Title

Stimulant use interventions may strengthen ‘Getting to Zero’ HIV elimination initiatives in Illinois: Insights from a modeling study

Authors

Lee, Francis
Sheeler, Daniel
Hotton, Anna
et al.

Publication Date

2022-05-01

DOI

10.1016/j.drugpo.2022.103628

Stimulant Use Interventions May Strengthen 'Getting to Zero' HIV Elimination Initiatives in Illinois: Insights from a Modeling Study

Francis Lee[1,2], Daniel Sheeler[1,2], Anna Hotton[1,2], Natascha Del Vecchio[1,2], Rey Flores[1,2], Kayo Fujimoto[3], Nina Harawa[4,5], John A. Schneider [1,2], Aditya S. Khanna[6,7]

[1]Chicago Center for HIV Elimination, The University of Chicago
[2]Department of Medicine, The University of Chicago
[3]Center for Health Promotion and Prevention Research, The University of Texas Health Science Center at Houston (UTHealth)
[4]Department of Epidemiology, University of California at Los Angeles
[5]Department of Psychiatry and Human Behavior, Charles R. Drew University
[6]Center for Alcohol and Addiction Studies, Brown University School of Public Health
[7]Department of Behavioral and Social Sciences, Brown University School of Public Health

Research Support
This work was supported by NIH R01 DA 039934, R03 DA 049662, T32DA043469, U2C DA 050098, and the Providence/Boston Center for AIDS Research (P30AI042853). A.S.K. was also supported by P20 GM 130414. NH received additional support from the California HIV/AIDS Research Program (CHRP) OS17-LA-003 (PI, Harawa), the UCLA Clinical and Translational Science Institute (CTSI) NIH/NCATS grant UL1-TR001881 (PI, Dubinett) and by the Center for HIV Identification, Prevention, and Treatment (CHIPTS) NIMH grant P30MH058107 (PI, Shoptaw).This work was completed in part with resources provided by the University of Chicago's Research Computing Center and the Center for Computation and Visualization, Brown University.

Author for Correspondence and Reprints
Aditya S. Khanna, Ph.D.
aditya_khanna@brown.edu

Word Count
Abstract: 318
Manuscript: 2956 (excluding Figures, Tables, References)

Highlights

Stimulant use is a key barrier to engagement in the HIV prevention and treatment continua.

We apply an agent-based model to examine the impact of stimulant use on population HIV outcomes.

We simulate behavioral and medication-assisted interventions to treat stimulant use.

Implementation of these interventions may positively impact efforts to eliminate HIV incidence.

Abstract:
Objective(s): Getting to Zero (GTZ) is an Illinois-based HIV elimination initiative. GTZ identifies younger Black men who have sex with men (YBMSM) as a population who have experienced disproportionate HIV incidence. Rising stimulant use among YBMSM has been determined to impede engagement in the HIV prevention and treatment continua for reducing onward HIV transmission. Given the limited development of dedicated or culturally appropriate interventions for this population, this modeling study explores the impact of stimulant use on HIV incidence among YBMSM and assesses the impact of such interventions on downstream HIV transmission to achieve GTZ goals.

Methods: A previously developed agent-based network model (ABNM), calibrated using data for YBMSM in Illinois, was extended to incorporate the impact of stimulant use (methamphetamines, crack/cocaine, and ecstasy) on sexual networks and engagement in HIV treatment and prevention continua. The model simulated the impact of a residential behavioral intervention (BI) for reducing stimulant use and an outpatient biomedical intervention (mirtazapine) for treating methamphetamine use. The downstream impact of these interventions on population-level HIV incidence was the primary intervention outcome.

Results: Baseline simulated annual HIV incidence in the ABNM was 6.93 [95% Uncertainty Interval (UI): 6.83,7.04] per 100 person years (py) and 453 [95% UI: 445.9,461.2] new infections annually. A residential rehabilitation intervention targeted to 25% of stimulant using persons yielded a 27.1% reduction in the annual number of new infections. Initiating about 50% of methamphetamine using persons on mirtazapine reduced the overall HIV incidence among YBMSM by about 11.2%. A 30% increase in antiretroviral treatment (ART) and preexposure prophylaxis (PrEP) uptake in the non-stimulant using YBMSM population combined with a 25% uptake of BI for stimulant using persons produces an HIV incidence consistent with HIV elimination targets (about 200 infections/year) identified in the GTZ initiative.

Conclusions: Behavioral and biomedical interventions to treat stimulant use, in addition to expanding overall ART and PrEP uptake, are likely to enhance progress towards achieving GTZ goals.

Keywords
Substance-Related Disorders; HIV infections; pre-exposure prophylaxis; computer simulation; sexual and gender minorities; preventive medicine

INTRODUCTION

Getting to Zero (GTZ) Illinois is an HIV elimination strategy that is being collaboratively implemented by a combination of state and county public health departments, academic medical centers, and community health organizations. GTZ Illinois assessments have found that the overall declines in HIV incidence have not been experienced equally by subpopulations; younger (18-34 years) Black gay, bisexual and other men who have sex with men (YBMSM) have experienced relatively stable incidence rates over recent years.[1,2] Improved engagement in the HIV prevention and treatment continua, achieved through a scale-up of antiretroviral treatment (ART) and preexposure prophylaxis (PrEP) use among YBMSM, is a centerpiece of the GTZ initiative.

The scale-up of ART and PrEP among YBMSM, however, is constrained by the many psychosocial and healthcare barriers faced by YBMSM.[3,4]Substance use is one such barrier, and it has been associated with suboptimal ART adherence and missed PrEP doses among MSM.[5–11]The use of stimulants – such as methamphetamines, crack/cocaine, and ecstasy – in particular, has been found to be associated with behaviors that may increase the risk of HIV transmission,[12] particularly condomless insertive and receptive anal sex.[13]Black MSM living with HIV and not using methamphetamines have been found to be less likely to miss clinical visits for ART care than those who have used methamphetamines.[14]Emerging evidence also suggests that Black MSM who use social networking sites are often younger and more likely to have used methamphetamines and cocaine in the past 12 months compared to persons who do not use such sites.[15]

Given the impact of stimulant use on disengagement from HIV care, stimulant use

treatment may be a key tool in achieving GTZ policy goals. Mirtazapine, in particular, has been shown in clinical trials to be an effective biomedical treatment for methamphetamine addiction.[16,17]While no FDA approved treatment exists for treating cocaine addiction, other interventions such as residential rehabilitation have found moderate success in treating stimulant use disorders (including methamphetamines and cocaine).[18–21]The success of these stimulant use treatments have led to calls for their integration in HIV care.[22,23]

The GTZ Illinois planning committee has explicitly identified addressing stimulant use as a crucial component of their policy planning efforts. GTZ aims to reduce the number of incident HIV cases among Black MSM in Illinois to a "functional zero" level, currently defined as fewer than 200 new infections per year.[24] Fewer studies, however, have examined the prevalence of stimulant use and its role in HIV transmission among Black MSM specifically.[25] Given that stimulant use treatment has not previously been incorporated in GTZ planning efforts,[24] transmission models that investigate the impact of stimulant use and sexual networks on the engagement in the HIV prevention and treatment continua can provide useful guidance for policy planning.

This study extends an existing agent-based network model (ABNM),[26] parameterized largely with data collected in Illinois, to assess the impact of stimulant (methamphetamines, crack/cocaine and ecstasy) use on the HIV prevention and treatment continua and downstream HIV incidence among YBMSM. We simulate stimulant use treatment interventions and project their impact on downstream HIV incidence to inform next steps in the GTZ planning efforts in Illinois.

METHODS

Agent-Based Network Model (ABNM) Development

The ABNM described below combines sexual network structure with a number of processes that impact HIV transmission. The sexual network structure was modeled using exponential random graph models (ERGMs),[27] a statistically robust approach to model complex network evolution over time, and implemented using the *statnet*[28] suite of packages in the R programming language. The ABM components were developed with the C++-based Repast HPC ABM toolkit.[29,30]Parameters and computer code to reproduce results are available in a public GitHub repository.[31]

Demographic, Network, Behavioral and Biological Data

The baseline model was parameterized with data sources that were representative of YBMSM in Illinois. Local data sources included cohort data on Chicago YBMSM from "uConnect"[32,33] and the Young Men's Affiliation Project (YMAP)[34,35]; both studies recruited participants in Chicago from 2013-2016 using systematic sampling schemes. Additional data on YBMSM were obtained from the National HIV Behavioral Surveillance (NHBS) survey in the Chicago Metropolitan Statistical Area.[36] Other local and national sources, described below, were included where representative data from Illinois were not available. All procedures and protocols were approved by relevant institutional review boards.

Baseline Model

Baseline HIV transmission was simulated to capture existing epidemic features among YBMSM (age 18 to 34 years), populated with 10,000 individuals at the start of the dynamic simulations, approximately consistent with the number of estimated YBMSM in Chicago. The substantive model components included arrivals, departures, dynamic sexual network structure, the temporal evolution of CD4 counts and HIV RNA ("viral load"), HIV testing and diagnosis,

dynamics of ART and PrEP use, external HIV infections, and HIV transmission dynamics (see Section A.4 of the Appendix for further details).

Modeling Impacts of Stimulant Use

HIV Treatment and Prevention Continua. The model examined the impact of methamphetamines, crack/cocaine and ecstasy use on HIV treatment and prevention continua. Population-based cohort data were used to estimate the usage rates of methamphetamines, crack/cocaine and ecstasy.[32,33] The model was seeded with users of the three stimulants in accordance with the estimated rates. Estimates of ART adherence among users of the three substances were also derived from the available cohort data. The PrEP continuum for stimulant users was modeled in terms of reduced initiation and retention relative to the general population, as estimated in the literature.[5,37,38] The ART and PrEP parameters for stimulant users are presented in Appendix Sections 4.9 and 4.10. The key model parameters are listed in Table 1.

Sexual Behavior. Stimulant users in the model, identified by indicator variables denoting methamphetamine, crack/cocaine and ecstasy use, were given a propensity to form partnerships cross-sectionally that was greater than that of a person not using these stimulants. This increased propensity was estimated by computing the ratio of the number of recent (i.e., past 6 months) partnerships for users of each of the stimulants relative to the number of partnerships reported by the overall YBMSM population (Table 1).

Model Calibration

Model simulations proceeded in daily time steps. The model was calibrated using previously described HIV incidence (about 5-7 per 100 person years) and prevalence (about 35-37%) set as targets,[26] estimated from population-based cohort data for Black MSM in Illinois.[39,40]

Interventions

This study incorporates two treatments for stimulant use: a residential behavioral intervention delivered via a rehabilitation facility for persons using any of the three stimulants, and a medication-assisted treatment program that consists of mirtazapine for treating methamphetamine use. We investigated the impact of these interventions on HIV incidence relative to the baseline model.

The residential behavioral intervention (BI) for users of crack/cocaine, ecstasy and methamphetamine users was motivated by previous empirical studies that demonstrated the impact of BIs on the behavior of persons who use stimulants.[41–43] We simulated the impact of a 3-month BI (consistent with the duration of a similar intervention implemented through a community rehabilitation program[44]). Simulations included HIV testing for HIV-undiagnosed persons at the time of their enrollment in the residential behavioral intervention. We considered scenarios in which varying proportions of persons using stimulants receive the intervention (see Sensitivity Analysis subsection below).

In accordance with empirical data, 87% of persons receiving residential BI changed their behavior.[45]Thus, 87% of persons diagnosed with HIV who receive BI are assumed to be always adherent to ART during their period of residential stay (see Table 1 for the levels of ART adherence in the model). Similarly, 87% of HIV-negative persons receiving BI are assumed to be optimally adherent (4+ doses/week) to PrEP during the course of the intervention. Upon completion of BI, agents return to their pre-intervention levels of engagement in the HIV treatment and prevention continua.

Additionally, a biomedical intervention, consisting of mirtazapine for treating methamphetamine use, was simulated. During the period of biomedical treatment, 48.5% of the mirtazapine users received a mirtazapine outpatient prescription for a period of 3 months,

consistent with common treatment mirtazapine treatment regimes.[16,17] These persons are parameterized to optimally adhere to their HIV medications (ART or PrEP) resulting in a 95% reduction in transmission of or risk for acquisition of HIV infection for the duration of their mirtazapine treatment (alternate scenarios that assume lower effectiveness are described in the Sensitivity Analysis subsection below). Upon completion of the mirtazapine treatment, agents returned to their pre-treatment levels of methamphetamine use. Thus, persons receiving BI or mirtazapine treatment experienced improved engagement in the HIV treatment and prevention continua during the course of receiving treatment.

Outcomes and Uncertainty Quantification

The primary outcomes for both residential BI and mirtazapine interventions were the mean number of HIV infections and the mean HIV incidence rate in the overall YBMSM population in the tenth year after the implementation at varying levels of uptake (Table 2A). HIV incidence among methamphetamine using persons who receive BI or mirtazapine was also estimated for the various levels of uptake (Table 2B). Additionally, scenarios that examined scale-up of ART and PrEP uptake in accordance with GTZ Illinois guidance, along with purposeful stimulant use interventions, were modeled to assess the impact of stimulant use interventions on overall GTZ policy goals (Table 3).

Uncertainty in the HIV incidence projection estimates was quantified by using bootstrap estimates derived via simulation. To do this, the 30 simulated HIV incidences at each time point under each policy scenario were sampled 1,000 times with replacement. The mean for each of the resampled datasets was computed, and the 2.5% and 97.5% quantiles of these means were taken to obtain the 95% bootstrap uncertainty interval (UI).

Sensitivity Analysis

For residential BI, sensitivity analyses examined uncertainty in the proportion of stimulant users who receive the intervention, considering scenarios in which 10%, 15%, 20%, and 25% of stimulant using persons received BI. For mirtazapine, sensitivity analyses considered varying proportions of methamphetamine using persons receiving mirtazapine treatment. Scenarios where 5%, 25%, 50%, 75%, and 100% of methamphetamine users are given mirtazapine were simulated. (We limited the proportion of stimulant users receiving residential BI to relatively lower levels because it is likely to be an expensive intervention and wider scale-up may be limited by its cost). Additional analyses presented in Appendix Section A.6 examine varying levels of engagement in the HIV treatment and prevention continua by the persons who received mirtazapine for methamphetamine use treatment. Given evidence that some persons using stimulants may change their patterns of use,[46] we conducted sensitivity analyses that considered scenarios modeling intermittent use behaviors. One scenario simulated a relatively shorter period of stimulant use (average duration of 1 year), and another considered a 5-year average duration of use. We compared the population-level HIV incidence results predicted by these models to our baseline assumption of lifetime use (Appendix Section A.7).

RESULTS

Figure 1A provides the mean HIV incidence rate (per 100 person years) in the overall population for 10 years following the implementation of BI for persons who use any of the three stimulants, with color bands that demonstrate the bootstrap uncertainty intervals. Correspondingly, Table 2A shows the overall annual HIV incidence rate and the mean number of HIV infections among YBMSM in the tenth year after the implementation of BI. The control case, with no purposeful intervention for stimulant using persons and ART and PrEP uptake maintained at baseline levels, yielded a mean HIV incidence rate of 6.93 (95% UI: 6.83, 7.04)

per 100 person years (py) in the overall population. In the tenth year, scaling up BI to 25% of stimulant using persons yielded a 35.0% decline in the HIV incidence rate to 4.51 (95% UI: 4.42, 4.6) per 100 py.

Figure 1B shows the mean HIV incidence rate in the overall population ten years after the implementation of the mirtazapine intervention. The declines in overall HIV incidence are modest relative to the BI intervention: Providing mirtazapine to all meth using persons resulted in a 20.1% decline in the HIV incidence rate in the overall population (Table 2A). The relatively lower decline in HIV incidence associated with mirtazapine treatment relative to BI is not surprising because all stimulant using persons in the model (approximately 28% of the population) are eligible for BI, but a relatively smaller proportion of persons use only methamphetamines (about 9% of the population) and are therefore eligible for a mirtazapine prescription.

In comparing the HIV incidence rate among persons who use methamphetamines, Table 2B shows that under the baseline model the HIV incidence rate among persons who use methamphetamines is about 10.6 per 100 py. Substantial (and comparable) declines in HIV incidence are seen when 15% of methamphetamine using persons receive the BI or 50% of methamphetamine using persons receive mirtazapine (about 6.3 per 100 py).

Notably, while stimulant use interventions are effective in substantially reducing population-level HIV incidence, functional zero HIV incidence was achieved only when ART and PrEP use are also scaled up in the overall population (Table 3). A 30% increase in ART and PrEP uptake in the general population combined with a 25% uptake of BI for stimulant users produces an HIV incidence of about 197 new infections per year.

DISCUSSION

Our findings provide an assessment of the relative benefits of BI and mirtazapine for reducing HIV risk among people who use stimulants and the added benefits such policies can have in achieving GTZ goals. On average, the residential BI implementation at 10% uptake among stimulant using persons (approximately 28% of the population) produced fewer new HIV infections annually than an outpatient mirtazapine intervention that reached all methamphetamine using persons (about 9% of the population). Approximately equal declines of HIV incidence among persons who use methamphetamine are accomplished by a BI uptake of about 15% or a mirtazapine uptake of 50%.

Additionally, a 30% scale-up in ART and PrEP in the general population, combined with BI for 25% of stimulant using persons, has the potential to achieve a "functional zero HIV incidence" in 10 years. Previous modeling work that focused on improving ART and PrEP engagement for all YBMSM but did not consider stimulant use interventions specifically has indicated that a functional zero HIV incidence may be achievable in 14 years if ART and PrEP uptake are both increased by 30% over the time period.[24] Here, we found that incorporating a purposeful intervention for persons who use stimulants may help reach a functional zero level in about 10 years.

Residential rehabilitation centers are likely to be expensive (costing approximately $215/day, according to some estimates[47]) and could be implemented via drug diversion programs or increased funding for voluntary addiction treatment. Increased funding for addiction treatment could also have downstream benefits in reducing HIV incidence and associated future treatment costs.[48]Such analyses, while beyond the scope of this paper, are important next steps to consider.

Broader structural problems, such as food insecurity, housing instability, and mental illness comorbidities often impact the ability of persons using stimulants to engage in the HIV

prevention and treatment continua. As residential drug rehabilitation facilities directly or indirectly address these problems, it is not surprising that engagement in the HIV treatment and prevention continua has been found to be higher during stay in a rehabilitation center. This study demonstrates the effectiveness of residential BI, even when persons undergoing treatment return to their baseline levels of care engagement upon leaving the rehabilitation facility.

We note several limitations in this study. First, the importance of more culturally sensitive interventions to address stimulant use among YBMSM is increasingly recognized, and more research is needed to develop such interventions that are effective.[49–52]We use a simulation model that was developed for a YBMSM population, and future iterations of this work will consider the development and deployment of interventions tailored to address YBMSM community needs. Second, meth can be injected, and sharing injection equipment may increase HIV risk. Because of lack of available data, we did not model this increased HIV risk due to sharing of injection equipment, focusing instead on the impacts of meth use on engagement in the prevention and treatment continua, an area of growing concern.[53,54] Third, due to limited data on underlying parameters, we modeled stimulant use as a binary variable and only considered a simplistic scenario of intermittent stimulant use in the sensitivity analysis. Future work might consider varying degrees of use of the stimulants that are considered here, and account for more realistic models of intermittent. use. Fourth, the financial costs of implementing behavioral and biomedical treatment programs for stimulant users, and the potential economic benefits of decarceration and rehabilitation were not examined here; such assessments will be important for future policymaking guidance. Fifth, evidence on the effectiveness of alternate PrEP dosing strategies, such as on-demand and long-acting injectable PrEP is emerging.[55,56] Future iterations of this model may incorporate such dosing strategies as components of GTZ planning efforts.

Sixth, our decision to focus the interventions presented here was based on priorities identified during the GTZ planning phase. Future efforts to refine these interventions may involve contingency management, which has been shown to be effective for treating stimulant use.[57–59] Finally, as in most simulation studies, the uncertainty quantification in this model is restricted to considering the stochasticity between model runs; the full range of model uncertainty, both due to the complexity of modeling human behavior and unforeseen developments in policy and treatment is likely much greater, and difficult to fully account for.

This work begins to investigate the efficacy of interventions in a simulation model designed for a YBMSM population. Achieving GTZ goals is contingent upon a broad scale-up of biomedical prevention modalities and addressing the psychosocial and structural barriers that reduce the impact of such barriers, particularly among YBMSM who experience disproportionate HIV incidence. Direct efforts to develop culturally sensitive interventions to treat stimulant use, when implemented at scale, may be an important component of efforts to realize HIV elimination goals. Computational modeling can continue to provide much needed data to guide the implementation of such interventions.

Author Declaration

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The study was reviewed by relevant Institutional Review Boards.

References

1. Illinois Department of Public Health. *Data and Statistics: HIV Fact Sheets: Men Who Have Sex with Men*.; 2016.
2. Illinois Department of Public Health. *Data and Statistics: HIV Fact Sheet: Blacks*.; 2014.
3. Hammett TM, Gaiter JL, Crawford C. Reaching seriously at-risk populations: health interventions in criminal justice settings. *Health education & behavior : the official publication of the Society for Public Health Education*. 1998;25(1):99-120.
4. Bowleg L, Teti M, Malebranche DJ, Tschann JM. "It's an Uphill Battle Everyday": Intersectionality, Low-Income

Black Heterosexual Men, and Implications for HIV Prevention Research and Interventions. *Psychology of men & masculinity*. 2013;14(1):25-34. doi:10.1037/a0028392
5. Hojilla JC, Vlahov D, Glidden D V, et al. Skating on thin ice: stimulant use and sub-optimal adherence to HIV pre-exposure prophylaxis. *Journal of the International AIDS Society*. 2018;21(3):e25103. doi:10.1002/jia2.25103
6. Grov C, Rendina HJ, John SA, Parsons JT. Determining the Roles that Club Drugs, Marijuana, and Heavy Drinking Play in PrEP Medication Adherence Among Gay and Bisexual Men: Implications for Treatment and Research. *AIDS and behavior*. Published online October 2018. doi:10.1007/s10461-018-2309-9
7. Wray TB, Chan PA, Kahler CW, Simpanen EM, Liu T, Mayer KH. Vulnerable Periods: Characterizing Patterns of Sexual Risk and Substance Use During Lapses in Adherence to HIV Pre-Exposure Prophylaxis among Men who have Sex with Men. *Journal of acquired immune deficiency syndromes (1999)*. Published online November 2018:1. doi:10.1097/QAI.0000000000001914
8. Stimulant Use and Viral Suppression in the Era of Universal Antiretroviral Therapy. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2019;80(1):89-93. doi:10.1097/QAI.0000000000001867
9. Carrico AW, Riley ED, Johnson MO, et al. Psychiatric risk factors for HIV disease progression: The role of inconsistent patterns of antiretroviral therapy utilization. *Journal of Acquired Immune Deficiency Syndromes*. 2011;56(2):146-150. doi:10.1097/QAI.0b013e318201df63
10. Hinkin CH, Barclay TR, Castellon SA, et al. Drug Use and Medication Adherence among HIV-1 Infected Individuals. *AIDS and Behavior*. 2007;11(2):185-194. doi:10.1007/s10461-006-9152-0
11. Marquez C, Mitchell SJ, Hare CB, John M, Klausner JD. Methamphetamine use, sexual activity, patient-provider communication, and medication adherence among HIV-infected patients in care, San Francisco 2004-2006. *AIDS care*. 2009;21(5):575-582. doi:10.1080/09540120802385579
12. Mimiaga MJ, Reisner SL, Fontaine YM, et al. Walking the line: stimulant use during sex and HIV risk behavior among Black urban MSM. *Drug and alcohol dependence*. 2010;110(1-2):30-37. doi:10.1016/j.drugalcdep.2010.01.017
13. Hermanstyne KA, Green HD, Tieu HV, Hucks-Ortiz C, Wilton L, Shoptaw S. The Association Between Condomless Anal Sex and Social Support Among Black Men Who Have Sex With Men (MSM) in Six U.S. Cities: A Study Using Data from the HIV Prevention Trials Network BROTHERS Study (HPTN 061). *AIDS and Behavior*. 2018;1:3. doi:10.1007/s10461-018-2315-y
14. Hightow-Weidman L, LeGrand S, Choi SK, Egger J, Hurt CB, Muessig KE. Exploring the HIV continuum of care among young black MSM. Paraskevis D, ed. *PLOS ONE*. 2017;12(6):e0179688. doi:10.1371/journal.pone.0179688
15. Young SD, Shoptaw S. Stimulant Use Among African American and Latino MSM Social Networking Users. *Journal of Addictive Diseases*. 2013;32(1):39-45. doi:10.1080/10550887.2012.759859
16. Colfax GN, Santos GM, Das M, et al. Mirtazapine to reduce methamphetamine use: A randomized controlled trial. *Archives of General Psychiatry*. 2011;68(11):1168-1175. doi:10.1001/archgenpsychiatry.2011.124
17. Coffin PO, Santos GM, Hern J, et al. Effects of Mirtazapine for Methamphetamine Use Disorder among Cisgender Men and Transgender Women Who Have Sex with Men: A Placebo-Controlled Randomized Clinical Trial. *JAMA Psychiatry*. 2020;77(3):246-255. doi:10.1001/jamapsychiatry.2019.3655
18. AshaRani P, Hombali A, Seow E, Ong WJ, Tan JH, Subramaniam M. Non-pharmacological interventions for methamphetamine use disorder: a systematic review. *Drug and Alcohol Dependence*. 2020;212. doi:10.1016/j.drugalcdep.2020.108060
19. Gossop M, Marsden J, Stewart D. Treatment outcomes of stimulant misusers. *Addictive Behaviors*. 2000;25(4). doi:10.1016/S0306-4603(00)00063-0
20. Gossop M, Marsden J, Stewart D, Kidd T. Changes in use of crack cocaine after drug misuse treatment: 4–5 year follow-up results from the National Treatment Outcome Research Study (NTORS). *Drug and Alcohol Dependence*. 2002;66(1). doi:10.1016/S0376-8716(01)00178-8
21. Gossop M, Marsden J, Stewart D, Kidd T. The National Treatment Outcome Research Study (NTORS): 4-5 year follow-up results. *Addiction*. 2003;98(3). doi:10.1046/j.1360-0443.2003.00296.x
22. Sylla L, Bruce RD, Kamarulzaman A, Altice FL. Integration and co-location of HIV/AIDS, tuberculosis and drug treatment services. *International Journal of Drug Policy*. 2007;18(4). doi:10.1016/j.drugpo.2007.03.001
23. Farrell M, Martin NK, Stockings E, et al. Responding to global stimulant use: challenges and opportunities. *The Lancet*. 2019;394(10209). doi:10.1016/S0140-6736(19)32230-5
24. Khanna AS, Edali M, Ozik J, et al. Projecting the number of new HIV infections to formulate the “Getting to Zero” strategy in Illinois, USA. *Mathematical Biosciences and Engineering*. 2021;18(4):3922-3938. doi:10.3934/mbe.2021196

25. Okafor CN, Hucks-Ortiz C, Hightow-Weidman LB, et al. Brief Report: Associations Between Self-Reported Substance Use Behaviors and PrEP Acceptance and Adherence Among Black MSM in the HPTN 073 Study. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2020;85(1). doi:10.1097/QAI.0000000000002407
26. Khanna AS, Schneider JA, Collier N, et al. A modeling framework to inform preexposure prophylaxis initiation and retention scale-up in the context of "Getting to Zero" initiatives. *AIDS (London, England)*. 2019;33(12):1911-1922. doi:10.1097/QAD.0000000000002290
27. Recent developments in exponential random graph (p*) models for social networks. *Social Networks*. 2007;29(2):192-215. doi:10.1016/J.SOCNET.2006.08.003
28. Handcock MS, Hunter DR, Butts CT, Goodreau SM, Morris M. statnet: Software tools for the Statistical Modeling of Network Data. Published online 2003.
29. Collier N, North M. Parallel agent-based simulation with Repast for High Performance Computing. *Simulation*. 2012;89(10):1215-1235.
30. Collier N, Murphy JT, Ozik J, Tatara E. Repast for High Performance Computing. Published online 2018.
31. Khanna AS, Collier N, Ozik J. BARS: Building Agent-based Models for Racialized Justice Systems.
32. Khanna AS, Michaels S, Skaathun B, et al. Preexposure Prophylaxis Awareness and Use in a Population-Based Sample of Young Black Men Who Have Sex With Men. *JAMA internal medicine*. 2016;176(1):136-138. doi:10.1001/jamainternmed.2015.6536
33. Schneider J, Cornwell B, Jonas A, et al. Network dynamics of HIV risk and prevention in a population-based cohort of young Black men who have sex with men. *Network Science*. Published online February 1, 2017:1-29. doi:10.1017/nws.2016.27
34. Kuhns LM, Hotton AL, Schneider J, Garofalo R, Fujimoto K. Use of Pre-exposure Prophylaxis (PrEP) in Young Men Who Have Sex with Men is Associated with Race, Sexual Risk Behavior and Peer Network Size. *AIDS and Behavior*. 2017;21(5):1376-1382. doi:10.1007/s10461-017-1739-0
35. Fujimoto K, Cao M, Kuhns LM, Li D, Schneider JA. Statistical adjustment of network degree in respondent-driven sampling estimators: Venue attendance as a proxy for network size among young MSM. *Social Networks*. 2018;54:118-131. doi:10.1016/j.socnet.2018.01.003
36. Paz-Bailey G, Mendoza MCB, Finlayson T, et al. Trends in condom use among MSM in the United States. *AIDS*. 2016;30(12):1985-1990. doi:10.1097/QAD.0000000000001139
37. Hojilla JC, Satre DD, Glidden D V., et al. Brief Report: Cocaine Use and Pre-exposure Prophylaxis: Adherence, Care Engagement, and Kidney Function. *Journal of Acquired Immune Deficiency Syndromes*. 2019;81(1):78-82. doi:10.1097/QAI.0000000000001972
38. Hojilla JC, Vlahov D, Crouch PC, Dawson-Rose C, Freeborn K, Carrico A. HIV Pre-exposure Prophylaxis (PrEP) Uptake and Retention Among Men Who Have Sex with Men in a Community-Based Sexual Health Clinic. *AIDS and Behavior*. 2018;22(4):1096-1099. doi:10.1007/s10461-017-2009-x
39. Preexposure prophylaxis awareness and use in a population-based sample of young black men who have sex with men. *JAMA Internal Medicine*. 2016;176(1). doi:10.1001/jamainternmed.2015.6536
40. Network dynamics of HIV risk and prevention in a population-based cohort of young Black men who have sex with men. *Network Science*. Published online February 2017:1-29. doi:10.1017/nws.2016.27
41. Wu E, El-Bassel N, Donald McVinney L, et al. Feasibility and Promise of a Couple-Based HIV/STI Preventive Intervention for Methamphetamine-Using, Black Men Who have Sex with Men. *AIDS and Behavior*. 2011;15(8):1745-1754. doi:10.1007/s10461-011-9997-8
42. Mimiaga MJ, Pantalone DW, Biello KB, et al. A randomized controlled efficacy trial of behavioral activation for concurrent stimulant use and sexual risk for HIV acquisition among MSM: project IMPACT study protocol. *BMC Public Health*. 2018;18(1):914. doi:10.1186/s12889-018-5856-0
43. Mimiaga MJ, Pantalone DW, Biello KB, et al. An initial randomized controlled trial of behavioral activation for treatment of concurrent crystal methamphetamine dependence and sexual risk for HIV acquisition among men who have sex with men. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*. 2019;31(9):1083-1095. doi:10.1080/09540121.2019.1595518
44. Moos RH, Moos BS, Andrassy JM. Outcomes of Four Treatment Approaches in Community Residential Programs for Patients With Substance Use Disorders. *Psychiatric Services*. 1999;50(12):1577-1583. doi:10.1176/ps.50.12.1577
45. Babudieri S, Dorrucci M, Boschini A, et al. Targeting Candidates for Directly Administered Highly Active Antiretroviral Therapy: Benefits Observed in HIV-Infected Injecting Drug Users in Residential Drug-Rehabilitation Facilities. *AIDS Patient Care and STDs*. 2011;25(6). doi:10.1089/apc.2010.0229

46. Lim SH, Ostrow D, Stall R, et al. Changes in Stimulant Drug Use Over Time in the MACS: Evidence for Resilience Against Stimulant Drug Use Among Men Who Have Sex with Men. *AIDS and Behavior*. 2012;16(1):151-158. doi:10.1007/s10461-010-9866-x
47. Recovery Centers of America. Economic Cost of Substance Abuse in the United States, 2016. Retrieved September 10, 2021 from https://recoverycentersofamerica.com/economic-cost-substance-abuse/.
48. Metzger DS, Woody GE, O'Brien CP. Drug Treatment as HIV Prevention: A Research Update. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2010;55(Supplement 1). doi:10.1097/QAI.0b013e3181f9c10b
49. Dangerfield DT, Cooper J, Heidari O, Allen S, Winder TJA, Lucas GM. Nursing and Health Care Preferences Among Opioid and Stimulant Using Black Sexual Minority Men: An Exploratory Study. *Journal of the Association of Nurses in AIDS Care*. 2021;32(5). doi:10.1097/JNC.0000000000000201
50. Sanchez K, Greer TL, Walker R, Carmody T, Rethorst CD, Trivedi MH. Racial and ethnic differences in treatment outcomes among adults with stimulant use disorders after a dosed exercise intervention. *Journal of Ethnicity in Substance Abuse*. 2017;16(4). doi:10.1080/15332640.2017.1317310
51. Sanchez K, Ybarra R, Chapa T, Martinez ON. Eliminating Behavioral Health Disparities and Improving Outcomes for Racial and Ethnic Minority Populations. *Psychiatric Services*. 2016;67(1). doi:10.1176/appi.ps.201400581
52. Saloner B, Cook BL. Blacks And Hispanics Are Less Likely Than Whites To Complete Addiction Treatment, Largely Due To Socioeconomic Factors. *Health Affairs*. 2013;32(1). doi:10.1377/hlthaff.2011.0983
53. Jin H, Ogunbajo A, Mimiaga MJ, et al. Over the influence: The HIV care continuum among methamphetamine-using men who have sex with men. *Drug and Alcohol Dependence*. 2018;192:125-128. doi:10.1016/j.drugalcdep.2018.07.038
54. Horvath KJ, Carrico AW, Simoni J, Boyer EW, Amico KR, Petroll AE. Engagement in HIV Medical Care and Technology Use among Stimulant-Using and Nonstimulant-Using Men who have Sex with Men. *AIDS Research and Treatment*. 2013;2013:1-11. doi:10.1155/2013/121352
55. Durand-Zaleski I, Mutuon P, Charreau I, et al. Costs and benefits of on-demand HIV preexposure prophylaxis in MSM. *AIDS*. 2018;32(1). doi:10.1097/QAD.0000000000001658
56. Kerrigan D, Mantsios A, Grant R, et al. Expanding the Menu of HIV Prevention Options: A Qualitative Study of Experiences with Long-Acting Injectable Cabotegravir as PrEP in the Context of a Phase II Trial in the United States. *AIDS and behavior*. 2018;22(11). doi:10.1007/s10461-017-2017-x
57. Shoptaw S, Landovitz RJ, Reback CJ. Contingent Vs. Non-Contingent Rewards: Time-Based Intervention Response Patterns Among Stimulant-Using Men Who Have Sex With Men. *Journal of Substance Abuse Treatment*. 2017;72. doi:10.1016/j.jsat.2016.09.004
58. Corsi KF, Shoptaw S, Alishahi M, Booth RE. Interventions to Reduce Drug Use Among Methamphetamine Users at Risk for HIV. *Current HIV/AIDS Reports*. 2019;16(1). doi:10.1007/s11904-019-00423-y
59. Stitzer ML, Gukasyan N, Matheson T, et al. Enhancing patient navigation with contingent financial incentives for substance use abatement in persons with HIV and substance use. *Psychology of Addictive Behaviors*. 2020;34(1). doi:10.1037/adb0000504
60. Centers for Disease Control and Prevention. CDC Wonder. Published 2017. Accessed January 15, 2022. http://wonder.cdc.gov/ucd-icd10.html.
61. Preexposure Prophylaxis Initiation and Retention in Care Over 5 Years, 2012-2017: Are Quarterly Visits Too Much? *Clinical infectious diseases*. 2018;67(2):283-287. doi:10.1093/cid/ciy160
62. Jenness SM, Weiss KM, Goodreau SM, et al. Incidence of Gonorrhea and Chlamydia Following HIV Preexposure Prophylaxis among Men Who Have Sex with Men: A Modeling Study. *Clinical Infectious Diseases*. Published online May 13, 2017. doi:10.1093/cid/cix439

Table 1: Parameters to Model HIV Transmission among young Black men who have sex with men (YBMSM), Illinois.		
Demography		
Parameter	**Estimate**	**Source**
Age range	[18 – 34) years	Defined population of interest
Departures from simulated population	- All agents achieving age > 34 years exit the population. - At any time in the simulation, agents uninfected with HIV experience mortality rates estimated in accordance with age-specific mortality for Chicago. Agents infected with HIV experience mortality rates determined by their CD4 counts.	-As per the defined age range of the population of interest - Estimated from the CDC Wonder database[60]
Stimulant Use		
Rates of stimulant use (% of all simulated agents)	Methamphetamines: 9.2% Crack/cocaine: 17.4% Ecstasy: 4.0%	Cohort data of YBMSM in Chicago (see Appendix Section A.4.9)
Sexual Behavior		
Mean partnership duration	All agents - Main: 512 days. Casual: 160 days. - No difference assumed between stimulant users and non-stimulant users.	Per NHBS data from Chicago[36] (see Appendix Section A.4.3)
Mean number of main partnerships of stimulant users (per person) on any given day	Stimulant users - Methamphetamines: 0.69 - Crack/cocaine: 0.61 - Ecstasy: 0.59	Cohort data of YBMSM in Chicago[32,33] and Appendix Section A.3
Mean number of casual partnerships (per person) on any given day	Stimulant users - Methamphetamines: 0.71 - Crack/cocaine: 0.63 - Ecstasy: 0.63	Cohort data of YBMSM in Chicago[32,33] and Appendix Section A.3
Adherence to Antiretroviral Treatment (ART)		
Distribution of ART adherence	Non-stimulant users: - Never adherent: 10% - Sometimes adherent: 30% - Usually adherent: 28% - Always adherent: 32% Stimulant users[*†] - Methamphetamines: 42% decline in percent always adherent - Crack/cocaine: 50% decline in percent always adherent - Ecstasy: 39% decline in percent always adherent	Cohort data of YBMSM in Chicago. [32,33](Details on ART adherence in the overall population are in Appendix Sections A.4.7 and adherence among stimulant using persons is described in Section A.4.9.)
PrEP Use		
Mean % of HIV-negative persons who are prescribed PrEP on any given day	Non-stimulant users: 13.7% Stimulant users: - Methamphetamines: 5.4% - Crack/cocaine: 7.1% - Ecstasy: 4.6%	Cohort data of YBMSM in Chicago[32,33] and Section A.4.10.

Mean time that a PrEP user is retained on PrEP	Non-stimulant users: 1 year Stimulant Users: 9 months	Clinic-based data from Chicago[61] (see additional details in Appendix Sections A.4.8 and A.4.10)
Adherence to PrEP among PrEP initiators	Non-stimulant users - Suboptimal adherence (0-3 pills/week): 38.1% -Optimal adherence (4+ pills/week): 61.9% Stimulant users: - Suboptimal adherence (0-3 pills/week):76% -High adherence (4+ pills/week):24%	Parameters for PrEP adherence in the overall population and among stimulant users are derived in Appendix Sections A.4.8 and A.4.10 respectively
Reduction in transmission associated with levels of PrEP adherence	Non-adherence: 0%; low: 31%; moderate: 81%; high: 95%	Consistent with PrEP effectiveness rates in other modeling studies [26,62]
[*]Persons always adherent to ART experiencing imperfect adherence due to stimulant use are uniformly distributed across the three other categories (usually, sometimes, and never adherent). [†]Users of multiple substances experience the highest declines associated with the substances of use.		

Table 2A: Mean HIV incidence rate and the number of new HIV infections in the overall population in the tenth year after the implementation of the behavioral and biomedical interventions for all persons who use stimulants.		
	10th year HIV Incidence in the full population (per 100 person years)	**New HIV Infections in 10th Year (full population)**
Scenario		
Baseline	6.93(6.83,7.04)	453 (445,461)
Behavioral Intervention (BI)		
Uptake†		
10%	5.39 (5.26,5.52)	379 (370,386)
15%	5.12 (5.02,5.23)	365 (358,372)
20%	4.84 (4.72,4.95)	348 (340,357)
25%	4.51 (4.42,4.6)	330 (324,337)
Mirtazapine		
Uptake††		
25%	6.11 (5.96,6.25)	411 (402,421)
50%	5.88 (5.74,5.99)	402 (394,410)
75%	5.76 (5.64,5.88)	400 (391,409)
100%	5.54 (5.43,5.66)	387 (380,396)

Table 2B: Mean HIV incidence rate and the number of new HIV infections among methamphetamine users in the tenth year after the implementation of the behavioral and biomedical interventions for persons who use methamphetamines only.		
Scenario	**10th year HIV Incidence among methamphetamine users** (per 100 person years)	**New HIV Infections in 10th Year (methamphetamine users)**
Baseline	10.63 (10.09,11.17)	47 (45,49)
Behavioral Intervention (BI)		
Uptake§		
10	7.14 (6.68,7.65)	37 (35,40)
15	6.34 (5.9,6.76)	34 (32,37)
20	5.92 (5.59,6.27)	33 (31,35)
25	5.58 (5.30,5.82)	31 (30,33)
Mirtazapine		
Uptake††		
25	7.18 (6.73,7.6)	37 (35,39)
50	6.37 (5.9,6.83)	34 (31,37)
75	5.66 (5.27,6.03)	32 (30,35)
100	4.71 (4.38,5.03)	28 (26,30)

†Proportion of persons using stimulants who receive the behavioral intervention (BI)
††Proportion of persons using methamphetamines who receive mirtazapine prescriptions
§Proportion of persons using methamphetamines who receive the Behavioral Intervention (BI)

Table 3: Impacts of Behavioral Intervention (BI) for stimulant users on mean HIV incidence rate and the number of new HIV infections in the overall population in the tenth year when ART and PrEP use are also scaled up for everyone			
ART and PrEP use for the full population	**Targeted Behavioral Intervention (BI) for Stimulant Using Persons***	**HIV Incidence in 10th Year (per 100 person years)**	**New HIV Infections in 10th Year**
20% increase in ART and PrEP use across the full population over 10 years	None	4.63 (4.52,4.75)	329 (321,337)
	10%	3.12 (3.04,3.21)	240 (234,246)
	15%	2.97 (2.9,3.03)	230 (225,236)
	20%	2.74 (2.67,2.82)	215 (209,221)
	25%	2.6 (2.52,2.68)	205 (199,211)
30% increase in ART and PrEP use across the full population over 10 years	None	3.86 (3.77,3.94)	281 (276,287)
	10%	2.87 (2.78,2.97)	222 (215,230)
	15%	2.72 (2.66,2.78)	212 (207,217)
	20%	2.6 (2.52,2.68)	205 (198,211)
	25%	2.48 (2.39,2.57)	197 (189,204)
*Proportion of persons using stimulants who receive BI			

Figure 1A: HIV incidence rate in the overall population after implementation of the residential behavioral intervention (BI) for persons who use any of the three stimulants (methamphetamines, ecstasy, or crack/cocaine).

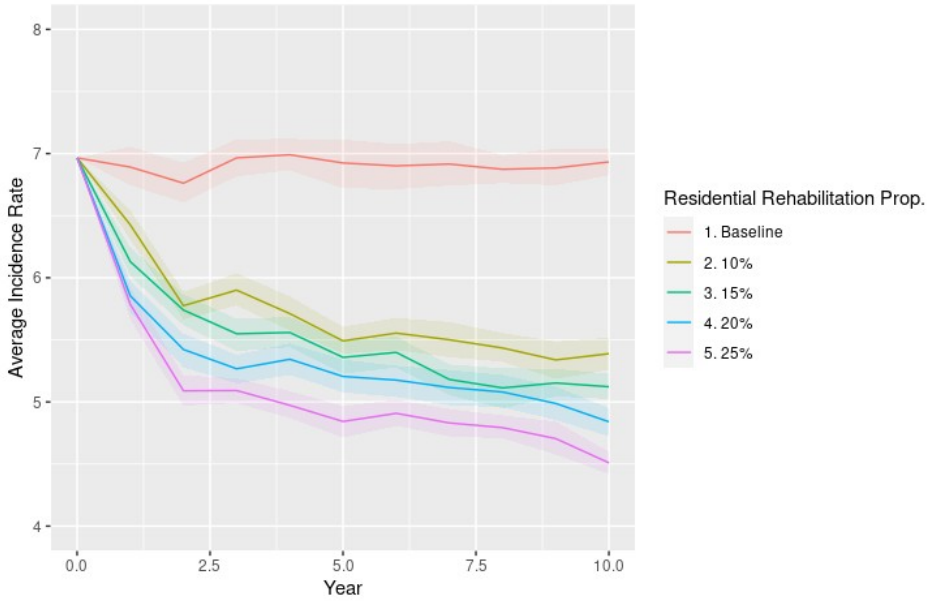

Figure 1B: HIV incidence rate in the overall population after implementation of the the mirtazapine intervention for persons who use methamphetamines.