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Title: Estimating the contribution of stimulant injection to HIV and HCV epidemics among people who inject drugs and implications for harm reduction: a modeling analysis

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ABSTRACT

Background: Stimulants, such as amphetamines and cocaine, are widely injected among people who inject drugs (PWID). Systematic reviews indicate stimulant injection is associated with HIV and HCV among PWID. Using these associations, we estimated the contribution of stimulant injection to HIV and HCV transmission among PWID.

Methods: We modeled HIV and HCV transmission among PWID, incorporating excess injecting and sexual risk among PWID who inject stimulants. We simulated three illustrative settings with different stimulants injected, prevalence of stimulant injecting, and HIV/HCV epidemiology. We estimated one-year population attributable fractions of stimulant injection on new HIV and HCV infections, and impact of scaling up needle-syringe programs (NSP).

Results: In low prevalence settings of stimulant injection (St. Petersburg-like, where 13% inject amphetamine), 9% (2.5-97.5% interval [95%I]: 6-15%) and 7% (95%I 4-11%) of incident HIV and HCV cases, respectively, could be associated with stimulant injection in the next year. With moderate stimulant injection (Montreal-like, where 34% inject cocaine), 29% (95%I: 19–37%) and 19% (95%I: 16-21%) of incident HIV and HCV cases, respectively, could be associated with stimulant injection. In high-burden settings like Bangkok where 65% inject methamphetamine, 23% (95%I:10–34%) and 20% (95%I: 9-27%) of incident HIV and HCV cases could be due to stimulant injection. High-coverage NSP (60%) among PWID who inject stimulants could reduce HIV (by 22-65%) and HCV incidence (by 7-11%) in a decade.

Discussion: Stimulant injection contributes substantially to HIV and HCV among PWID. NSP scale-up and development of novel interventions among PWID who inject stimulants are warranted.

Keywords: stimulants, modeling, injection drugs, harm reduction

1. INTRODUCTION

After opioids, stimulants, including amphetamines and cocaine contribute to the second highest proportion of disease attributed to drug use disorder worldwide (United Nations Office on Drugs Crime, 2017). Manufacturing and seizures of stimulants increased by approximately 20% from 2015-2016 (United Nations Office on Drugs and Crime, 2018) and stimulant use has been recognized as an important cofactor in rising drug-related mortality in North America (Seth et al., 2018; United Nations Office on Drugs and Crime, 2018). Among people who inject drugs (PWID), stimulant injection varies regionally, from nearly 20% PWID reporting stimulants as the main drug injected in Western Europe, to 40-50% in North America, Latin America, and Eastern Europe (United Nations Office on Drugs and Crime, 2018).

PWID who inject stimulants exhibit elevated injection (e.g. frequent injecting and syringe sharing (Tyndall et al., 2003)) and sexual risks (e.g. more unprotected sex acts and sexual partners (Colfax et al., 2010)) thereby increasing their risk for HIV and hepatitis C virus (HCV) infection. Based on a systematic review, cocaine injection was associated with 3-fold increased risk of HIV infection (Tavitian-Exley et al., 2015) and 2.9-fold increased odds of prevalent HCV infection compared to PWID who did not use cocaine as their primary substance (Butler et al., 2017). The magnitude of these risks was similar among PWID who injected amphetamines (2-fold increased risk of HIV (Tavitian-Exley et al., 2015) and 2.4-fold increased odds of prevalent HCV infection compared to those who did not inject amphetamines as their primary substance) (Miller et al., 2009). Unlike opioid use disorder, effective pharmacotherapies to treat stimulant use disorder are not yet available. Thus, in the absence of effective treatment, harm reduction services, such as needle/syringe programs (NSP) and condoms are needed to tackle the excess risks of HIV and HCV transmission in this group.

Despite documented associations between stimulant injection and blood borne viruses among PWID at the individual level (Farrell et al., 2019), the contribution of stimulant injection to HIV and HCV epidemics among PWID has not been quantified. Unlike statistical models which examine associative relationships between variables, epidemic models incorporate these associations to provide a mechanistic relationship to simulate complex transmission dynamics and provide insights into epidemic drivers and future epidemic trajectories. Epidemic modeling can be used to guide decision-makers on implementing effective public health responses, such as assessing how drug policies and harm reduction scale-up could affect these epidemics (Farrell et al., 2019). We used systematic review associations between

stimulant injection and HIV and HCV to assess the population-level contribution of stimulant injection on HIV and HCV transmission among PWID, and future impact of interventions among PWID who inject stimulants using dynamic modeling across several illustrative settings.

2. MATERIALS AND METHODS

2.1 Mathematical model

We developed a dynamic, deterministic compartmental joint model of HIV and HCV transmission among PWID (**Figure 1**). The model incorporated sexual and injecting-related transmission of HIV, and injecting-related transmission of HCV. We estimated differential sexual and injecting risks associated with stimulant injection which generated observed patterns in HCV (injecting risk) and HIV (sexual and injecting risk). We stratified the model by HIV and HCV infection status (including coinfection states), stimulant injection (yes/no), and intervention status (on/off) for PWID who injected stimulants. HIV status was stratified by disease stage (susceptible, acute, latent, pre-AIDS, AIDS) and ART status (latent on ART, pre-AIDS on ART, and AIDS on ART). After HIV infection, individuals entered a short period of acute infection (characterized by high viremia and high transmissibility (Boily et al., 2009; Hollingsworth et al., 2008)), followed by a longer latent phase, and then a pre-AIDS phase (of high viremia and high transmissibility (Boily et al., 2009; Hollingsworth et al., 2008)) and AIDS phase (where we assumed individuals did not engage in injecting or sexual activity and did not contribute to transmission). Individuals in the latent stage or later could be recruited on and drop out of ART, which reduced HIV progression rates, HIV-related mortality from AIDS, sexual and parenteral transmission (to a lower and more uncertain extent than sexual transmission). HCV infection was stratified by susceptible and chronic HCV. We neglected HCV treatment based on historically low HCV treatment rates among PWID (<1% treated globally), and because stimulant injection was the focus of our analysis which has not been associated with HCV treatment uptake. HIV-infected individuals were less likely to spontaneously clear HCV infection (Micallef et al., 2006) and individuals coinfected with HIV not receiving ART were assumed to more readily transmit HCV due to elevated viral loads (Thein et al., 2008). The model was open where PWID entered through injecting initiation and exited through death or permanent cessation of injection drug use. HIV-related deaths were not replaced, resulting in a declining PWID population in all settings.

For our baseline analysis, PWID entered injecting stimulants or not and remained in that risk group. For simplicity, we defined the stimulant injecting category (amphetamines or cocaine) by the most widely injected type in that setting. For consistency with systematic review data on elevated HIV and HCV risk among PWID who inject stimulants, the stimulant group included those who injected multiple substances (Butler et al., 2017; Tavitian-Exley et al., 2015). However, estimates for excess HIV risk among PWID who inject stimulants as the primary drug (compared to not) were similar for all stimulants: (IRRs: 2.3 (95%CI 1.0-5.8) opioids and stimulants, 3.1 (95%CI 1.8-5.5) cocaine, 2.0 (95%CI 1.2-3.4) amphetamine) (Farrell et al., 2019; Tavitian-Exley et al., 2015). We assumed proportional (random) mixing between all groups. We incorporated both elevated injecting and sexual risk among PWID who inject stimulants compared to PWID who did not inject stimulants. The magnitudes of these relative risks were varied, and calibrated to systematic review data on observed differences in HIV incidence (due to elevated injecting and sexual risks) and HCV prevalence (due to elevated injecting risk) among PWID who injected stimulants compared PWID who did not, accounting for minor differences observed by stimulant type (cocaine or amphetamine) (Tavitian-Exley et al., 2015). The model implicitly incorporated existing harm reduction interventions at baseline to generate the observed HIV and HCV epidemics, but assumed that PWID who injected stimulants did not have access to high coverage NSP, as stimulant-using PWID need more syringes and have lower coverage compared to opioid-using PWID even when accessing NSPs (O'Keefe et al., 2018). PWID who injected stimulants could be recruited onto or drop off from high-coverage NSP, which reduced injecting-related risks only.

2.2 Modeled settings

We modeled three illustrative settings with varying levels of main stimulant injected (cocaine or amphetamine), and differing epidemics of HIV and HCV among PWID. Specifically, we modeled settings with low prevalence (13%) of amphetamine injecting (St. Petersburg-like), moderate prevalence (34%) of cocaine injecting (Montreal-like), and high prevalence (65%) of methamphetamine injecting (Bangkok-like). The Montreal and Bangkok-like setting had low HIV incidence (<1 per 100 PY) whereas the St. Petersburg-like setting had higher HIV incidence (~7 per 100py). All settings had high chronic HCV prevalence (55-75%).

2.3 Parameterization and calibration

Calibration and parameterization values are in **Tables 1-2**. Calibration data varied, but input parameters were identical across settings. The exception was the upper uncertainty bound for duration of injection in the St. Petersburg-like setting based on evidence that this could be longer.(Vickerman et al., 2014) We used Latin Hypercube Sampling to generate 500 parameter sets from uncertainty distributions. We seeded the epidemic with 0.75% of the population infected with HIV and HCV, while the remaining population was assumed to be susceptible for both HIV and HCV. The model was run to reach a steady state prevalence and incidence. For each parameter set, the model was calibrated at steady-state to setting-based values for HIV incidence, HCV prevalence, ART coverage among HIV-positive PWID, the proportion of incident HIV infections due to sexual transmission (see appendix Figures S1-S6), and systematic review data on elevated HIV incidence among people who inject stimulants as their primary drug (amphetamine incidence rate ratio [IRR]: 2.0, 95% CI: 1.2-3.4 and cocaine IRR: 3.1, 95% CI: 1.8-5.5) compared to PWID who did not inject stimulants as their primary drug(Tavitian-Exley et al., 2015), and increased odds of prevalent HCV among PWID who injected stimulants (amphetamine odds ratio [OR]: 2.43, 95% CI: 1.33-4.43 and cocaine OR: 2.92, 95% CI: 2.50-.40) compared to PWID who did not (Butler et al., 2017; Miller et al., 2009). Due to uncertainty in the increased risk of HIV and odds of HCV infection among PWID who inject stimulants, we calibrated to sampled values for these outputs to generate simulations representing the uncertainty ranges. Calibration was achieved through varying the following parameters: HCV transmission rate among PWID who did not inject stimulants, relative transmissibility of injecting-related HIV compared to HCV among PWID who did not inject stimulants, relative transmissibility of sexual-related HIV compared to injecting-related HIV, ART recruitment rate, proportion who entered as stimulant injecting PWID, relative risk of parenteral transmission of HIV and HCV among PWID who injected stimulants compared to not, and relative risk of sexual transmission of HIV among PWID who injected stimulants compared to not. The model was calibrated using a global optimization solver in MATLAB (fmincon with MultiStart search algorithm to ensure global minima were obtained) which minimized the sum log-likelihood of the calibration values given the data. We accepted fits with projections within the 95% CI of the observed HIV incidence data and 99% CI of the HIV IRR and HCV OR among PWID who injected stimulants compared to PWID who did not.

2.4 Model analyses

For each setting, we simulated the epidemic assuming no change in stimulant injection or intervention coverage. As population size estimates of PWID are uncertain (Abdul-Quader et al., 2014), rather than presenting absolute changes,

we calculated relative changes in new HIV and HCV infections in each scenario compared to the base case. We estimated the proportion of incident HIV and HCV infections projected to occur over the next year among PWID who injected stimulants by dividing the expected number of incident cases among PWID who injected stimulants by the number of all incident cases. We calculated the 1-year population attributable fraction (PAF) of stimulant injection by comparing the total expected number of HIV and HCV infections over one year in our baseline epidemic to a counterfactual scenario where we assumed no increased injecting or sexual risk associated with stimulant injection. In other words, the PAF corresponds to scenarios where stimulant using PWID transition to and remain in non-stimulant injection drug use group. Finally, we determined the impact of scaling-up high-coverage NSP (100% of injections covered by a sterile needle/syringe) over the next decade to 60% coverage among PWID who inject stimulants, consistent with the highest level achieved in global settings (Larney et al., 2017). High-coverage NSP was assumed to reduce only parenteral transmission of HIV (RR: 0.42 [95%CI 0.22-0.81]) and HCV (RR: 0.79 [95%CI 0.39-1.61]) based on global systematic review data, (Aspinall et al., 2014; Platt, L. et al., 2017) but we also examined impact using the European effect estimate for HCV (RR: 0.44 [95% 0.24-0.80]) (Platt et al., 2018).

2.5 Sensitivity analyses

We examined the sensitivity of several assumptions, such as the impact of 50% preferential (assortative) mixing by stimulant injecting (versus fully proportional). We additionally assessed three alternative scenarios regarding stimulant injection (see appendix for calibration methods): 1) PWID entered as not injecting stimulants, and if they began injecting stimulants then they remained injecting stimulants, and 2) PWID entered as not injecting stimulants, and if they began injecting stimulants remained injecting stimulants for five years and then transitioned to not injecting stimulants and 3) 20% increase in the recruitment proportion of stimulant using PWID.

3. RESULTS

Overall, model projections calibrated well to the data in all three illustrative settings (posterior parameter distributions and calibration shown in **Figures S1-S3, Tables S1-S2**). Despite slightly increased HIV mortality, the proportion of PWID injecting stimulants remained stable over time (**Figures S4-S6 panel A**). Calibration to the elevated odds of prevalent HCV among PWID who injected stimulants resulted in a 2.5-fold simulated relative HCV incidence among PWID who injected stimulants compared to PWID who did not, regardless of stimulant class (RR: 2.4 [2.5-97.5%

interval [95% interval, 95%I]: 1.7-3.8], RR: 2.9 [95%I: 2.5–3.4], RR: 2.3 [95%I: 1.4–3.4] in the St. Petersburg-like, Montreal-like and Bangkok-like settings, respectively). The simulations estimated a 2-3 fold relative injecting HIV risk among PWID who injected stimulants compared to PWID who did not (RR: 2.5 [95%I: 1.7–3.8], RR: 2.9[95%I: 2.5–3.4], and RR: 2.2 [95%I: 1.4–3.4], in the St. Petersburg-like, Montreal-like, and Bangkok-like settings, respectively). Greater uncertainty was observed for the relative sexual risk among PWID who inject stimulants: RR: 1.0 (95%I: 1.0–9.6), RR: 4.2 (95%I: 1.0–15.1), and RR: 1.2 (95%I: 1.0–5.5) in the St. Petersburg-like, Montreal-like, and Bangkok-like settings, respectively. This uncertainty is likely due to the relatively minor contribution of sexual risk to overall HIV transmission among PWID across the settings (**Figure S1-S3, panel G**).

3.1 Proportion of incident HIV and HCV occurring among PWID who inject stimulants

PWID who injected stimulants shouldered a disproportionate burden of new HIV and HCV infections (**Figure 2)**. For each 10% of PWID who injected stimulants across the scenarios, 11-15% of incident HIV and HCV infections would occur among this group over the next year. In the St. Petersburg-like setting, characterized by a relatively low proportion (13%) of recent amphetamine injection, 19% (95%I: 13-23%) of incident HIV cases and 17% (95%I 15-19%) of incident HCV cases could occur among PWID who inject stimulants over the next year. In the Montreal-like setting, where a moderate level (34%) of PWID inject cocaine, 52% (95%I: 33-57%) and 44% (95%I: 39–46%) of incident HIV and HCV cases, respectively, would occur among PWID who inject stimulants in the next year. In a Bangkok-like setting, defined by a high proportion (65%) of PWID who inject methamphetamine, over 75% of incident infections (71% (95%I: 63-81%) and 70% (95%I: 67–73%) of HIV and HCV respectively), could occur among PWID who injected stimulants in the next year.

3.2 PAF of stimulant injection on HIV and HCV

If the excess risk associated with stimulant injection were removed in the St. Petersburg-like setting, 9% (95%I 6-15%) and 7% (95%I: 4-11%) of incident HIV and HCV cases, respectively, could be prevented in the next year (1-year PAF, from 2020-2021; **Figure 3**). Across all settings, the HIV PAF was predominantly associated with elevated injection risk; in the St. Petersburg-like setting, 8% (95%I: 4-14%) and <1% (95% I: 0-6%) of HIV infections could be prevented if only the injection or sexual-related risks associated with stimulant injection were removed, respectively. In the Montreal-like setting with higher prevalence of stimulant injecting, 29% (95%I: 19–37%) and 19% (95%I: 16-21%) of incident HIV

and HCV cases, respectively could be associated with cocaine injection (1-year PAF, from 2020-2021). Approximately 22% (95%I: 16-24%) and 7% (95%I: 0-21%) of HIV infections could be prevented if only the injection or sexual-related risks associated with cocaine injection were removed, respectively. In the Bangkok-like setting, despite higher prevalence of stimulant injection (65%), the observed HIV PAF (23% [95%I: 10–34%]), was similar to the Montreal-like setting. Compared to the other scenarios, the Bangkok-like setting exhibited the highest HCV PAF: 20% (95%I: 9-27%). Across all settings, a median additional 4-9% of new HIV and 3-6% of new HCV infections in the next year could be attributable to each 10% increase in prevalence of stimulant injection.

3.4 Impact of NSP scale-up among PWID who inject stimulants

If high coverage NSP increased to 60% coverage among PWID who inject stimulants in each of these settings, this could reduce overall HIV incidence by 22% (95%I: 8-38%) in the St. Petersburg-like setting, 63% (95% I: 30%-80%) in the Montreal-like setting, and 65% (95% I: 30% - 81%) in the Bangkok-like setting over the next decade (from 2020-2030). Nonetheless, HIV incidence among PWID who inject stimulants would still exceed that of non-stimulant injecting PWID (**Figure S7-S9**). Compared to HIV, less impact was achieved on HCV incidence due to lower effect estimate of NSP on HCV, where the median reduction in incidence at 10 years ranged from 7-11% across settings. When using the NSP effect estimate on HCV from European studies(World Health Organization, 2007), the median reduction in HCV incidence over the next decade (from 2020-2030) ranged from 13-30%.

3.5 Sensitivity analyses

Compared to the base-case results, preferential mixing (50% assortative by stimulant injection) resulted in moderate reductions in the 1-year PAF (**Figure S10**), with median HIV-related PAFs ranging from 6-24% across settings compared to 9-29%. The sensitivity analyses with varying stimulant turnover assumptions and increasing stimulant population had minimal impact on the HIV and HCV PAFs (<2% difference).

4. DISCUSSION

PWID who inject stimulants are disproportionately affected by HIV and HCV, and elevated injecting and sexual risks associated with stimulant injection could be important contributors to HIV and HCV epidemics among PWID. Across three illustrative settings, for each 10% of the population who inject stimulants, 11-15% of HIV and HCV

infections occur among this group. Further, stimulant injection could contribute to 9-29% of new HIV and 7-20% of new HCV infections in the next year. Scale-up of high coverage NSP for PWID who inject stimulants could ameliorate, but not eliminate excess risks associated with stimulant injection. In terms of policy implications, interventions to reduce injecting risk among stimulant-using PWID are urgently needed across settings regardless of main type of stimulant injected. Second, in the absence of medication assisted treatment for stimulant use disorder, higher levels of NSP might be needed to prevent transmission compared to PWID who primarily inject non-stimulants. For example, methamphetamine injecting PWID in Melbourne, Australia, which has one of the highest NSP coverage levels (Larney et al., 2017), had lower coverage of clean syringe provision (O'Keefe et al., 2018). Third, scaled-up harm reduction interventions targeting PWID who inject stimulants should include condom distribution and other sexual risk interventions. However, our analysis indicates sexual risk contribution likely varies by setting depending on overall sexual risk and should therefore be further informed by a local understanding of epidemic drivers. Fourth, our modeling highlights additional interventions are needed to address elevated blood-borne virus risks among stimulant-using PWID, which could include supervised consumption rooms (SCRs), pre-exposure prophylaxis (PrEP), and treatment for HIV and HCV. Indeed, evidence from numerous settings indicate PWID who inject stimulants frequently use SCRs, suggesting they could serve as critical settings for HIV and HCV testing and treatment (Reddon et al., 2011; Toth et al., 2016). Given increased HIV transmission risks, initiating PrEP should also be considered. However findings from the Bangkok Tenofovir trial indicate lower PrEP adherence among PWID who injected methamphetamine so particular attention might be needed in this group (Martin et al., 2015).

Previous modeling studies have incorporated increased risks of HCV transmission among ‘high-risk’ PWID who either injected crack cocaine or experienced homelessness, but these did not quantify the independent contribution of stimulant injecting (Platt, LS et al., 2017; Vickerman et al., 2014; Ward et al., 2018). An economic modeling analysis explored the impact of crack smoking rooms on averting HIV and HCV in Vancouver but only focused on provision of clean pipes (Jozaghi, 2014). Our model is consistent with modeling and economic analyses showing the effectiveness of high coverage NSP on preventing HIV and HCV transmission among PWID, although these did not examine PWID who injected stimulants specifically (Kwon et al., 2012; Kwon et al., 2009; Vickerman et al., 2012).

4.1 Limitations

We note several limitations, mainly involving parameter uncertainty. First, due to lack of detailed data on stimulant injection, we purposely modelled illustrative settings. Thus, our results were not intended to generate specific predictions in these settings. While we recognize that our estimates might not be directly applicable to settings with growing or declining proportions of people who inject stimulants, for simplicity and comparison across settings, we simulated epidemics in steady-state. This might not be true in all settings, particularly where scale-up of HCV treatment is occurring as in Montreal (Makarenko et al., 2019). However, changes in these background dynamics would likely have minimal impact on the one-year PAFs and the relative contribution of stimulant injection. Additionally, since our goal was to examine the contribution of stimulant use broadly, due to differences in other parameter values across the settings, the results were not solely explained by the prevalence of stimulants, but also the type of stimulant injected and other epidemic characteristics. Lack of systematic review data also precluded us from comparing drug-related mortality among stimulant using PWID to opioid only using PWID.

Secondly, our modeling was based on global systematic reviews and meta-analyses of elevated HIV incidence and HCV prevalence among PWID who injected stimulants as a primary drug compared to those who did not. These associations were based on limited studies, some of which were dated. Further, we simulated this excess burden through elevated sexual and injecting risks among PWID who injected stimulants. However, additional work examining the causal associations underlying the observed infection patterns are warranted, especially for HCV where higher odds of prevalent HCV could be due to other factors. Nevertheless, our simulated mechanisms (stimulant injection increasing sexual and injecting risk) are consistent with several studies (Vickerman et al., 2014; Ward et al., 2018).

Third, we neglected any potential additional risk among polysubstance-using PWID who inject stimulants and opioids. HIV incidence among those who inject opioids and stimulants and those who inject primarily stimulants was higher although uncertainty was wide and few studies examined this specifically (Tavitian-Exley et al., 2015). Polysubstance injection is common ,and injection of stimulants and opioids might be associated with injecting and sexual risks and longer injecting duration compared to those who injected only one drug class (Tavitian-Exley et al., 2018). Thus, our simulations could underestimate the potential contribution of stimulant injection.

Fourth, data on duration of stimulant injection and mixing by stimulant injection status were unavailable. Thus, we assumed no turnover and proportional mixing at baseline, and sensitivity analyses found minimal differences. Nevertheless, investigation on the trajectory of stimulant injection and mixing patterns is warranted to identify key intervention targets. Latent class analyses among PWID in California revealed distinct sociodemographic, behavioral, and disease related outcomes between PWID who primarily injected methamphetamine versus heroin (Meacham et al., 2018; Roth et al., 2015). Conversely, polysubstance use could potentially increase mixing between PWID who use stimulants and other substances and PWID who do not use stimulants.

Fifth, because stimulant injection was of primary interest, it was the only source of heterogeneity, which might not capture all contributors of the epidemics. However, by including more heterogeneity, it might have prevented us from examining the independent contribution of stimulant injection and making inferences across all settings. For example, we observed a similar HIV PAF of stimulant injection in our moderate stimulant prevalence setting (Montreal-like, 34%) and high stimulant prevalence setting (Bangkok-like, 65%), which was in part due to higher effect estimates for the HIV incidence rate ratio among cocaine injectors (the main stimulant injected in Montreal) compared to methamphetamine injectors (the main stimulant injected in Bangkok). Additionally, HIV incidence was very low in our Montreal-like scenario (0.3/100py), so the elevated risks among stimulant injectors may, in part, be sustaining the HIV epidemic. Nevertheless, additional sources of heterogeneity would allow for refinement of predictions across settings, We likely did not capture other potentially negative outcomes associated with stimulant injection and HIV, such as lower ART adherence rates (Jin et al., 2018).

Sixth, the effect estimate for NSP was not among PWID who injected stimulants specifically (Platt, L. et al., 2017). This is reasonable because for HCV the exposure was defined as receiving one or more sterile syringes for each injection, so even if PWID who inject stimulants require a different number of sterile syringes, provided they receive a syringe for each injection, then impact on HIV and HCV transmission should be similar. Additionally, in a UK-based analysis for the effect of high-coverage NSP on HCV, the authors controlled for crack injection and found no interaction (Platt et al., 2018). Due to geographical heterogeneity for the NSP effect estimate between North America and Europe (Platt, L. et al., 2017), and data lacking for other global regions, we used the pooled effect estimate but acknowledge the uncertainty which might vary by setting depending on program and population characteristics. Additionally, this

uncertainty could explain why less impact NSP on HCV incidence was observed compared to the NSP impact on HIV incidence.

4.2 Conclusions

Our modeling could assist policymakers in mounting the appropriate public health response to prevent HIV and HCV associated with stimulant injection. Our findings indicate PWID who inject stimulants shoulder a disproportionate share of HIV and HCV, and elevated sexual and injecting risks associated with stimulant injection could contribute to many new HIV and HCV infections among PWID. Substantial impact in abating the contribution of stimulant injection can be achieved if evidence-based prevention interventions, particularly NSPs, are scaled-up. Lastly, development of effective novel interventions reducing sexual and injecting risk among PWID who inject stimulants is urgently needed.

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