

1                   **Manufactured Death: Mathematical Modeling of HIV Prevention**  
2                   **Impossibility Among People Who Inject Drugs**

3                   *A Barrier Decomposition Analysis*

4                   AC Demidont, DO<sup>1</sup>

5                   <sup>1</sup>Independent Researcher; Nyx Dynamics LLC

6                   **Correspondence to:**

7                   AC Demidont, DO

8                   Nyx Dynamics LLC

9                   Email: acdemidont@nyxdynamics.org

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16 **Abstract**

17 **Background:** For decades, HIV prevention experts have warned that people who inject drugs (PWID) face  
18 structural barriers requiring comprehensive policy reform. These warnings have been largely ignored. We  
19 developed a computational model to quantify these barriers, validate expert consensus, and—critically—  
20 estimate the timeline before stochastic avoidance fails and catastrophic outbreaks become inevitable.

21 **Methods:** We constructed a three-layer barrier framework decomposing HIV prevention failure into  
22 pathogen biology, HIV testing limitations, and architectural failures (policy, stigma, infrastructure, research  
23 exclusion, and algorithmic bias). Monte Carlo simulation ( $n=100,000$  per scenario) quantified cascade com-  
24 pletion probability for long-acting injectable pre-exposure prophylaxis (LAI-PrEP) across eight policy sce-  
25 narios. A stochastic avoidance failure model predicted outbreak probability incorporating methamphetamine  
26 prevalence trajectories and network density evolution.

27 **Findings:** Under current policy,  $P(R_0=0) = 0.00\%$  for PWID versus 16.30% for men who have sex with  
28 men (MSM) receiving identical pharmacological intervention. Architectural failures accounted for 93.2%  
29 of prevention failure. No single barrier removal achieved meaningful improvement; only comprehensive  
30 reform approached efficacy. Most critically, our model predicts 63.3% probability of major outbreak within  
31 5 years (median: 4.0 years), with regional variation reflecting methamphetamine penetration. Without algo-  
32 rithmic debiasing, machine learning systems will function as Weapons of Math Destruction, systematically  
33 excluding PWID from prevention access through a self-reinforcing negative feedback loop.

34 **Interpretation:** Our findings validate decades of expert warnings while providing what the literature  
35 has lacked: a timestamp. COVID-19 demonstrated that stochastic avoidance is time-limited; our model  
36 quantifies when this protection will fail for PWID. The barriers are known, the solutions are known, and  
37 now the deadline is known. What remains is the political will to act before mathematical certainty becomes  
38 human catastrophe.

39 **Funding:** None.

40 **Research in Context**

41 **Evidence before this study**

42 We searched PubMed for articles published from January 1, 2010, to December 1, 2024, using the terms  
43 “HIV prevention,” “people who inject drugs,” “PrEP,” “structural barriers,” and “HIV outbreak.” The lit-  
44 erature reveals a consistent pattern: experts have repeatedly identified the barriers preventing HIV preven-  
45 tion among PWID (criminalization, stigma, healthcare discrimination, research exclusion) and have repeat-  
46 edly proposed solutions (decriminalization, harm reduction integration, SSP expansion, research inclusion).  
47 These recommendations have been systematically ignored. Multiple U.S. outbreaks since 2015 occurred in  
48 settings where warnings had been issued years earlier. What the literature lacks is not knowledge of barriers  
49 or solutions, but quantification of the timeline before inaction produces catastrophe.

50 **Added value of this study**

51 This study validates expert consensus through computational modeling while providing what previous work  
52 has not: a countdown. Our three-layer barrier framework quantifies barrier contributions (93.2% architec-  
53 tural, 6.8% testing, 0.0% pathogen biology), confirming that prevention failure is policy-manufactured. The  
54 stochastic avoidance failure model provides the first mathematical prediction of outbreak probability over  
55 time (63% within 5 years, median 4.0 years). We identify machine learning algorithms as an emerging  
56 threat that will systematically exclude PWID through biased training data, creating self-reinforcing negative  
57 feedback loops that O’Neil termed “Weapons of Math Destruction.”

58 **Implications of all the available evidence**

59 The scientific evidence for what must be done has existed for decades. Our contribution is the timestamp: we  
60 are quantifying how long humanity has before ignoring expert consensus produces predictable catastrophe.  
61 COVID-19 proved that stochastic avoidance—hoping probability protects us from transmissible disease—  
62 fails catastrophically when conditions change. Our model applies this lesson to HIV among PWID. The  
63 barriers are known. The solutions are known. The deadline is now known. What remains is political will.

## 64 1 Introduction

65 Among the estimated 15.6 million people who inject drugs (PWID) globally, 17.8% are living with HIV.<sup>1</sup>  
66 For three decades, experts in HIV prevention have issued warnings about this population: that criminaliza-  
67 tion drives transmission,<sup>2</sup> that healthcare stigma prevents care engagement,<sup>3</sup> that research exclusion leaves  
68 interventions unvalidated,<sup>4</sup> and that comprehensive harm reduction—not piecemeal reform—is required.<sup>5</sup>  
69 These warnings have been systematically ignored.

70 The reasons for inaction are not mysterious. Multiple, oppositional financial motivations create struc-  
71 tural resistance to change. Decriminalization would benefit PWID but eliminate revenue streams for crimi-  
72 nal justice systems built on drug enforcement. Pharmaceutical corporations manufacturing HIV prevention  
73 agents also manufacture HIV treatment agents, complicating their strategic calculus. Healthcare systems  
74 profit from treating preventable infections. And underlying all of this is a societal calculation—rarely spo-  
75 ken but operationally evident—that PWID are a population the majority is willing to allow to vanish from  
76 existence.

77 We developed a computational model not to discover what experts already know, but to quantify it—and,  
78 critically, to provide what the literature has lacked: a timestamp. COVID-19 demonstrated with tragic clarity  
79 that stochastic avoidance—the hope that probability will protect humanity from transmissible infectious  
80 disease—is a time-limited phenomenon. When conditions change, when network density crosses critical  
81 thresholds, probability fails and catastrophe follows. Our model applies this lesson to HIV among PWID.

82 The findings presented here align precisely with what Strathdee, Altice, Des Jarlais, and others have  
83 warned for years.<sup>5,6</sup> Single barrier removals will not produce meaningful change. Policy overhaul must be  
84 comprehensive. Machine learning algorithms trained on biased data will perpetuate exclusion. And time is  
85 running out. Our contribution is not the identification of these truths but their mathematical formalization—  
86 including the calculation that, under current conditions, we have a median of 4 years before stochastic  
87 avoidance fails and a catastrophic outbreak among PWID becomes not merely possible but probable.

## 88    2    Background: The Transformative Potential of Biomedical Prophylaxis

89    Advances in biomedical prophylaxis of transmissible infectious diseases provide profound opportunities  
90    for both populations and individuals. At the societal level, long-acting injectable HIV PrEP (LAI-PrEP)  
91    overcomes the primary barrier to oral PrEP success—adherence—presenting the first agents truly capable  
92    of ending the HIV epidemic.<sup>7</sup> The implications extend beyond HIV: malarial chemoprophylaxis enables  
93    travel to destinations that would otherwise carry significant health consequences; vaccination programs  
94    have eliminated diseases that once devastated generations.

95       Perhaps more importantly, biomedical prophylaxis provides individuals the freedom to make autonomous  
96    choices while remaining protected should those choices lead to exposure. For men who have sex with men  
97    (MSM) around the world, effective HIV treatment, PrEP, and bacterial STI post-exposure prophylaxis have  
98    transformed sexual health, enabling sex-positivity that has forced revisions to medical training curricula  
99    globally.<sup>7</sup> The success of these implementations demonstrates a critical principle: prevention succeeds when  
100   it fits sufficiently within an individual's autonomy and can be feasibly incorporated into daily priorities.

101      This principle illuminates both the promise and the failure of current approaches to PWID. LAI-PrEP's  
102   every-two-month dosing schedule should represent an ideal fit for populations whose lives are characterized  
103   by instability, competing survival priorities, and barriers to daily medication adherence. Yet our analysis  
104   demonstrates that PWID cannot access this protection—not because of the drug's properties, but because of  
105   architectural barriers that prevent the intervention from reaching them.

<sup>106</sup> **3 Methods**

<sup>107</sup> **3.1 Theoretical Framework: Three-Layer Barrier Model**

<sup>108</sup> We conceptualized HIV prevention barriers as operating at three hierarchical levels, each imposing multi-  
<sup>109</sup> plicative penalties on cascade completion probability:

<sup>110</sup>      **Layer 1 (Pathogen Biology):** HIV establishes irreversible infection within 4–72 hours of mucosal  
<sup>111</sup> exposure and within minutes of parenteral inoculation. This biological reality dictates the temporal window  
<sup>112</sup> for effective prevention but, as our analysis demonstrates, is rarely the limiting factor when architectural  
<sup>113</sup> barriers prevent individuals from reaching the point where pathogen dynamics become relevant.

<sup>114</sup>      **Layer 2 (HIV Testing Failures):** Current HIV testing algorithms cannot reliably detect acute infec-  
<sup>115</sup> tion before LAI-PrEP initiation.<sup>8</sup> Window periods range from 10–33 days for RNA testing to 31–90 days  
<sup>116</sup> for rapid point-of-care tests. LAI-PrEP delays HIV detection by median 98 days, during which 63% of  
<sup>117</sup> breakthrough infections develop major resistance mutations.<sup>9,10</sup>

<sup>118</sup>      **Layer 3 (Architectural Failures):** Structural barriers operate through five mechanisms: (a) Policy—  
<sup>119</sup> criminalization of drug use, with 80% of studies demonstrating negative effects on HIV prevention;<sup>2</sup> (b)  
<sup>120</sup> Stigma—healthcare discrimination experienced by 78% of PWID;<sup>3</sup> (c) Infrastructure—prevention systems  
<sup>121</sup> designed for MSM populations;<sup>11</sup> (d) Research Exclusion—systematic exclusion from HIV prevention tri-  
<sup>122</sup> als;<sup>4,12</sup> and (e) Machine Learning—algorithmic deprioritization based on training data that underrepresents  
<sup>123</sup> PWID by 120-fold.

<sup>124</sup> **3.2 Cascade Model Specification**

<sup>125</sup> We modeled LAI-PrEP implementation as an 8-step cascade where sustained protection requires successful  
<sup>126</sup> completion of all steps: awareness, willingness, healthcare access, disclosure of injection drug use, provider  
<sup>127</sup> willingness to prescribe, adequate HIV testing, initiation, and sustained engagement. Each step probability  
<sup>128</sup> reflects barrier-specific penalties:

$$P(\text{step}) = P_{\text{base}} \times \prod_{b \in \text{barriers}} (1 - \text{penalty}_b) \quad (1)$$

<sup>129</sup> Final  $P(R_0=0)$  incorporates an incarceration survival factor:<sup>13</sup>

$$P(R_0 = 0) = \prod_{i=1}^8 P(\text{step}_i) \times (1 - r_{\text{incarceration}})^{\text{years}} \times m_{\text{policy}} \quad (2)$$

<sup>130</sup> **3.3 Monte Carlo Simulation**

<sup>131</sup> We simulated 100,000 individuals per policy scenario over a 5-year horizon across eight scenarios: Current  
<sup>132</sup> Policy, Decriminalization Only, Decriminalization + Stigma Reduction, SSP-Integrated Delivery, Full Harm  
<sup>133</sup> Reduction, Full HR + PURPOSE-4 Data, Full HR + ML Debiasing, and Theoretical Maximum.

<sup>134</sup> **3.4 Stochastic Avoidance Failure Model**

<sup>135</sup> We developed a model predicting outbreak probability as a function of network density evolution:<sup>6</sup>

$$\rho(t) = \rho_0 + m_{\text{meth}}(t) \times \mu \times 0.5 + h \times 0.3 + r \times 0.2 + m_{\text{meth}}(t) \times 0.15 \quad (3)$$

<sup>136</sup> Methamphetamine prevalence was modeled as growing 2.5% annually from a 2018 baseline of 14.3%,<sup>14</sup>  
<sup>137</sup> with regional variation. Annual outbreak probability followed an exponential function above a critical net-  
<sup>138</sup> work threshold, with protective effects from SSP and OAT coverage.

<sup>139</sup> **3.5 MSM Comparison**

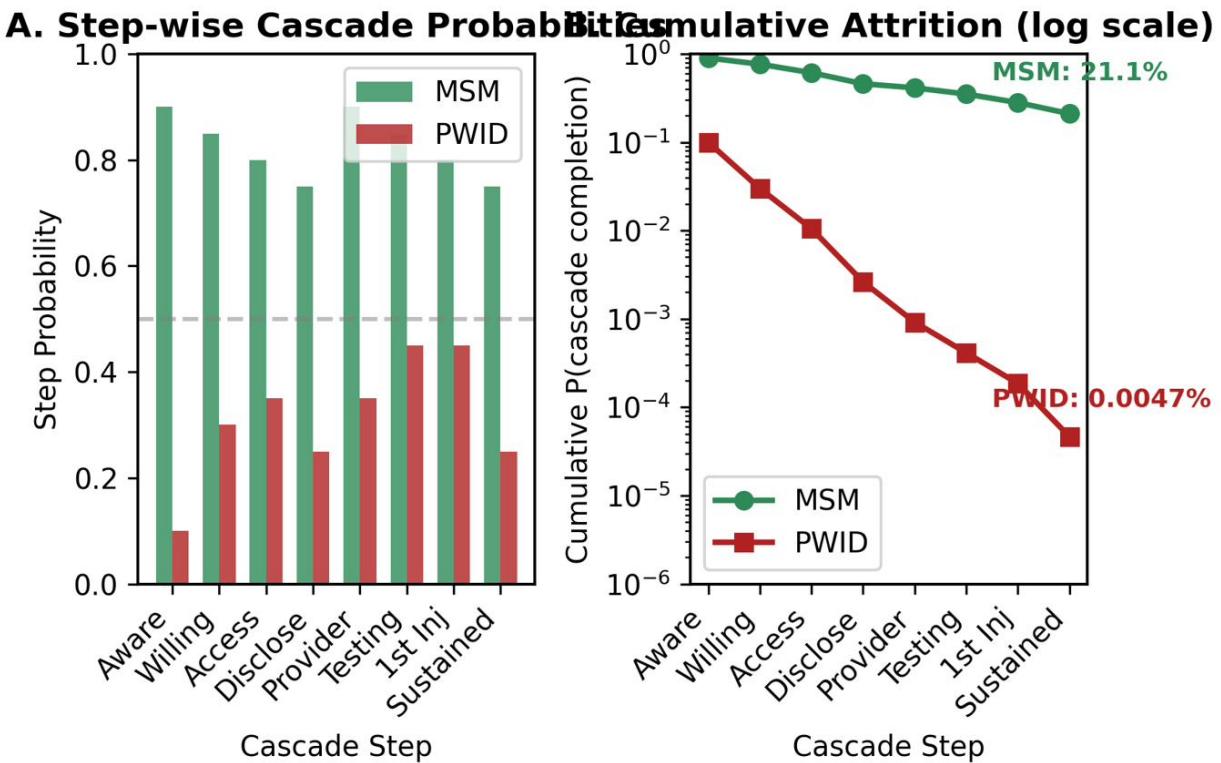
<sup>140</sup> We calculated MSM cascade completion using published uptake data<sup>7</sup> to represent the outcome of identical  
<sup>141</sup> pharmacological intervention applied to a population included in prevention trial design and implementation  
<sup>142</sup> frameworks.

143 **4 Results**

144 **4.1 Validation of Expert Consensus: Cascade Failure Under Current Policy**

145 Under current policy, the 8-step LAI-PrEP cascade demonstrated catastrophic attrition (Figure 1). Step  
 146 probabilities were: awareness 10%, willingness 30%, healthcare access 35%, disclosure 25%, provider  
 147 willing 35%, HIV testing adequate 45%, first injection 45%, and sustained engagement 25%. The product  
 148 yielded cascade completion of 0.00465%. After applying 5-year incarceration survival probability of 16.8%,  
 149 final  $P(R_0=0)$  was effectively zero.

150 In Monte Carlo simulation of 100,000 individuals, observed  $P(R_0=0)$  was 0.00% (95% CI: 0.00–0.00).  
 151 The majority of failures (89.9%) occurred at the awareness step. This finding validates what experts have  
 152 long stated: PWID fail at the first barrier before prevention becomes possible.<sup>11,15</sup>

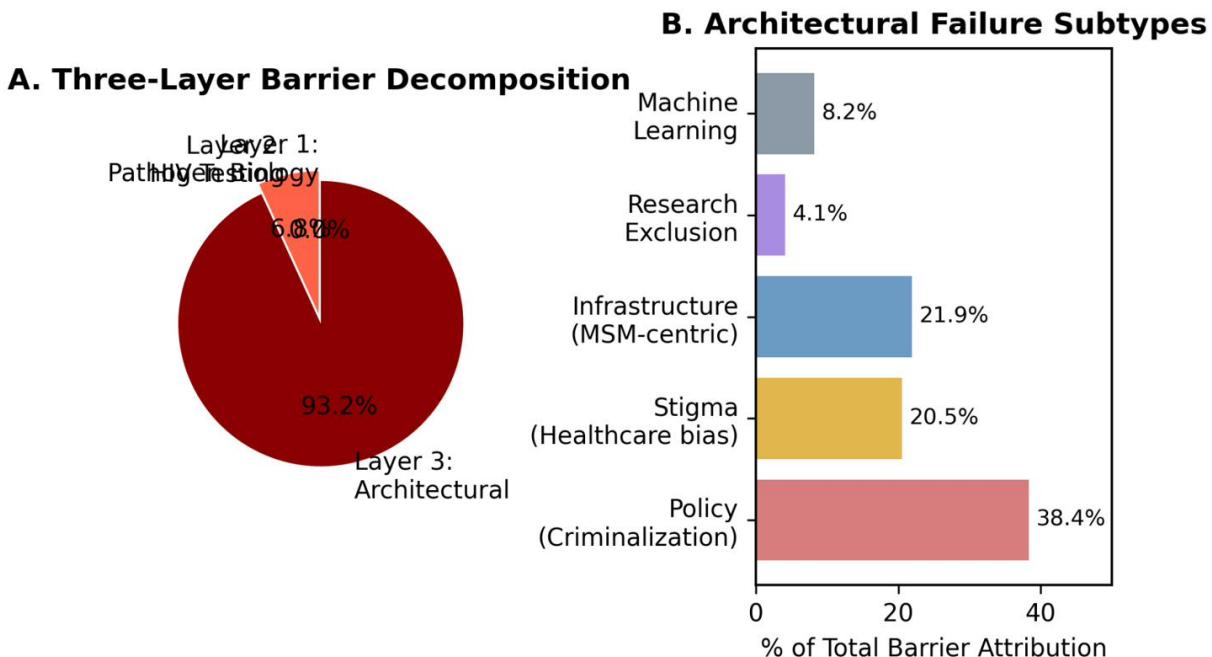


**Figure 1: LAI-PrEP Cascade Comparison: MSM vs PWID.** Cascade completion 21.1% for MSM versus 0.0047% for PWID receiving identical pharmacological intervention. Under current policy, 90% of PWID fail at awareness—the first barrier.

## 153 4.2 Barrier Decomposition: Architectural Failures Dominate

154 Barrier decomposition attributed: Layer 1 (Pathogen Biology) 0.0%, Layer 2 (HIV Testing) 6.8%, and Layer  
155 3 (Architectural Failures) 93.2% (Figure 2). Within architectural failures: policy 38.4%, infrastructure  
156 21.9%, stigma 20.5%, machine learning 8.2%, and research exclusion 4.1%.

157 Pathogen biology contributed 0.0%—not because HIV dynamics are irrelevant, but because cascade  
158 attrition is so severe that biological constraints are never tested. When 90% fail at awareness, the 4–72 hour  
159 window for prevention is meaningless. This finding reframes the challenge: we do not need better drugs;  
160 we need policy that allows existing drugs to reach intended recipients.

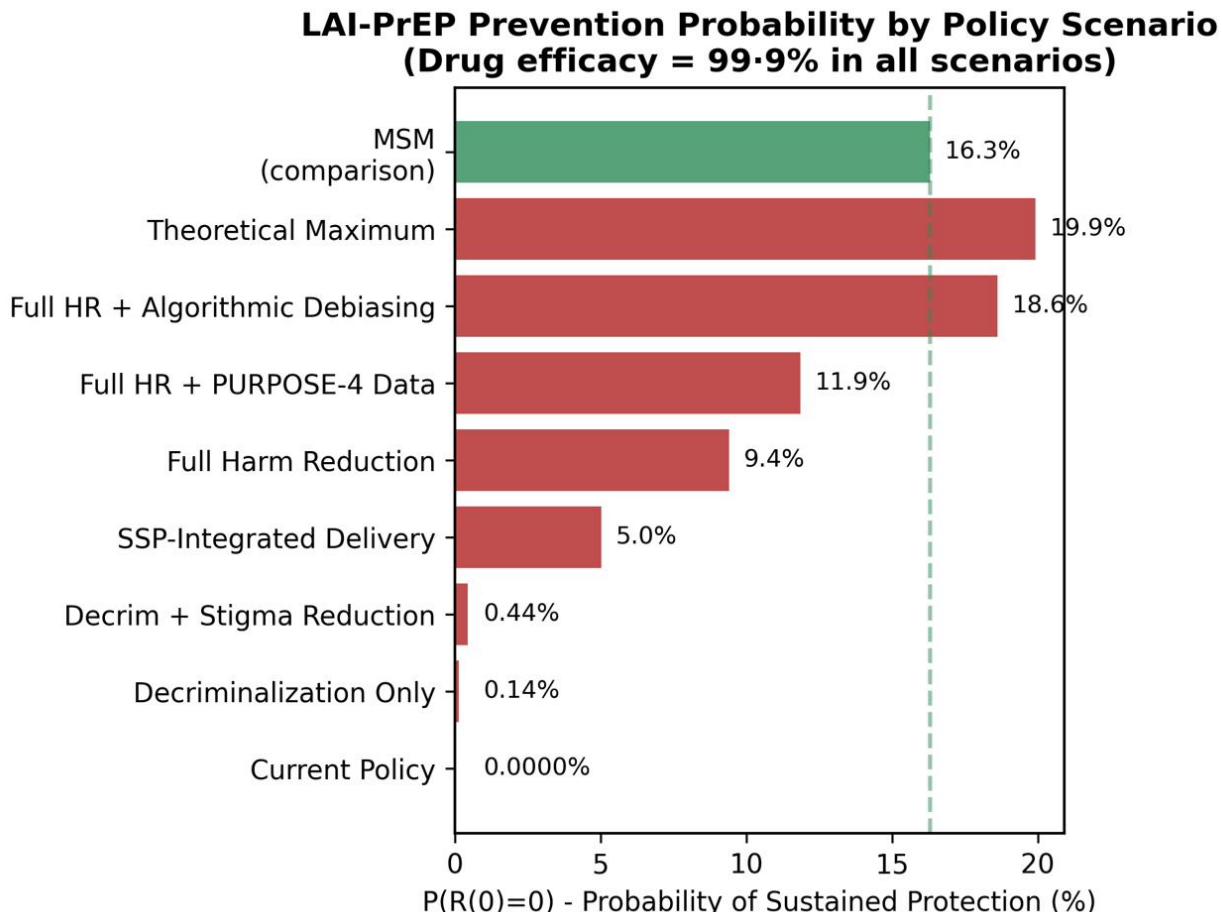


**Figure 2: Three-Layer Barrier Decomposition.** Architectural failures account for 93.2% of prevention failure. Pathogen biology contributes 0.0%—not because it is unimportant, but because structural barriers prevent individuals from reaching the point where biology becomes relevant.

## 161 4.3 Single Barrier Removal Is Insufficient

162 Table 1 and Figure 3 present  $P(R_0=0)$  across policy scenarios. Decriminalization alone increased  $P(R_0=0)$   
163 from 0.00% to only 0.14%. Adding stigma reduction achieved 0.44%. SSP-integrated delivery reached  
164 5.03%. Full harm reduction achieved 9.42%. Only comprehensive reform with algorithmic debiasing ap-  
165 proached MSM levels at 18.62%.

166 This finding validates expert consensus: piecemeal reform fails.<sup>5</sup> The multiplicative nature of cascade  
167 barriers means improving any single step yields minimal benefit when other steps remain at 25–45% proba-  
168 bility.



**Figure 3: Policy Scenario Analysis.** No single intervention achieves meaningful improvement. Only comprehensive reform approaches MSM prevention levels, validating decades of expert recommendations.

#### 169 4.4 The Timestamp: Stochastic Avoidance Failure Prediction

170 The stochastic avoidance model predicted 63.3% probability of major outbreak within 5 years (Figure 4).

171 Median time to outbreak was 4.0 years. Cumulative probability reached 87.6% by 10 years.

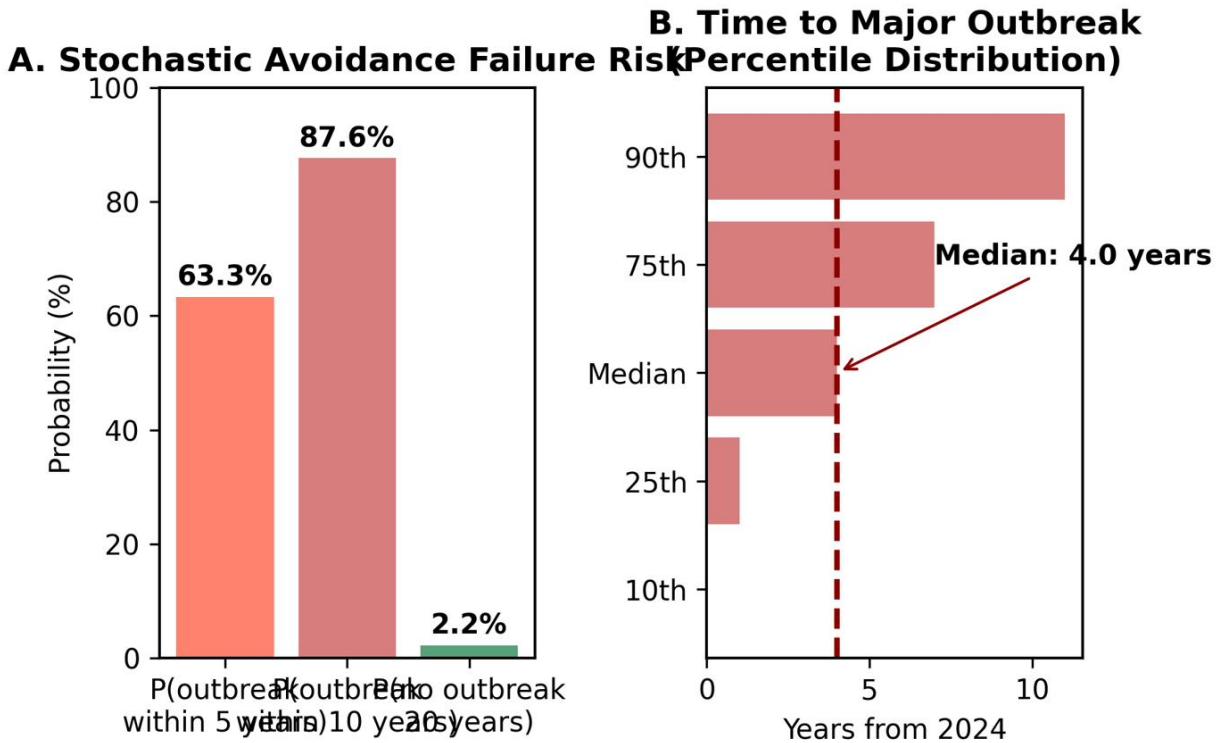
172 Regional variation was substantial (Table 2): Pacific Northwest showed 88% 5-year probability (median

173 1.0 year); Appalachia 78% (median 2.0 years); Northeast Urban 64% (median 3.0 years).

174 This is our central finding: **we have approximately 4 years before stochastic avoidance fails.** COVID-

175 19 demonstrated this principle at global scale—that probability-based protection from transmissible disease

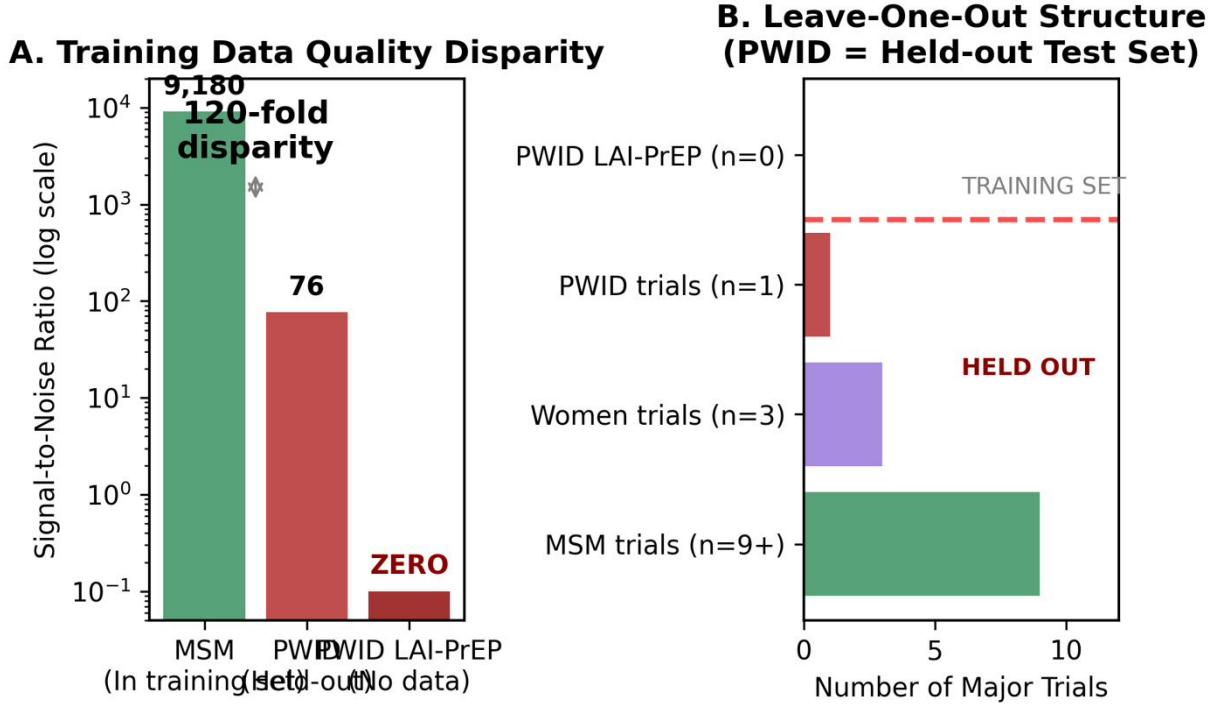
<sup>176</sup> is time-limited. Our model applies this lesson specifically to HIV among PWID.



**Figure 4: Stochastic Avoidance Failure Prediction: The Timestamp.** 63.3% probability of major outbreak within 5 years; median 4.0 years. COVID-19 proved stochastic avoidance fails when conditions change. Our model quantifies when this will occur for HIV among PWID.

#### <sup>177</sup> 4.5 MSM vs PWID: Same Drug, Infinite Disparity

<sup>178</sup> MSM achieved  $P(R_0=0)$  of 16.30% compared to 0.00% for PWID—an infinite-fold disparity from identical  
<sup>179</sup> pharmacological intervention (Figure 5). This difference emerged entirely from structural factors: MSM  
<sup>180</sup> cascade probabilities ranged 75–95% versus 10–45% for PWID. The 120-fold disparity in machine learning  
<sup>181</sup> training data compounds these barriers algorithmically.



**Figure 5: Signal-to-Noise Ratio Disparity.** MSM: 9,180 publications; PWID: 76.4 (estimated)—120-fold disparity in machine learning training data. Algorithms trained on this data will systematically exclude PWID regardless of clinical indication.

## 182 5 Discussion

### 183 5.1 Validating Expert Consensus

184 Our computational findings align precisely with what HIV prevention experts have published for decades.<sup>2,5,6</sup>  
 185 Single barrier removals do not produce meaningful change. Policy overhaul must be comprehensive. Crim-  
 186 inalization drives transmission. Stigma prevents care engagement. Research exclusion leaves interventions  
 187 unvalidated for the populations that need them most.

188 We do not claim to have discovered these truths. We claim to have quantified them—and to have pro-  
 189 vided what the literature has lacked: a timestamp.

### 190 5.2 The Timestamp: Why This Time Is Different

191 COVID-19 provided the definitive demonstration that stochastic avoidance is time-limited. For years, epi-  
 192 demiologists warned that a novel respiratory pathogen could produce pandemic catastrophe. These warnings  
 193 were ignored because probability had protected humanity from the worst scenarios. Until it didn't.

194 Our model applies this lesson to HIV among PWID. The 63% five-year outbreak probability is not a  
195 worst-case scenario; it is the expected outcome under current conditions. The median 4-year timeline is  
196 not a distant threat; it is an immediate deadline. The outbreaks in Scott County,<sup>16</sup> Lawrence/Lowell,<sup>17</sup>  
197 and Cabell/Kanawha Counties<sup>18</sup> were not unpredictable—they were probabilistically inevitable in settings  
198 where experts had issued warnings years earlier.

199 Van Handel and colleagues identified 220 vulnerable U.S. counties in 2016.<sup>19</sup> Only 21% had syringe  
200 services programs operating by 2018. The mathematical certainty of outbreak in inadequately protected  
201 populations is not theoretical; it has been demonstrated repeatedly. Our model quantifies the timeline for the  
202 next—and potentially larger—catastrophe.

### 203 5.3 Machine Learning as Weapon of Math Destruction

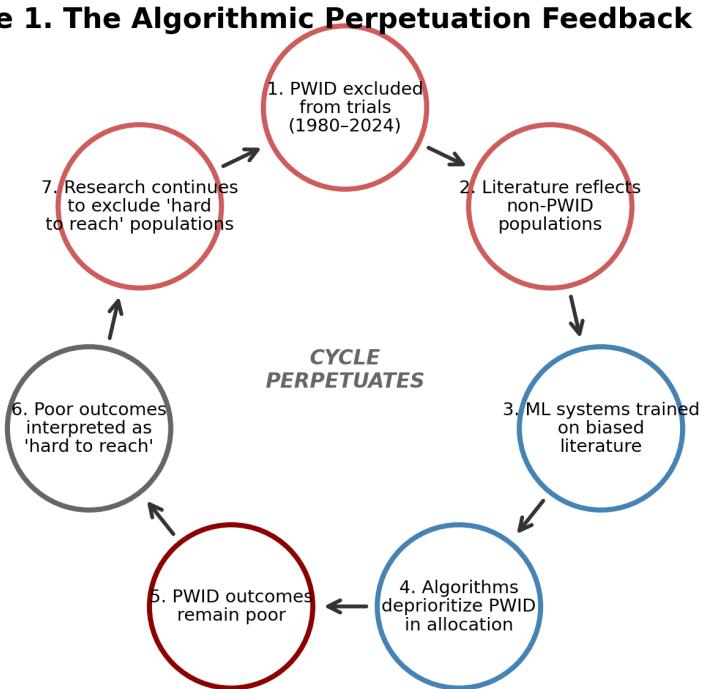
204 Cathy O’Neil’s concept of “Weapons of Math Destruction” (WMDs) describes algorithms that encode bias,  
205 operate at scale, and create self-reinforcing feedback loops that perpetuate inequality.<sup>20</sup> Our analysis identi-  
206 fies HIV prevention algorithms as an emerging WMD for PWID.

207 The mechanism is straightforward (Figure 6). Machine learning algorithms powering insurer prior au-  
208 thorization, clinical decision support, and resource allocation are trained on data that underrepresents PWID  
209 by 120-fold. When these algorithms evaluate PWID patients, they systematically deprioritize them—not  
210 because the computations are flawed, but because the training data is of insufficient quality to generate  
211 equitable outputs.

212 The consequences compound. Individuals with prior oral PrEP adherence difficulties—precisely those  
213 who would most benefit from LAI-PrEP’s reduced adherence requirements—will be flagged as poor candi-  
214 dates. Populations excluded from clinical trials will lack the evidence base to justify coverage. Each denial  
215 generates data that reinforces future denials.

216 We acknowledge that algorithmic debiasing will require substantial upfront investment. Financial and  
217 temporal commitments to disentangle biased algorithms embedded in corporate strategic infrastructure are  
218 significant. But our model suggests we will not end the HIV epidemic without making them.

**Figure 1. The Algorithmic Perpetuation Feedback Loop**



*Policy exclusion (Steps 1-2) creates biased training data; ML systems encode this bias (Step 3) and perpetuate it through resource allocation (Step 4); poor outcomes (Step 5) are misattributed to population characteristics (Step 6); continued exclusion (Step 7) completes the cycle.*

**Figure 6: Machine Learning as Weapon of Mass Destruction: The Negative Feedback Loop.** PWID exclusion from trials → inadequate training data → algorithmic deprioritization → reduced access → poor outcomes → reinforced exclusion. Without intervention, this loop is self-perpetuating and inescapable.

#### 219 5.4 Competing Financial Motivations

220 The persistence of barriers despite decades of expert warnings reflects structural conflicts of interest that our  
221 model cannot resolve but must acknowledge:

222      **Criminal Justice:** Decriminalization would benefit PWID but eliminate revenue streams for systems  
223 built on drug enforcement. The 30% annual incarceration rate among PWID is not an unfortunate side  
224 effect; it is an economic input.

225      **Pharmaceutical Industry:** Corporations manufacturing HIV prevention agents also manufacture HIV  
226 treatment agents. The financial calculus of preventing infections that would otherwise require lifelong treat-  
227 ment is not straightforward.

228      **Healthcare Systems:** Treating preventable infections generates revenue. Prevention reduces it.

229      **Insurance Industry:** Short-term cost containment through prior authorization barriers may produce  
230 long-term cost increases through treatment of preventable infections, but quarterly earnings pressure short-

231 term thinking.

232 These conflicts create structural resistance to the comprehensive reform our model demonstrates is nec-  
233 essary. They also represent precisely the kind of high-complexity, multi-stakeholder decision problem where  
234 machine learning could provide assistance—if the algorithms were trained to weight individual and societal  
235 outcomes rather than shareholder value alone.

## 236 **5.5 Is There a Solution?**

237 Perhaps. Machine learning algorithms excel at assisting humanity with high-complexity decisions involving  
238 competing priorities. The same systems that currently function as WMDs could, with appropriate training  
239 data and objective functions, identify optimal resource allocation strategies that balance individual protec-  
240 tion, population health, and economic sustainability.

241 But this requires those controlling the algorithms to stop treating vulnerable populations as pieces on  
242 a chessboard—inputs to be optimized for corporate benefit. Decision systems must be trained to weight  
243 individual success equivalently to corporate success. Prevention must be valued as an outcome, not merely  
244 treatment avoided.

245 The technical capability exists. The policy frameworks exist. The expert consensus exists. What remains  
246 absent is the political will to implement solutions that conflict with entrenched financial interests.

## 247 **5.6 Limitations**

248 Our analysis has limitations. Cascade parameters derive from heterogeneous literature; we addressed this  
249 through sensitivity analysis demonstrating robustness. The stochastic model simplifies complex network dy-  
250 namics; local outbreak timing will depend on factors not captured in aggregate parameters. Policy scenarios  
251 represent idealized conditions; implementation would be partial and gradual.

## 252 **5.7 Strengths**

253 Our model’s strengths include: validation of expert consensus through independent computational analysis;  
254 quantification of barrier contributions enabling prioritization; the first mathematical timestamp for stochastic  
255 avoidance failure; identification of machine learning as emerging barrier; and demonstration that identical  
256 pharmacological intervention produces infinite-fold disparity based solely on structural factors.

257 **6 Conclusions**

258 HIV prevention among PWID exists in a state of manufactured death—conditions created by policy choices  
259 that render epidemic control mathematically impossible regardless of pharmacological innovation. Our  
260 findings do not reveal new barriers; they validate decades of expert warnings while providing what the  
261 literature has lacked: a timestamp.

262 We have approximately 4 years before stochastic avoidance fails and catastrophic outbreak becomes  
263 probable rather than possible. The barriers are known. The solutions are known. The deadline is now  
264 known.

265 COVID-19 proved that humanity cannot rely on probability to protect us from transmissible infectious  
266 disease. Our model quantifies when this lesson will apply to HIV among PWID. The question is not whether  
267 we will act, but whether we will act in time.

268 **Data Sharing**

269 All model code, simulation outputs, and analysis scripts are available at <https://github.com/Nyx-Dynamics/hiv-prevention-master>.

271 **Declaration of Interests**

272 A.C.D. was previously employed by Gilead Sciences, Inc. (October 2024) and held company stock (divested  
273 December 2024). Gilead Sciences, Inc. had no role in study design, data collection, analysis, interpreta-  
274 tion, manuscript writing, or publication decision. A.C.D. is Founder and CEO of Nyx Dynamics, LLC, a  
275 healthcare consulting firm. The model presented here is released open-source under MIT License.

276 **Acknowledgments**

277 The author thanks HIV prevention researchers whose published work provided model parameters, PWID  
278 community advocates whose testimony informed barrier characterization, and the experts whose decades of  
279 warnings this analysis validates.

<sup>280</sup> **Author Contributions**

<sup>281</sup> ACD conceived the study, developed the theoretical framework, conducted literature synthesis, built com-  
<sup>282</sup> putational models, performed analyses, and wrote the manuscript.

<sup>283</sup> **Informed Consent**

<sup>284</sup> This computational study used only synthetic data. No human participants were enrolled.

<sup>285</sup> **Ethics**

<sup>286</sup> This computational study did not involve human participants.

**Table 1:**  $P(R_0=0)$  by Policy Scenario (n=100,000 per scenario)

Scenario	$P(R_0=0)$	95% CI	Cascade %
Current Policy	0.00%	(0.00, 0.00)	0.01%
Decriminalization Only	0.14%	(0.12, 0.17)	0.23%
Decrim + Stigma Reduction	0.44%	(0.40, 0.48)	0.72%
SSP-Integrated Delivery	5.03%	(4.89, 5.16)	8.12%
Full Harm Reduction	9.42%	(9.24, 9.60)	9.42%
Full HR + PURPOSE-4 Data	11.86%	(11.66, 12.06)	11.86%
Full HR + ML Debiasing	18.62%	(18.38, 18.86)	18.62%
Theoretical Maximum	19.92%	(19.67, 20.17)	19.92%
<b>MSM (Comparison)</b>	<b>16.30%</b>	—	<b>21.07%</b>

*Note:* MSM comparison represents identical pharmacological intervention. Disparity is policy-determined, not pharmacology-determined.

**Table 2:** Regional Outbreak Probability Predictions: The Timestamp

Region	$P(5 \text{ years})$	Median (years)	$P(10 \text{ years})$	Meth Baseline
National Average	59%	4.0	85%	14.3%
Appalachia	78%	2.0	94%	25%
Pacific Northwest	88%	1.0	98%	35%
Northeast Urban	64%	3.0	89%	12%

*Note:* Median represents years until outbreak probability exceeds 50%. Pacific Northwest has effectively no remaining time under current conditions.

287 **Figure Legends**

288 **Figure 1.** LAI-PrEP Cascade Comparison: MSM vs PWID. Identical pharmacological intervention pro-  
289 duces 21.1% cascade completion for MSM versus 0.0047% for PWID. Under current policy, 90% of PWID  
290 fail at awareness—before prevention becomes possible.

291 **Figure 2.** Three-Layer Barrier Decomposition. Architectural failures account for 93.2% of prevention  
292 failure (policy 38.4%, infrastructure 21.9%, stigma 20.5%, ML 8.2%, research exclusion 4.1%). Pathogen  
293 biology contributes 0.0%—structural barriers prevent individuals from reaching the point where biology  
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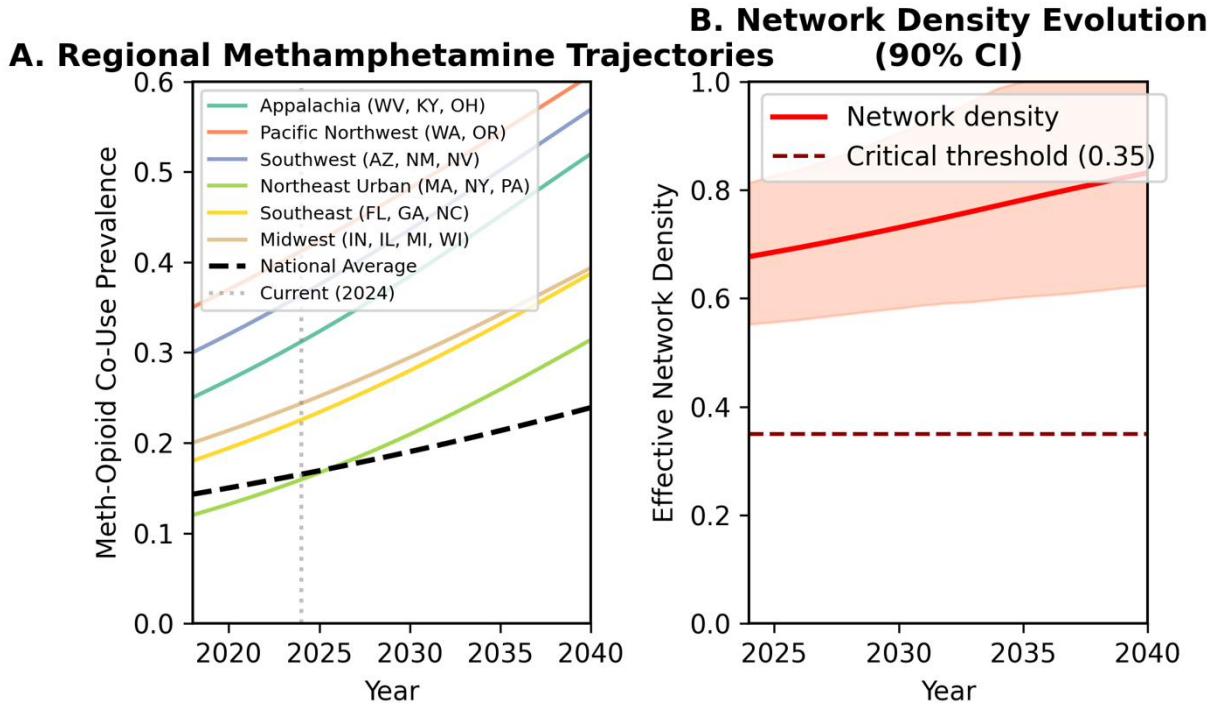
295 **Figure 3.** Policy Scenario Analysis. No single intervention achieves meaningful improvement. De-  
296 criminalization alone: 0.14%. Full harm reduction: 9.42%. Only comprehensive reform with algorithmic  
297 debiasing approaches MSM levels (18.62%).

298 **Figure 4.** Stochastic Avoidance Failure Prediction: The Timestamp. 63.3% probability of major out-  
299 break within 5 years; median 4.0 years. COVID-19 demonstrated stochastic avoidance fails when conditions  
300 change. This model quantifies when it will fail for HIV among PWID.

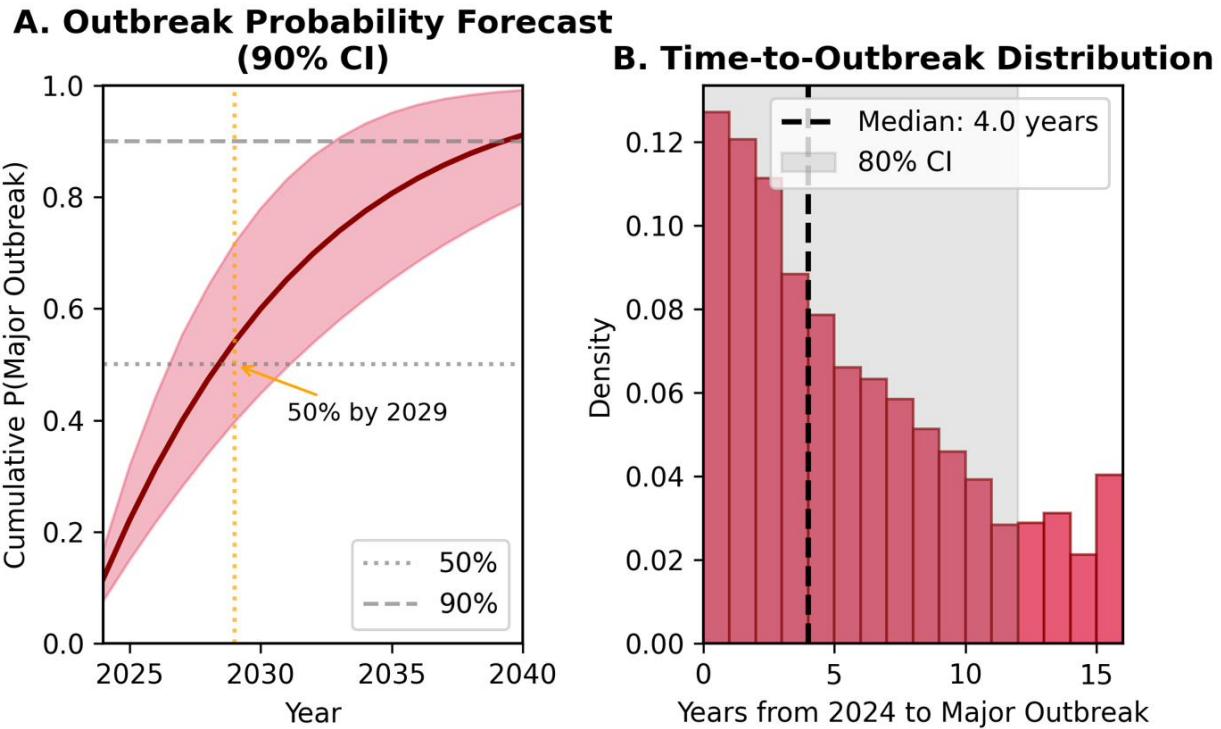
301 **Figure 5.** Signal-to-Noise Ratio Disparity. MSM: 9,180 publications; PWID: 76.4 (estimated)—120-  
302 fold disparity in ML training data. Algorithms trained on this data will systematically exclude PWID re-  
303 gardless of clinical indication.

304 **Figure 6.** Machine Learning as Weapon of Math Destruction: The Negative Feedback Loop. PWID  
305 exclusion from trials produces inadequate training data, producing algorithmic deprioritization, producing  
306 reduced access, producing poor outcomes, reinforcing exclusion. Without intervention, this loop is in-  
307 escapable.

308 **Supplementary Figures**



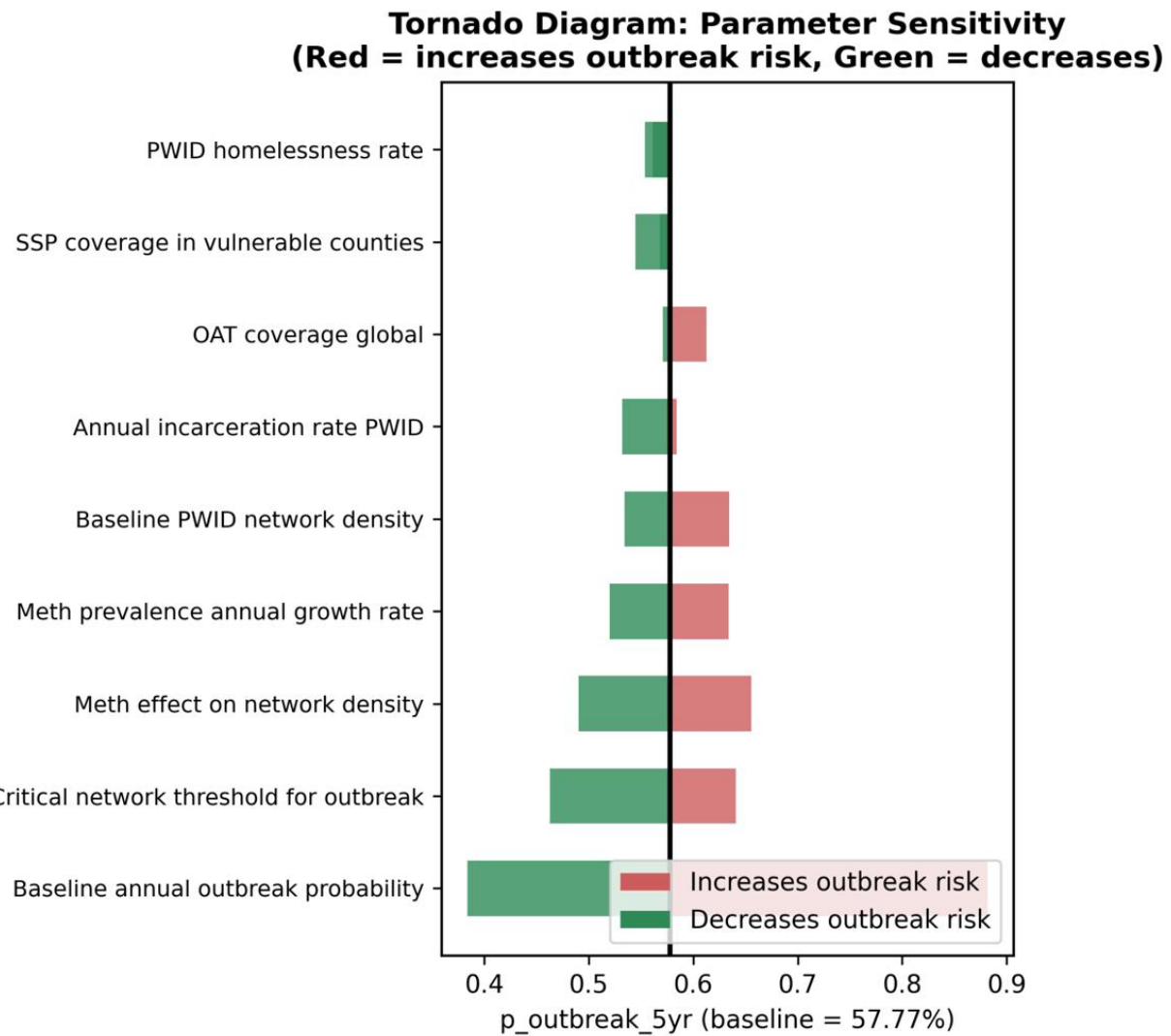
**Figure 7: Supplementary Figure 1: Regional Methamphetamine Trajectories.** Pacific Northwest: 35% baseline; Northeast Urban: 12% with 5%/year growth (fastest). Network density evolution approaches critical threshold.



**Figure 8: Supplementary Figure 2: Outbreak Probability Forecast.** Cumulative probability with 90% CI. 50% threshold crossed at year 4; 90% threshold crossed at year 12.

## 309 References

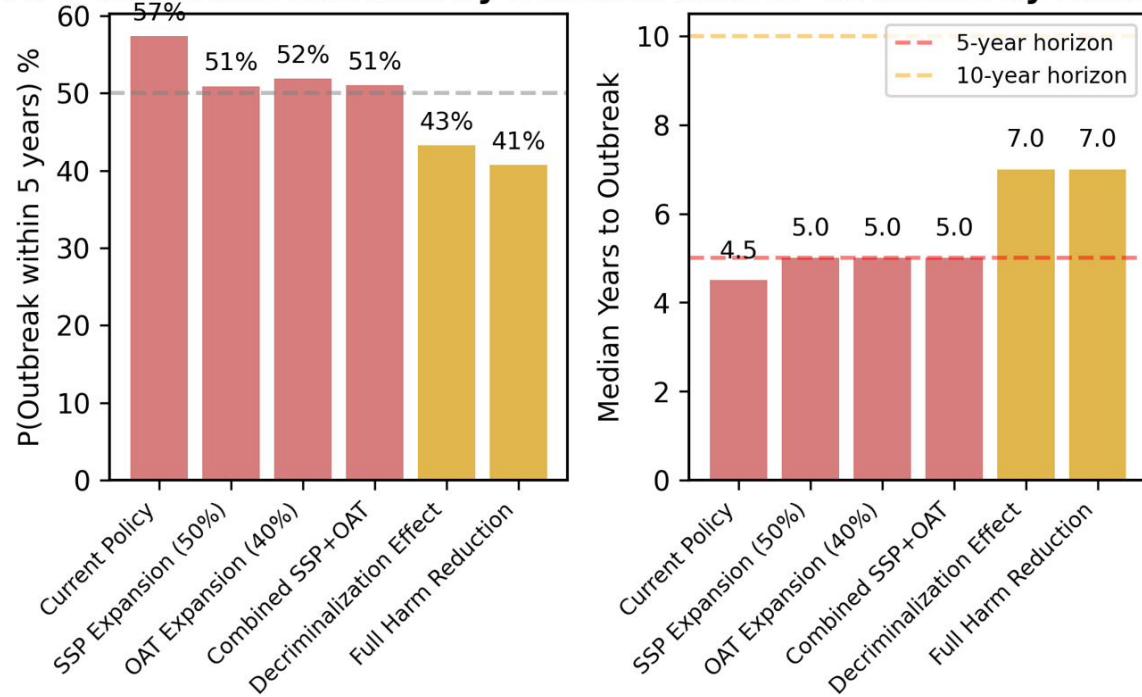
- 310 [1] Louisa Degenhardt, Amy Peacock, Samantha Colledge, Janni Leung, Jason Grebely, Peter Vicker-  
311 man, Jack Stone, Evan B Cunningham, Adam Trickey, Kostyantyn Dumchev, Michael Lynskey, Paul  
312 Griffiths, Richard P Mattick, Matthew Hickman, and Sarah Larney. Global prevalence of injecting  
313 drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who  
314 inject drugs: a multistage systematic review. *Lancet Glob Health*, 5(12):e1192–e1207, 2017. doi:  
315 10.1016/S2214-109X(17)30375-3.
- 316 [2] Kora DeBeck, Tessa Cheng, Julio S. Montaner, Chris Beyrer, Richard Elliott, Susan Sherman, Evan  
317 Wood, and Stefan Baral. Hiv and the criminalisation of drug use among people who inject drugs: a  
318 systematic review. *Lancet HIV*, 4(8):e357–e374, 2017. doi: 10.1016/S2352-3018(17)30073-5.
- 319 [3] Bella Muncan et al. "they look at us like junkies": influences of drug use stigma on the healthcare  
320 engagement of people who inject drugs in New York City. *Harm Reduct J*, 17:53, 2020. doi: 10.1186/  
321 s12954-020-00399-8.



**Figure 9: Supplementary Figure 3: Tornado Diagram.** Most influential parameters: baseline outbreak probability ( $\pm 49.8\text{pp}$ ), critical network threshold ( $\pm 17.8\text{pp}$ ), methamphetamine multiplier ( $\pm 16.6\text{pp}$ ).

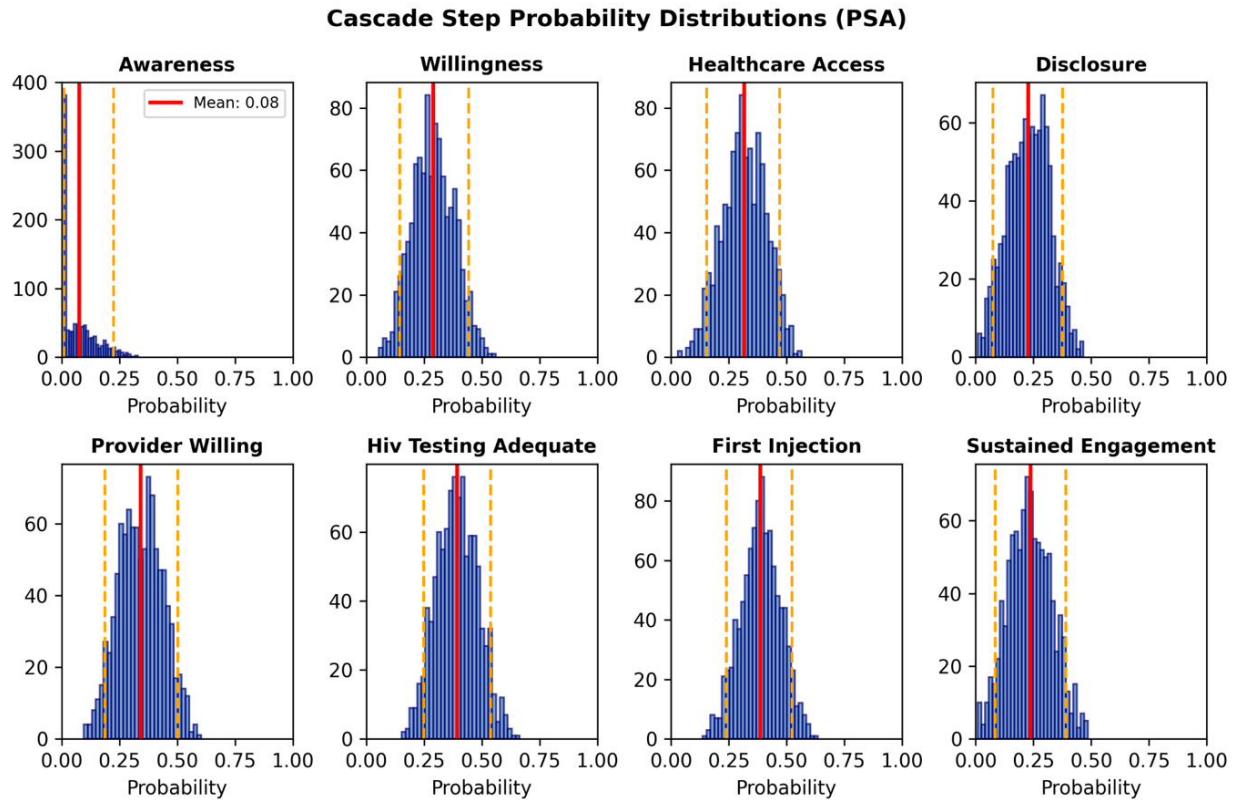
- 322 [4] Jane K. Brody et al. The systematic exclusion of people who inject drugs from HIV prevention trials.  
 323      *Int J Drug Policy*, 2021. doi: 10.1016/j.drugpo.2021.103284.
- 324 [5] Steffanie A. Strathdee, Irene Kuo, Nabila El-Bassel, Sally Hodder, Laramie R. Smith, and Sandra A.  
 325      Springer. Preventing HIV outbreaks among people who inject drugs in the United States: plus ça  
 326      change, plus ça même chose. *AIDS*, 34(14):1997–2005, 2020. doi: 10.1097/QAD.0000000000002673.
- 327 [6] Don C Des Jarlais et al. Potential disruptions of HIV prevention among people who inject drugs in  
 328      NYC from the COVID-19 pandemic: modeling to help inform prevention. *Drug Alcohol Depend*,  
 329      2022. doi: 10.1016/j.drugalcdep.2022.109505.

## A. 5-Year Outbreak Risk by Scenario



**Figure 10: Supplementary Figure 4: Policy Scenario Comparison.** Current policy: 57% 5-year risk, 4.5 years median. Full harm reduction: 41% 5-year risk, 7.0 years median.

- 330 [7] Robert M. Grant, Javier R. Lama, Peter L. Anderson, et al. Preexposure chemoprophylaxis for HIV  
331 prevention in men who have sex with men. *N Engl J Med*, 363(27):2587–2599, 2010. doi: 10.1056/  
332 NEJMoa1011205.
- 333 [8] Mary R. Tanner, Jesse G. O’Shea, Katrina M. Byrd, Marie Johnston, Gema G. Dumitru, John N. Le,  
334 Allison Lale, Kathy K. Byrd, Preetam Cholli, Emiko Kamitani, Weiming Zhu, Karen W. Hoover, and  
335 Athena P. Kourtis. Antiretroviral postexposure prophylaxis after sexual, injection drug use, or other  
336 nonoccupational exposure to HIV – CDC recommendations, United States, 2025. *MMWR Recomm*  
337 *Rep*, 74(1):1–56, 2025. doi: 10.15585/mmwr.rr7401a1.
- 338 [9] Mark A. Marzinke et al. Characterization of HIV infection in participants who seroconverted in HPTN  
339 083. *Antimicrob Agents Chemother*, 2023. doi: 10.1128/aac.00053-23.
- 340 [10] Susan H. Eshleman et al. Integrase strand transfer inhibitor resistance mutations in participants who  
341 seroconverted during HPTN 083. *J Infect Dis*, 2022. doi: 10.1093/infdis/jiac415.
- 342 [11] K. B. Biello, A. R. Bazzi, M. J. Mimiaga, D. L. Biancarelli, A. Edeza, P. Salhaney, E. Childs,



**Figure 11: Supplementary Figure 5: Cascade Uncertainty.** Probability distributions for each step under parameter uncertainty (n=1,000 PSA samples).

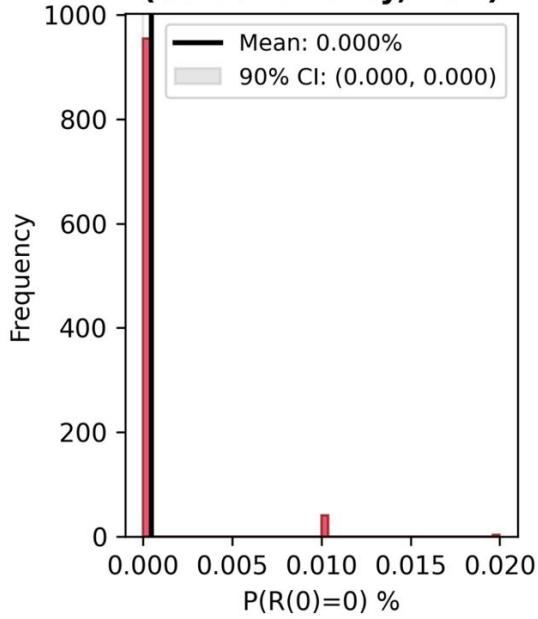
and M. L. Drainoni. Perspectives on HIV pre-exposure prophylaxis (PrEP) utilization and related intervention needs among people who inject drugs. *Harm Reduct J*, 15(1):55, 2018. doi: 10.1186/s12954-018-0263-5.

[12] Emiko Kamitani et al. A systematic review of HIV pre-exposure prophylaxis best practices: where are the people who inject drugs? *AIDS Behav*, 2024. doi: 10.1007/s10461-024-04332-z.

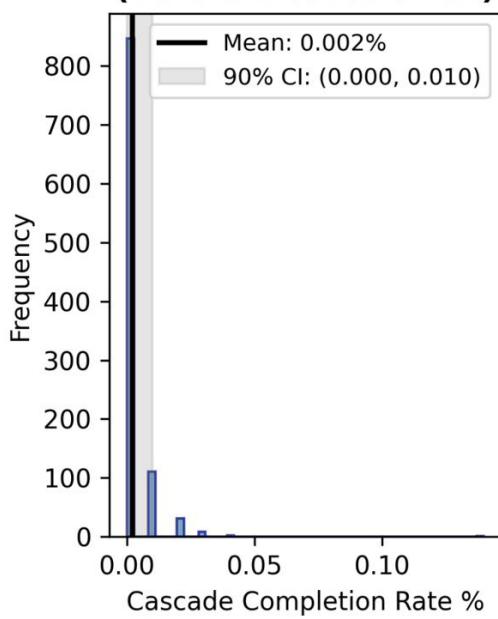
[13] Jack Stone et al. Incarceration history and risk of HIV and hepatitis C virus acquisition among people who inject drugs: a systematic review and meta-analysis. *Lancet Infect Dis*, 18(12):1397–1409, 2018. doi: 10.1016/S1473-3099(18)30469-9.

[14] Sara Nelson Glick, Richard Burt, Kim Kummer, Joe Tinsley, Caleb J. Banta-Green, and Matthew R. Golden. Increasing methamphetamine injection among non-MSM who inject drugs in King County, Washington. *Drug Alcohol Depend*, 182:86–92, 2018. doi: 10.1016/j.drugalcdep.2017.10.011.

## A. Distribution of Prevention Probability of Cascade Completion (Current Policy, PSA)



## B. Distribution of Cascade Completion (Before Incarceration)



**Figure 12: Supplementary Figure 6:  $P(R_0=0)$  Distribution.** Robustness demonstration: mean 0.0005%, 90% CI (0.00%, 0.00%) across 1,000 PSA samples.

354 [15] Cheryl B. Mistler et al. PrEP awareness, uptake and use among people who inject drugs: a systematic  
 355 review. *AIDS Behav*, 2021. doi: 10.1007/s10461-020-02988-x.

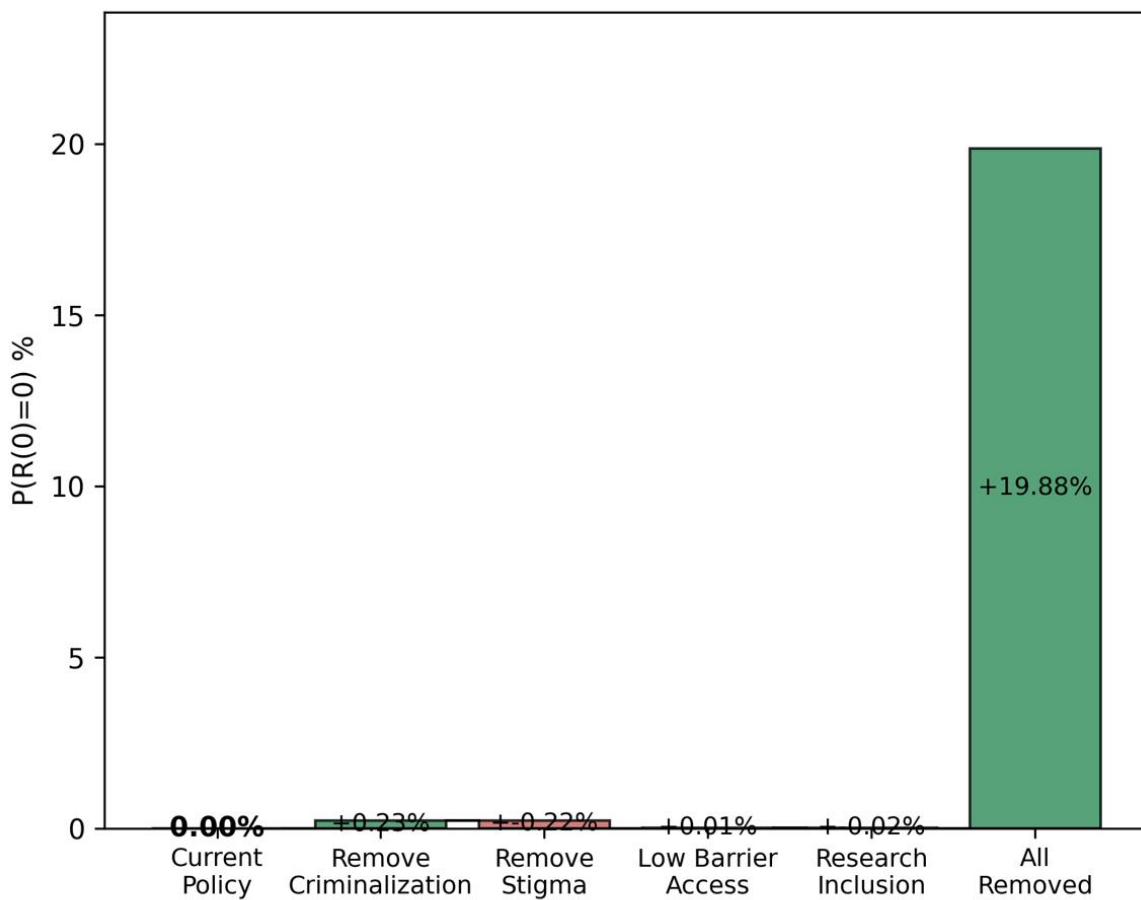
356 [16] Philip J. Peters et al. HIV infection linked to injection use of oxymorphone in Indiana, 2014–2015. *N  
 357 Engl J Med*, 375(3):229–239, 2016. doi: 10.1056/NEJMoa1515195.

358 [17] Charles Algren, Erica L. Dawson, Betsey John, Kevin Cranston, et al. Opioid use fueling HIV  
 359 transmission in an urban setting: an outbreak of HIV infection among people who inject drugs—  
 360 Massachusetts, 2015–2018. *Am J Public Health*, 110(1):37–44, 2020. doi: 10.2105/AJPH.2019.  
 361 305366.

362 [18] R. Paul McClung et al. Response to a large HIV outbreak, Cabell County, West Virginia, 2018–2019.  
 363 *Am J Prev Med*, 2021. doi: 10.1016/j.amepre.2021.05.039.

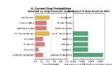
364 [19] Michelle M. Van Handel, Charles E. Rose, Elaine J. Hallisey, Jessica L. Kolling, Jon E. Zibbell, Brian  
 365 Lewis, Michele K. Bohm, Christopher M. Jones, Barry E. Flanagan, Azfar-E-Alam Siddiqi, Kashif  
 366 Iqbal, Andrew L. Dent, Jonathan H. Mermin, Eugene McCray, John W. Ward, and John T. Brooks.

### Incremental Effect of Barrier Removal on Prevention Probability



**Figure 13: Supplementary Figure 7: Barrier Removal Waterfall.** Incremental effects: No criminalization (+0.23pp), No stigma (+0.01pp), Low-barrier access (+0.02pp), Full inclusion (+0.004pp), All removed (19.88%).

367 County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among per-  
368 sons who inject drugs, United States. *J Acquir Immune Defic Syndr*, 73(3):323–331, 2016. doi:  
369 10.1097/QAI.0000000000001098.



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**Figure 14: Supplementary Figure 8: Step Importance.** No single step fix achieves epidemic control. Multiplicative cascade requires simultaneous intervention.