Supplement S2: Additional Figures

Outbreak Forecasting, Methamphetamine Trajectories, Scenario Comparisons, Cascade Uncertainty, R_0ZeroDistributions, Barrier Removal Impact and Step Importance

Supporting the manuscript:

Structural barriers drive near-zero population-level effectiveness of Long Acting Injectable HIV prevention (LAI-PrEP) among people who inject drugs: A Computational Modeling Study

AC Demidont, DO

Independent Researcher, Nyx Dynamics LLC
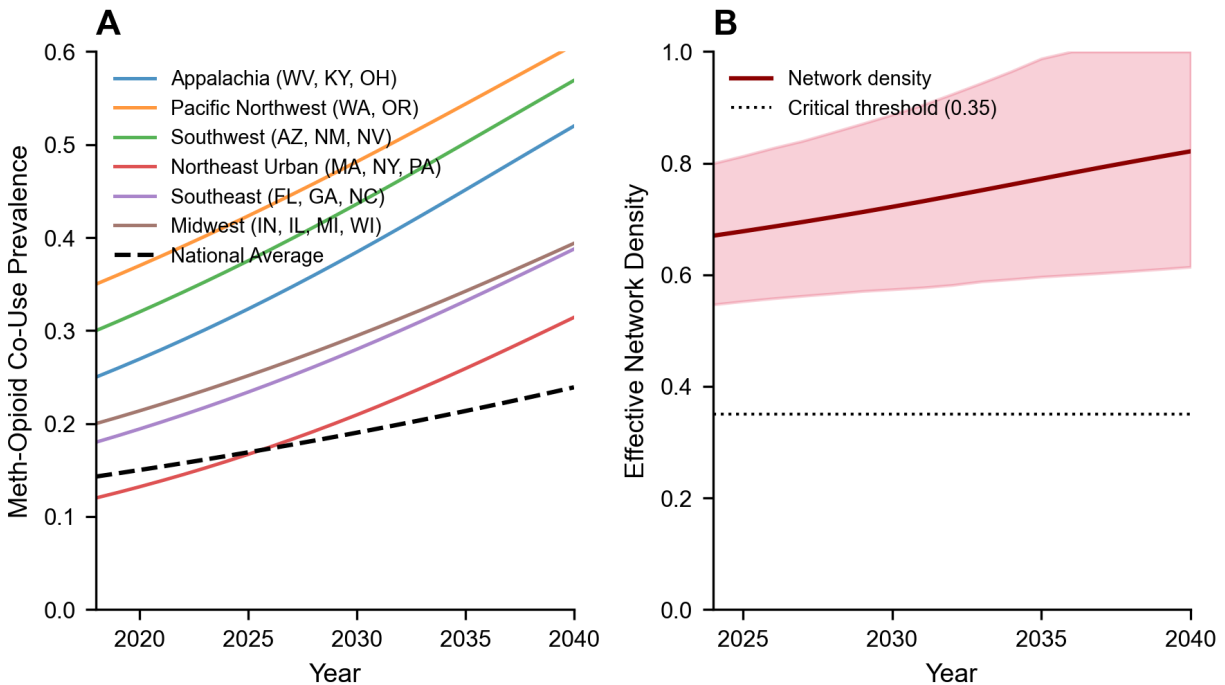
December 27, 2025

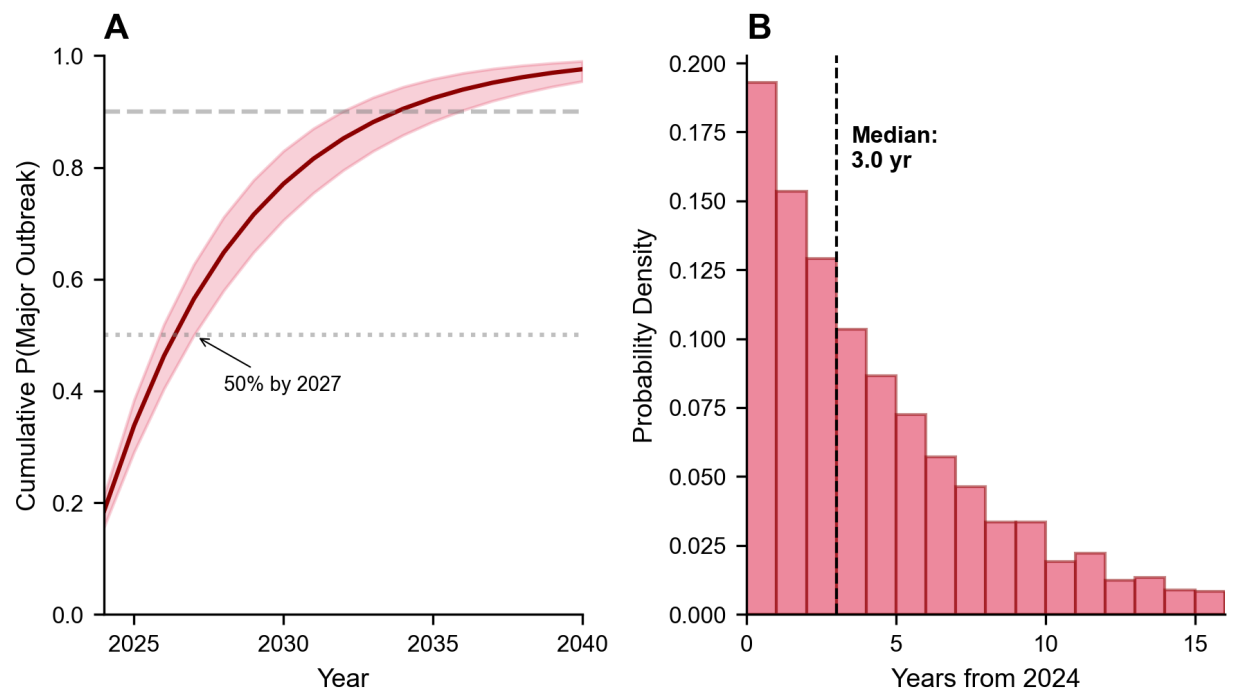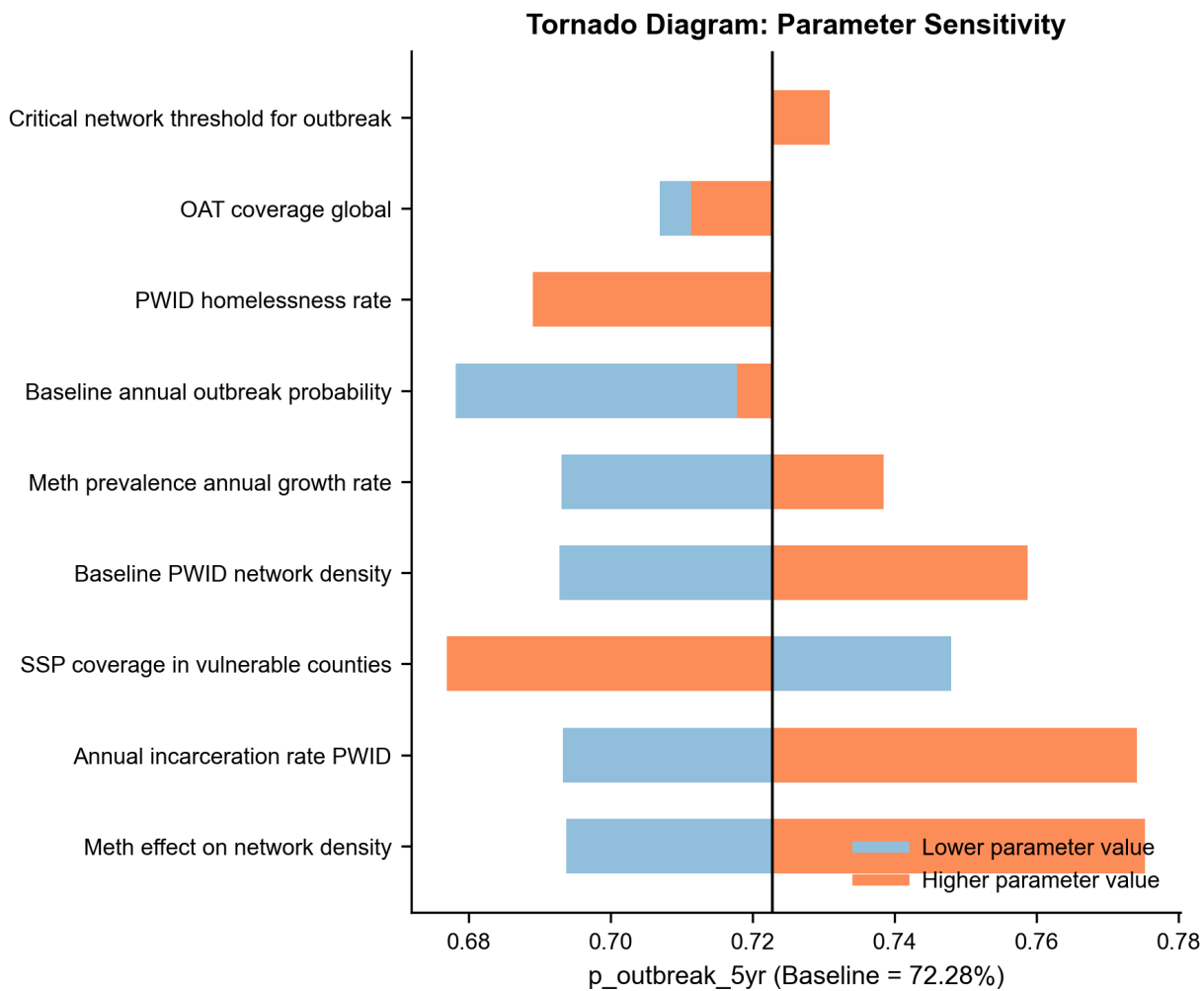## Supplementary Figures

Figure S1

A

Cumulative P(Major Outbreak)

50% by 2027

Year

B

Probability Density

Median:
3.0 yr

Years from 2024

Figure S2

Tornado Diagram: Parameter Sensitivity

Critical network threshold for outbreak
OAT coverage global
PWID homelessness rate
Baseline annual outbreak probability
Meth prevalence annual growth rate
Baseline PWID network density
SSP coverage in vulnerable counties
Annual incarceration rate PWID
Meth effect on network density

Lower parameter value
Higher parameter value

p_outbreak_5yr (Baseline = 72.28%)

Figure S3

A

OAT Expansion (40%)	
Current Policy	
SSP Expansion (50%)	
Decriminalization Effect	
Combined SSP+OAT	
Full Harm Reduction	

P(Outbreak within 5 years) %

B

Median Years to Outbreak

Figure S4

Awareness	Willingness	Healthcare Access	Disclosure

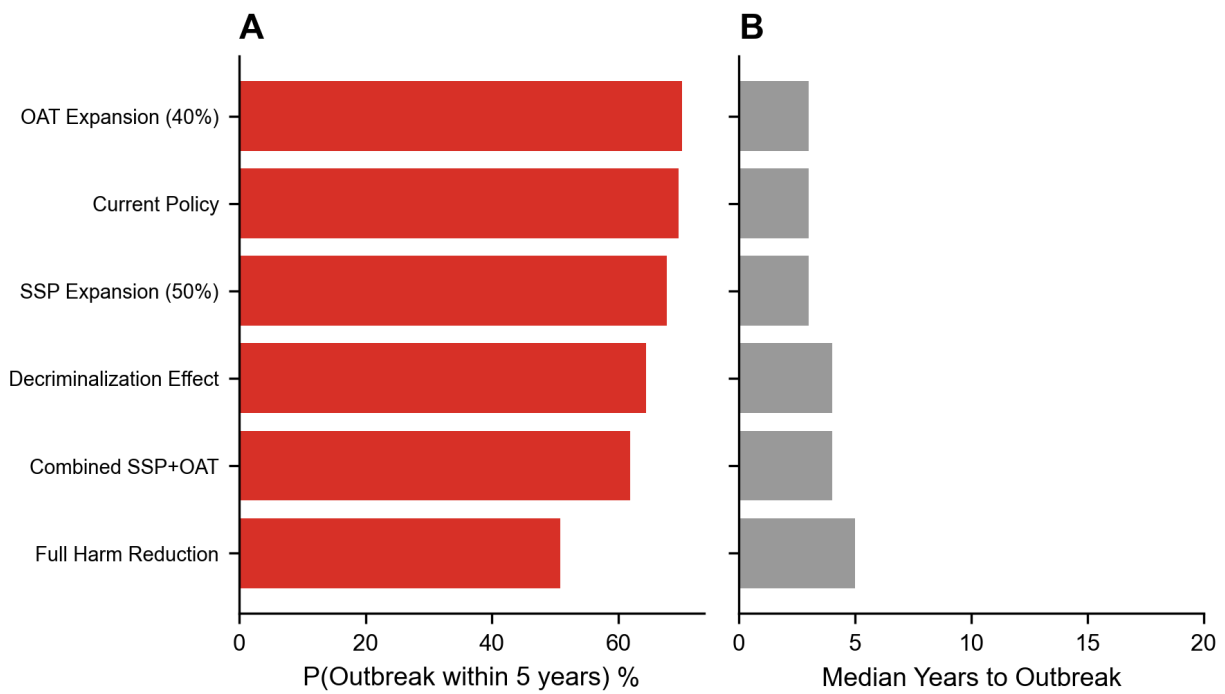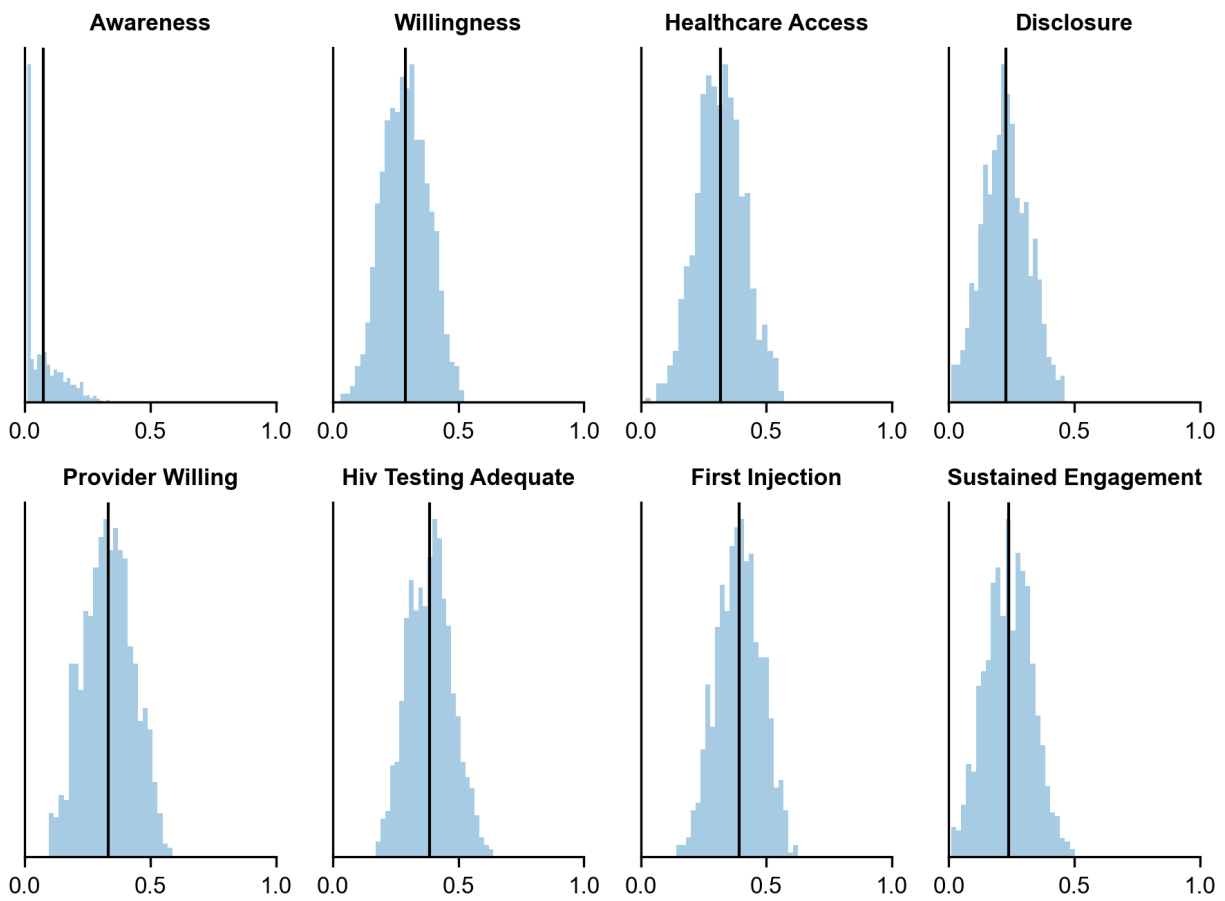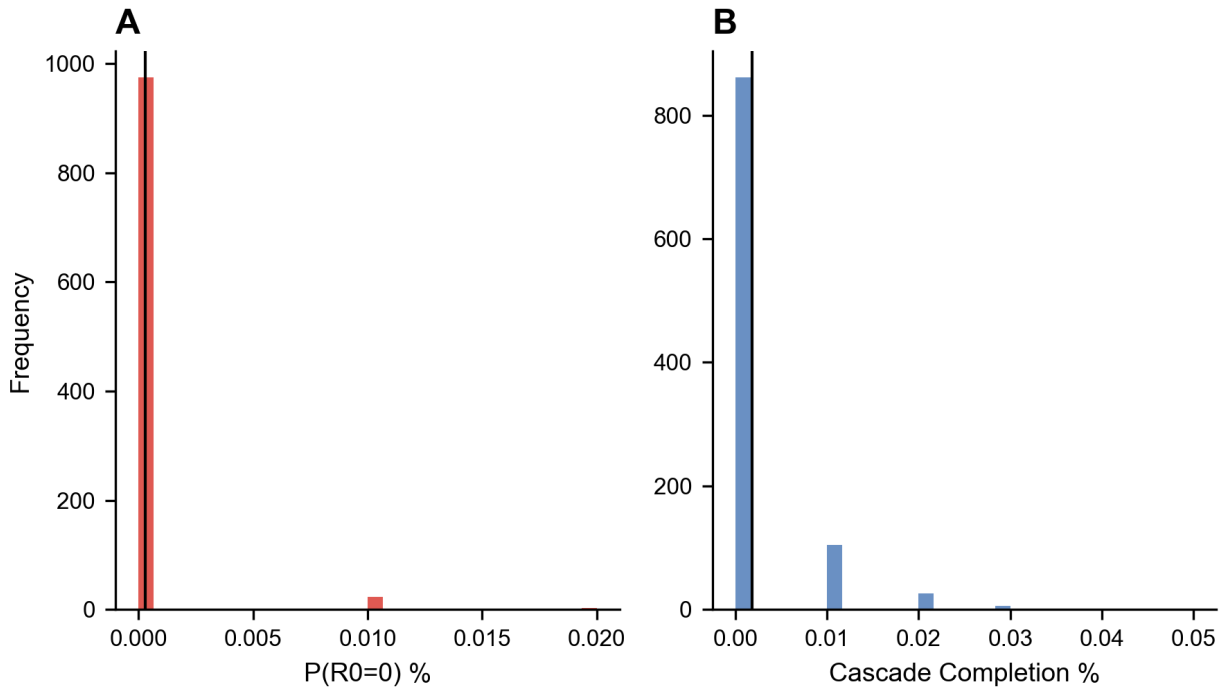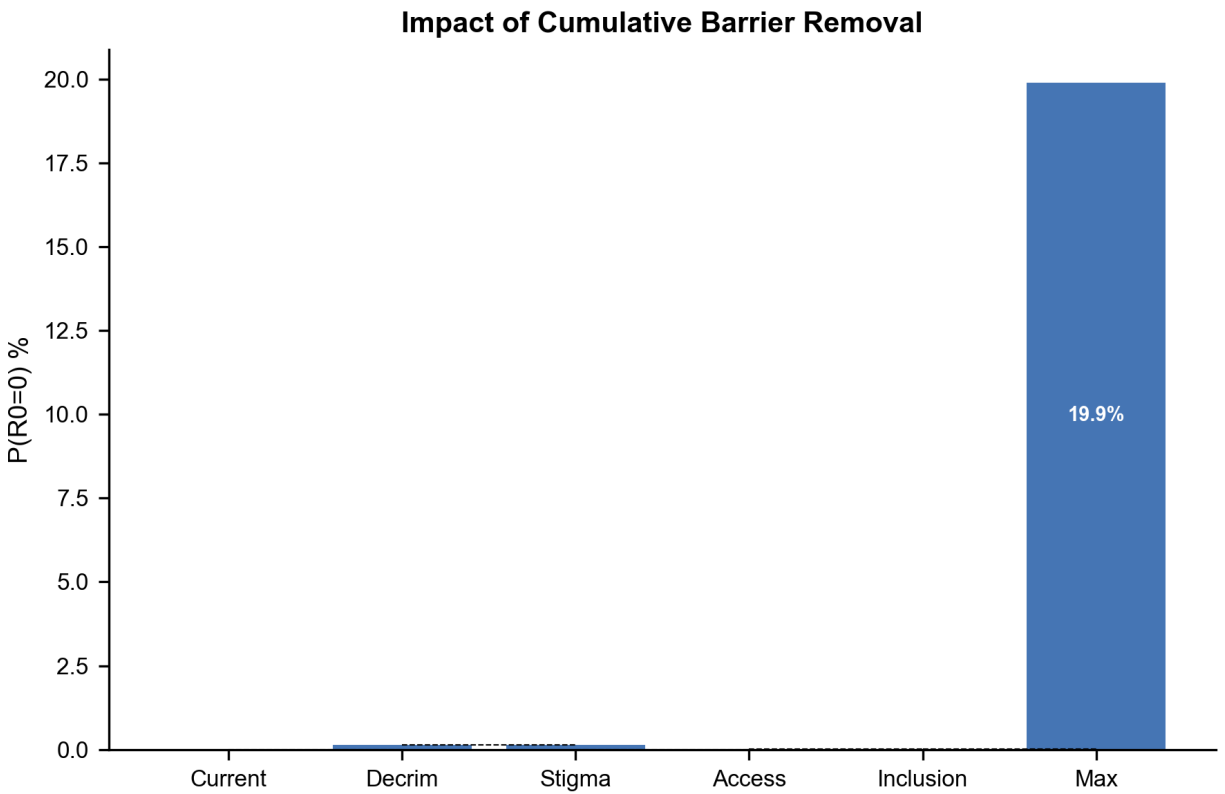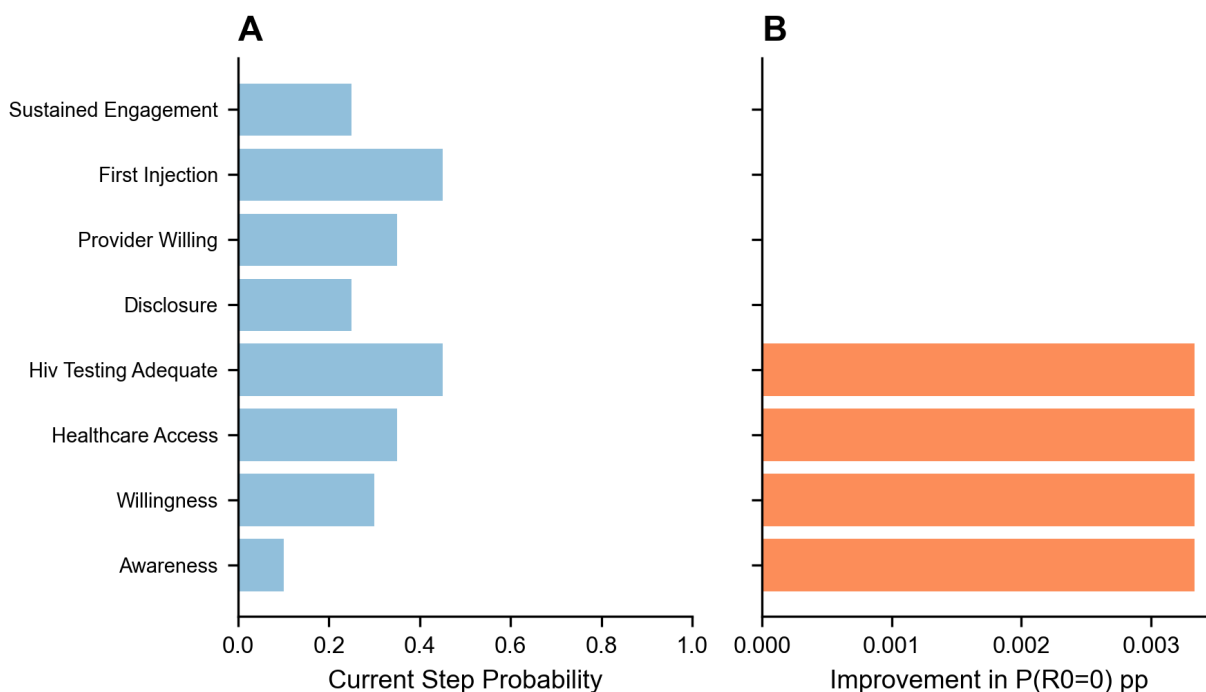| Provider Willing	Hiv Testing Adequate	First Injection	Sustained Engagement

Figure S5

5

Figure S6

Figure S7

Figure S8

Supplementary Figure Legends

Figure S1–S8. Supplementary analyses supporting cascade failure, barrier dominance, and outbreak inevitability among PWID.

Figure S1. Methamphetamine prevalence trajectories used in stochastic avoidance modeling. Projected regional methamphetamine prevalence trajectories among people who inject drugs (PWID) over a 10-year horizon, stratified by U.S. region. Trajectories were parameterized from national surveillance and cohort data demonstrating increasing stimulant injection and opioid–methamphetamine co-use.[1, 2, 3, 4, 5, 6, 7]

Figure S2. Stochastic avoidance failure and outbreak probability over time. Cumulative probability of a major HIV outbreak among PWID under current policy conditions, estimated using Monte Carlo simulation incorporating network density evolution, methamphetamine prevalence, housing instability, and incarceration rates.

Figure S3. Tornado diagram of parameter sensitivity for 5-year outbreak probability. One-way sensitivity analysis showing the relative influence of model parameters on predicted outbreak probability at 5 years.

Figure S4. Policy scenario comparison for achieving sustained protection ($R_0 = 0$). Comparison of eight policy scenarios illustrating the probability of achieving sustained HIV protection among PWID over 5 years.

Figure S5. Cascade uncertainty and probabilistic completion distribution. Distribution of prevention cascade completion probabilities across probabilistic sensitivity analyses.

7

Figure S6. Distribution of $R_0 = 0$ outcomes under Monte Carlo simulation. Histogram of achieved sustained protection outcomes across 100,000 simulated PWID under current policy conditions.

Figure S7. Barrier removal analysis showing incremental gains in prevention probability. Sequential removal of individual barrier classes illustrating their incremental contribution to prevention probability.

Figure S8. Relative importance of cascade steps in determining prevention failure. Step-importance analysis quantifying the proportion of total cascade failure attributable to each prevention stage.

References

[1] M. R. Golden, R. Lechtenberg, S. N. Glick, J. Dombrowski, J. Duchin, J. R. Reuer, S. Dhanireddy, S. Neme, S. E. Buskin, Outbreak of Human Immunodeficiency Virus Infection Among Heterosexual Persons Who Are Living Homeless and Inject Drugs — Seattle, Washington, 2018, MMWR. Morbidity and Mortality Weekly Report 68 (15) (2019) 344–349. doi:10.15585/mmwr.mm6815a2.
URL http://www.cdc.gov/mmwr/volumes/68/wr/mm6815a2.htm?s_cid=mm6815a2_w

[2] S. N. Glick, R. Burt, K. Kummer, J. Tinsley, C. J. Banta-Green, M. R. Golden, Increasing methamphetamine injection among non-MSM who inject drugs in King County, Washington, Drug Alcohol Depend 182 (2018) 86–92. doi:10.1016/j.drugalcdep.2017.10.011.

[3] J. Walters, L. Busy, C. Hamel, K. Junge, T. Menza, J. Mitchell, T. Pinsent, K. Toevs, J. Vines, Use of injection drugs and any form of methamphetamine in the Portland, OR metro area as a driver of an HIV time-space cluster: Clackamas, Multnomah, and Washington Counties, 2018-2020, AIDS Behav 26 (6) (2022) 1717–1726. doi:10.1007/s10461-021-03522-3.

[4] M. M. Van Handel, C. E. Rose, E. J. Hallisey, J. L. Kolling, J. E. Zibbell, B. Lewis, M. K. Bohm, C. M. Jones, B. E. Flanagan, A.-E.-A. Siddiqi, K. Iqbal, A. L. Dent, J. H. Mermin, E. McCray, J. W. Ward, J. T. Brooks, County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among persons who inject drugs, United States, J Acquir Immune Defic Syndr 73 (3) (2016) 323–331. doi:10.1097/QAI.0000000000001098.

[5] R. A. Bonacci, A. C. Moorman, D. Bixler, M. Penley, S. Wilson, A. Hudson, R. P. McClung, Prevention and care opportunities for people who inject drugs in an HIV outbreak - Kanawha County, West Virginia, 2019-2021, J Gen Intern Med 38 (3) (2023) 828–831. doi:10.1007/s11606-022-07875-w.

[6] R. P. McClung, et al., Response to a large HIV outbreak, Cabell County, West Virginia, 2018–2019, Am J Prev Med (2021). doi:10.1016/j.amepre.2021.05.039.

[7] M. W. Plankey, et al., The relationship between methamphetamine and popper use and risk of HIV seroconversion in the multicenter AIDS cohort study, J Acquir Immune Defic Syndr 45 (1) (2007) 85–92. doi:10.1097/QAI.0b013e318032beca.