5719
29	limit 28 to human	5155
30	*sexually transmitted disease/ or men who have sex with men.mp. or *sexual behaviour/ or *condom/ or *homosexuality/ or *Human immunodeficiency virus/ or *acquired immune deficiency syndrome/ or *Human immunodeficiency virus infection/ or *men who have sex with men/ or *high risk population/	289894
31	limit 30 to human	249403
32	21 or 23 or 25 or 27 or 29 or 31	421395
33	19 and 32	4214
34	<b>limit 33 to yr="2004 -Current"</b>	<b>2520</b>

**FREE TEXT SEARCHING: Embase (1980 to 2015 Week 12), HMIC Health Management Information Consortium (1979 to January 2015), Ovid MEDLINE(R) (1946 to March Week 4 2015), PsycINFO (1806 to March Week 4 2015), Global Health (1973 to 2015 Week 11)**

#	Searches	Results
1	(stimulant? or central nervous system stimulant? or CNS stimulant? or stimulant drug? or central nervous stimulant? agent? or stimulant? agent?).tw.	55054
2	(crack-cocaine or cocain or cocaine or crack or crack cocaine or cocaine hydrochloride or base cocaine).tw.	92530
3	(amphetamine? or amphetamine-type or meta-amphetamine?).tw.	55272
4	(Ecstasy or MDMA).tw.	13377
5	(Methylphenidate or Methylamphetamine).tw.	16492
6	(new psychoactive substance? or synthetic cathinone? or cathinone? or ketamine or piperazine? or phenethylamine? or kratom or BZP or methcathinone or 4-methylmethcathinone or mephedrone).tw.	48141
7	(kath or paramethoxyamphetamine or fenetylline or ephedrine or pseudoephedrine or dexamphetamine or dextroamphetamine or mixed amphetamine salt? or dextromethamphetamine or lisdexamphetamine).tw.	14458
8	(ampakine? or phenmetrazine or xanthines or amfepramone or diethylpropion or phentermine or fenfluramine-phentermine or aka fenphen or phenylpropanolamine).tw.	5867
9	(crystal methamphetamine or crystalline methamphetamine or crystal meth).tw.	633
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	258292
11	(route of administration or non-injecting drug user? or IDU? or injecting drug user? or injector? or smoker?).tw.	222897
12	(Human immunodeficiency virus or HIV or aids associated virus or aids related virus or AIDS virus or Human immuno deficiency virus or Human immunodeficiency virus 1 or Human immunodeficiency virus 2 or seroprevalence or HIV Seropositivity).tw.	754721
13	(Viral hepatitis or HCV or Hepatitis C virus type 1 or Hepatitis C virus 1 or Hepatitis C virus or Hepatitis C virus subtype 1a or Hepatitis C virus subtype 1b or HBV or Hepatitis virus B or human hepatitis B virus or hepatitis B or hepatitis C).tw.	340117
14	(Sexually transmitted disease? or sexually transmitted infection? or blood-borne viruse? or viral disorder? or providing sex in exchange for money or multiple sexual partner? or sex in exchange for drug? or sex for drug? or sex worker? or sexual behaviour or men who have sex with men or MSM or Homosexuality or needle sharing).tw.	162279
15	12 or 13 or 14	1133926
16	10 and 15	9642
17	limit 16 to human	8957
18	limit 17 to yr="2004 -Current"	5509

**Additional Searches using Broad terms:**

Data bases	Results
CINAHL	49
SCOPUS	1631
Cochrane Library	139

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