

Epidemics

The Prevention Theorem: Time-Dependent Constraints on Post-Exposure Prophylaxis for HIV --Manuscript Draft--

Manuscript Number:	
Article Type:	Research Paper
Keywords:	HIV prevention; Mathematical modeling; Prevention Theorem; PEP timing; Irreversible dynamics
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Abstract:	Antiretroviral agents for HIV prevention are typically evaluated in terms of trial efficacy and programmatic coverage, but rarely in terms of whether they admit a true mathematical solution to prevention. Here we introduce the Prevention Theorem, which formalizes prevention for a given exposure e as the condition $R_0(e)=0$, meaning that the probability of establishing a productive, transmissible infection is exactly zero. Within this framework, post-exposure prophylaxis (PEP) is not delayed treatment but a time-dependent operator acting on within-host infection establishment dynamics. Using a mechanistic model of reservoir seeding and proviral integration, we derive the PEP Window Corollary: PEP can enforce $R_0(e)=0$ only when initiated within a finite biological window prior to irreversible integration and initial reservoir establishment. Beyond this window, all reachable system states satisfy $R_0(e)>0$ and are irreducible by post-exposure intervention. Parameterization using virological data indicates that this window extends to approximately 72 hours for mucosal exposures but is compressed to roughly 12–24 hours for parenteral exposures due to bypass of early immune bottlenecks. As an applied example, we show that structural access delays in high-risk populations—such as people who inject drugs—frequently exceed this compressed parenteral window. Consequently, for such exposures the condition $R_0(e)=0$ is mathematically and biologically unreachable before access is even attempted, rendering the failure of post-exposure prevention a consequence of violated biological boundary conditions rather than pharmacological efficacy.
Suggested Reviewers:	Bryan Grenfell, PhD Professor of Ecology and Evolutionary Biology, Princeton University grenfell@princeton.edu Experience in intervention timing and mechanistic modeling of infectious disease control; appropriate for evaluation of feasibility-focused analyses. Sally Blower, PhD Professor-in-Residence, University of California Los Angeles sblower@mednet.ucla.edu Extensive expertise in mathematical modeling of HIV transmission and intervention limits, including foundational work on uncertainty and feasibility in infectious disease models. Well suited to evaluate theorem-driven analyses of intervention controllability. Simon Levin, PhD George M. Moffett Professor of Biology, Princeton University slevin@princeton.edu Internationally recognized authority on controllability, irreversibility, and limits of intervention in complex biological systems. Well suited to evaluate existence and non-existence results in theorem-driven epidemiological analyses.
Opposed Reviewers:	

Dear Editors of *Epidemics*,

Please consider our manuscript entitled "**The Prevention Theorem: Time-Dependent Constraints on Post-Exposure Prophylaxis for HIV**" for publication as a Research Paper in *Epidemics*.

This manuscript introduces a formal feasibility framework for HIV prevention by defining prevention as the condition $R_0(e)=0$ for a given exposure event. Within this framework, we demonstrate that post-exposure prophylaxis (PEP) functions as a strictly time-dependent operator acting on within-host infection establishment dynamics and admits a finite biological window beyond which prevention is mathematically unattainable. We derive a closed-form prevention solution, state an explicit PEP Window Corollary, and illustrate the resulting irreducible infection state once proviral integration has occurred. The analysis distinguishes between mucosal and parenteral exposures and demonstrates how bypass of early immune bottlenecks compresses the prevention window for parenteral transmission.

The contribution is intended as a feasibility and constraint analysis rather than a population-level transmission model. The work focuses on existence and non-existence of prevention solutions under biologically realistic timing assumptions, which we believe aligns well with *Epidemics*' emphasis on mechanistic insight into epidemic control and intervention limits. An applied example involving people who inject drugs is included to illustrate violation of biological boundary conditions, but the primary contribution is generalizable to pathogens characterized by irreversible genomic integration or long-lived latent reservoirs.

This manuscript has not been published previously and is not under consideration elsewhere. The study involved no human participants and relied exclusively on publicly available data and published literature. A declaration of interests and ethics statement are included in the manuscript.

Thank you for your consideration. We believe this work will be of interest to readers of *Epidemics* concerned with the fundamental limits of reactive interventions and the conditions under which prevention can—and cannot—be achieved.

Sincerely,

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The Prevention Theorem: Time-Dependent Constraints on Post-Exposure Prophylaxis for HIV

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Abstract

Antiretroviral agents for HIV prevention are typically evaluated in terms of trial efficacy and programmatic coverage, but rarely in terms of whether they admit a true mathematical solution to prevention. Here we introduce the Prevention Theorem, which formalizes prevention for a given exposure e as the condition $R_0(e) = 0$, meaning that the probability of establishing a productive, transmissible infection is exactly zero. Within this framework, post-exposure prophylaxis (PEP) is not delayed treatment but a time-dependent operator acting on within-host infection establishment dynamics. Using a mechanistic model of reservoir seeding and proviral integration, we derive the PEP Window Corollary: PEP can enforce $R_0(e) = 0$ only when initiated within a finite biological window prior to irreversible integration and initial reservoir establishment. Beyond this window, all reachable system states satisfy $R_0(e) > 0$ and are irreducible by post-exposure intervention. Parameterization using virological data indicates that this window extends to approximately 72 hours for mucosal exposures but is compressed to roughly 12–24 hours for parenteral exposures due to bypass of early immune bottlenecks. As an applied example, we show that structural access delays in high-risk populations—such as people who inject drugs—frequently exceed this compressed parenteral window. Consequently, for such exposures the condition $R_0(e) = 0$ is mathematically and biologically unreachable before access is even attempted, rendering the failure of post-exposure prevention a consequence of violated biological boundary conditions rather than pharmacological efficacy.

Keywords: HIV prevention, Mathematical modeling, Prevention Theorem, PEP timing,

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Highlights

- Prevention is defined mathematically as the condition $R_0(e) = 0$.
- PEP operates as a time-dependent function racing against irreversible integration.
- A finite biological window exists beyond which prevention is mathematically impossible.
- Parenteral exposures compress this window to 12–24 hours, bypassing mucosal bottlenecks.
- Structural access delays in PWID invariably exceed this compressed biological limit.

¹ 1. Introduction

² Despite the availability of antiretroviral agents with trial efficacies approaching or exceeding
³ 99%, HIV prevention following exposure remains constrained by the biological dynamics
⁴ of infection establishment [1, 2]. Prevention is often discussed as a matter of coverage, adherence,
⁵ or early treatment, implicitly assuming that post-exposure intervention remains feasible
⁶ at all times following contact. A formal evaluation of this assumption requires specifying what
⁷ prevention means in mathematical terms. Previous work has shown that HIV transmission
⁸ and progression models are often highly sensitive to uncertain biological parameters, under-
⁹ scoring the difficulty of drawing robust conclusions from long-horizon simulations without
¹⁰ strong constraints on initial conditions and system dynamics[3].

¹¹ We define prevention for a specific viral exposure e as the condition $R_0(e) = 0$, correspond-
¹² ing to zero probability that the exposure establishes a productive, transmissible infection.
¹³ Any state satisfying $R_0(e) > 0$ admits non-zero onward transmission and therefore cannot be
¹⁴ considered complete prevention. Within this formulation, pre-exposure prophylaxis enforces
¹⁵ $R_0(e) = 0$ by rendering the host non-susceptible prior to contact, whereas post-exposure
¹⁶ prophylaxis (PEP) attempts to enforce $R_0(e) = 0$ after contact but before infection estab-
¹⁷ lishment becomes irreversible.

18 Crucially, PEP operates as a time-dependent operator acting on within-host establish-
19 ment dynamics, racing against irreversible biological processes including proviral integration
20 and latent reservoir seeding. Once these processes are complete, the system undergoes a
21 phase transition to an irreducible infection state in which $R_0(e) > 0$ is permanently fixed,
22 independent of subsequent therapeutic intervention [4, 5, 6]. This formulation applies to any
23 pathogen in which irreversible genomic integration or long-lived latent reservoirs fix infection
24 status beyond a critical temporal threshold.

25 In the sections that follow, we formalize this constraint through the Prevention Theorem
26 and its corollaries, derive the finite temporal window during which PEP can enforce preven-
27 tion, and illustrate the consequences of violating this boundary condition using the structural
28 context of injection drug use as an applied example.

29 2. Methods

30 2.1. Theoretical Framework: The Prevention Theorem

31 We define the state of true prevention for a specific viral exposure e as the condition
32 where the basic reproductive number for that exposure, $R_0(e)$, is exactly zero.

$$\text{Condition for Prevention: } R_0(e) = 0 \quad (1)$$

33 This condition implies that the probability of the exposure establishing a productive,
34 transmissible infection is zero [7, 8]. Interventions are classified by their ability to enforce this
35 condition. Pre-exposure prophylaxis (PrEP) enforces $R_0(e) = 0$ by rendering the host non-
36 susceptible prior to contact. Post-exposure prophylaxis (PEP) attempts to enforce $R_0(e) = 0$
37 by extinguishing the virus after contact but before the infection becomes self-sustaining.

38 2.2. Closed-Form Prevention Solution

39 Let $R(t)$ denote the total number of infected cells resulting from a single exposure event
40 at time t . The system admits exactly one closed-form prevention solution:

$$R(0) = 0 \Rightarrow R(t) = 0 \quad \forall t. \quad (2)$$

41 If no infected cells exist at the initial condition, no infected cells can arise at any fu-
 42 ture time. For any initial condition satisfying $R(0) > 0$, no post-exposure or therapeutic
 43 intervention can mathematically guarantee $R(t) = 0$; all such interventions act only on the
 44 subsequent trajectory of $R(t)$ and not on its initial condition [9].

45 *2.3. Infection Establishment Dynamics*

46 We model within-host establishment dynamics following a single exposure event using
 47 logistic formulations for reservoir seeding, $P_{\text{seed}}(t)$, and proviral integration, $P_{\text{int}}(t)$ [4]. These
 48 functions describe the cumulative probability that irreversible biological transitions have
 49 occurred by time t .

50 *2.4. Master Equation for Time-Dependent Prevention*

51 The efficacy of post-exposure intervention is time-dependent. We define the reproductive
 52 number as a function of intervention timing:

$$R_0(e, t) = 1 - E_{\text{PEP}}(t) \quad (3)$$

53 with the efficacy function defined as:

$$E_{\text{PEP}}(t) = (1 - P_{\text{seed}}(t)) \varepsilon_{\max} + (P_{\text{seed}}(t) - P_{\text{int}}(t)) \varepsilon_{\text{mid}} + P_{\text{int}}(t) \varepsilon_{\min} \quad (4)$$

54 Here, ε_{\max} represents efficacy prior to seeding, ε_{mid} represents efficacy during the seed-
 55 ing window, and ε_{\min} represents efficacy after integration is established (typically zero for
 56 prevention purposes).

57 Because $E_{\text{PEP}}(t)$ depends on cumulative probabilities of irreversible biological transitions,
 58 once integration is established, this operator, $E_{\text{PEP}}(t) \rightarrow 0$ and $R_0(e, t)$, admits a hard
 59 temporal cutoff once established.[10]

60 **Corollary 1 (PEP Window Corollary):** *Post-exposure prophylaxis can enforce the*
 61 *prevention condition $R_0(e) = 0$ if and only if initiated within a finite biological window*
 62 *$t < t_{\text{crit}}$ prior to irreversible proviral integration. Beyond this critical threshold, all reachable*
 63 *system states satisfy $R_0(e) > 0$ and are irreducible by post-exposure intervention or any*
 64 *therapeutic option currently available.*

65 **3. Results**

66 *3.1. Visualization of the Theorem*

67 Figure 1 illustrates the four core components of the Prevention Theorem. Panel A shows
 68 the timeline of infection establishment, with reservoir seeding preceding proviral integration.
 69 Panel B demonstrates the time-dependent efficacy function $E_{PEP}(t)$, which decays mono-
 70 tonically toward zero as irreversible transitions accumulate. Panel C visualizes the phase
 71 transition into the irreducible infection state, where the probability of infection approaches
 72 certainty. Panel D summarizes the mathematical formalism.

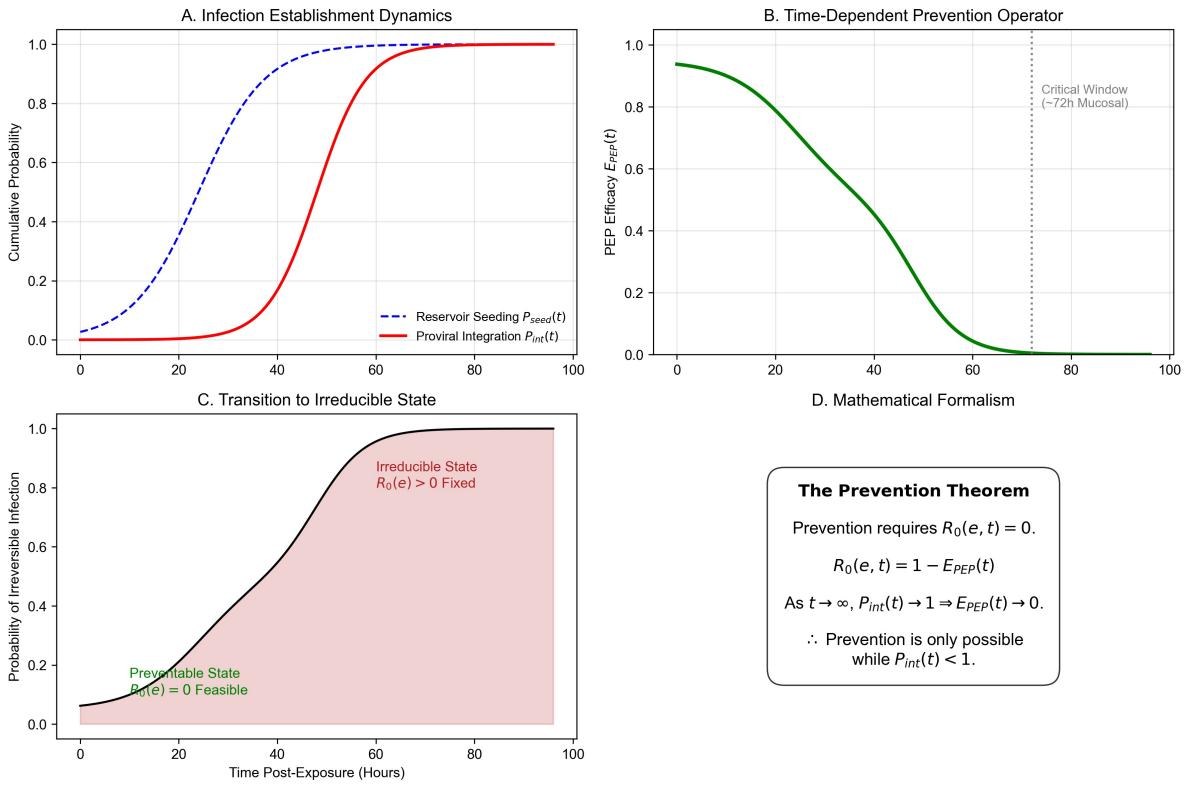


Figure 1: **The Prevention Theorem: Dynamics of Infection Establishment and Post-Exposure Prevention.** Panel A shows cumulative probabilities of reservoir seeding (dashed blue) and proviral integration (solid red) over time. Panel B displays the time-dependent efficacy function $E_{PEP}(t)$, which decays as integration progresses. Panel C illustrates the transition from preventable to irreducible states, with the green zone representing the window during which $R_0(e) = 0$ is achievable and the red zone representing the irreducible infection state. Panel D restates the theorem: prevention requires $R_0(e) = 0$, which is only achievable while $P_{int}(t) < 1$.

73 3.2. Finite Prevention Window for Post-Exposure Prophylaxis

74 Model parameterization indicates that the window for enforcing $R_0(e) = 0$ extends to
75 approximately 72 hours for mucosal exposures, constrained by local immune bottlenecks
76 [10]. However, for parenteral exposures (e.g., injection), this window is compressed to roughly
77 12–24 hours due to the bypass of early mucosal barriers and rapid systemic dissemination
78 [11]. This “left-shift” of the critical window significantly reduces the timeframe for effective
79 intervention.

80 Figure 2 demonstrates the quantitative compression of the prevention window between
81 mucosal and parenteral exposures. The parenteral route (red dashed line) shows a precipitous
82 decline in prevention efficacy within the first 24 hours, whereas the mucosal route (blue solid
83 line) maintains higher efficacy through 72 hours. This differential is driven by the distinct
84 immunological bottlenecks encountered in each tissue compartment.

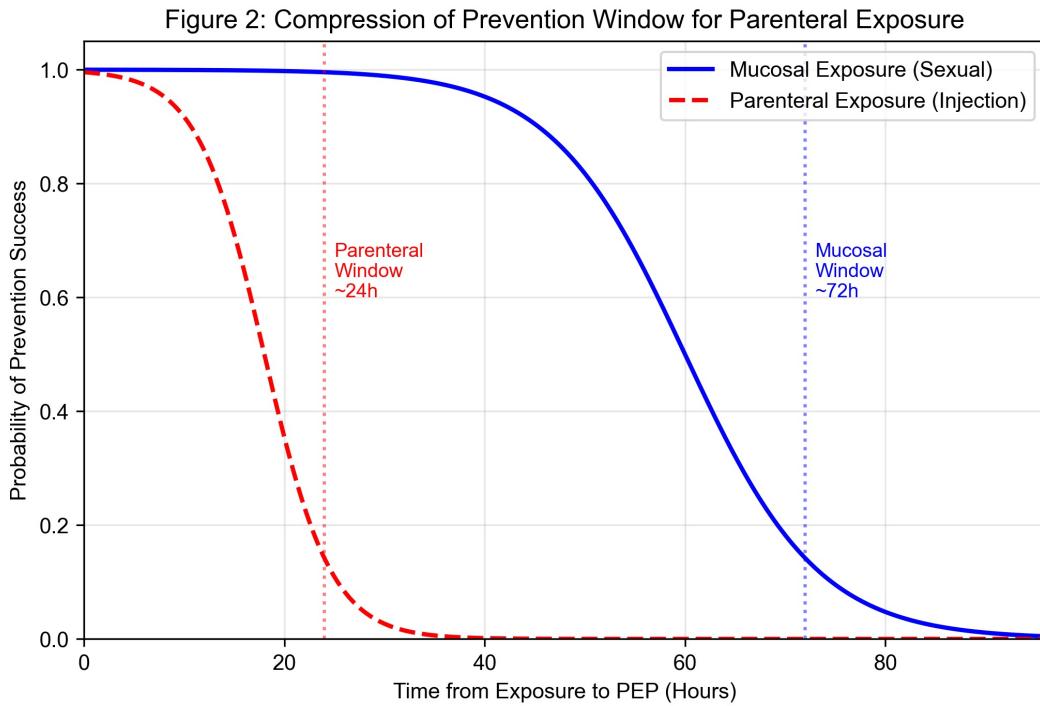


Figure 2: **Compression of the Prevention Window for Parenteral Exposure.** The solid blue line shows the probability of prevention success following mucosal exposure, which remains effective through approximately 72 hours. The dashed red line shows the dramatically compressed window for parenteral exposure, with prevention efficacy approaching zero by 24 hours. The differential reflects the bypass of mucosal immune barriers in systemic exposures, allowing more rapid establishment of productive infection.

85 3.3. *Irreducible Infection State*

86 Proviral integration represents a thermodynamically irreversible transformation of the
87 host genome. Once integrated, viral DNA persists for the lifetime of the cell and is propagated
88 to all daughter cells during division, producing clonal expansion independent of ongoing viral
89 replication [5].

$$G(t+1) = G(t) + \text{HIV}_{\text{provirus}} \quad (5)$$

90 No biologically realizable inverse transformation exists that restores the pre-integration
91 genomic state. Consequently, once integration occurs, the condition $R_0(e) = 0$ is mathemati-
92 cally unattainable [12, 13].

93 3.4. *Reservoir Stratification*

94 Long-lived viral reservoirs persist in specific cellular compartments, including naïve T-
95 cells, central memory T-cells (T_{CM}), stem cell-like memory T-cells (T_{SCM}), and microglial
96 cells [5, 14]. These compartments are characterized by self-renewal capacity and longevity,
97 allowing viral persistence independent of viral replication [15].

98 3.5. *Applied Example: Structural Infeasibility Under Access Delays*

99 Comparison of the derived biological windows against empirically observed access delays
100 in high-risk populations (e.g., people who inject drugs) reveals a fundamental mismatch.
101 Surveillance data indicates that while 85% of sexual exposure cases present to Emergency
102 Departments within 72 hours, structural delays for injection-related exposures consistently
103 exceed the compressed 24-hour parenteral window [16, 17].

104 For this population, the cycle time required to navigate arrest, withdrawal, and housing
105 instability (T_{struct}) almost invariably exceeds the biological cycle time (T_{bio}). Consequently,
106 the condition $R_0(e) = 0$ is biologically unreachable before access is even attempted. In
107 these scenarios, failure is not a probabilistic outcome of drug efficacy or adherence, but a
108 deterministic result of timing constraints.

109 **4. Discussion**

110 *4.1. Theoretical Implications*

111 Prevention is fundamentally an existence problem: does a state $R_0(e) = 0$ exist and is it
112 reachable? Our analysis shows that PEP failure often represents a boundary violation rather
113 than adherence failure; late intervention cannot alter the initial condition $R(0) > 0$ once it
114 has been established [9].

115 *4.2. Biological Proof of Concept: CCR5-Δ32*

116 The only known “cure” scenarios involve CCR5-Δ32 transplantation, which effectively
117 eliminates the susceptibility term in the transmission equation [13]:

$$\frac{dR}{dt} = \lambda SV \cdot 0 = 0 \quad (6)$$

118 This intervention functions as a system replacement rather than a reversal of the infection
119 state, reinforcing the irreversibility of the integrated provirus in susceptible hosts.

120 *4.3. Implications for Epidemic Control*

121 Reactive interventions cannot achieve epidemic control when biological establishment pre-
122 cedes access. Prevention architectures must therefore be evaluated against biological feasi-
123 bility constraints, not solely pharmacological efficacy [18].

124 **5. Future Work**

125 Future analyses will explore stochastic population dynamics and network-level avoidance
126 collapse resulting from these constraints. The specific impact of architectural failure on
127 population-level incidence is explicitly deferred to subsequent analysis.

128 **References**

- 129 [1] R. M. Grant, J. R. Lama, P. L. Anderson, V. McMahan, A. Y. Liu, L. Vargas, et al.,
130 Preexposure chemoprophylaxis for HIV prevention in men who have sex with men, New
131 England Journal of Medicine 363 (27) (2010) 2587–2599. doi:10.1056/NEJMoa1011205.

- 132 [2] P. L. Anderson, D. V. Glidden, A. Liu, S. Buchbinder, J. R. Lama, J. V. Guanira,
133 et al., Emtricitabine–tenofovir concentrations and pre-exposure prophylaxis efficacy in
134 men who have sex with men, *Science Translational Medicine* 4 (151) (2012) 151ra125.
135 doi:10.1126/scitranslmed.3003707.
- 136 [3] S. M. Blower, H. Dowlatabadi, Sensitivity and uncertainty analysis of complex models
137 of disease transmission: An HIV model as an example, *International Statistical Review*
138 62 (2) (1994) 229–243. doi:10.2307/1403510.
- 139 [4] A. J. McMichael, S. L. Rowland-Jones, The immune response to HIV, *Immunity* 33 (4)
140 (2010) 431–441. doi:10.1016/j.immuni.2010.08.006.
- 141 [5] A. Wahl, L. Al-Harthi, HIV infection of non-classical cells in the brain, *Retrovirology*
142 20 (1) (2023) 1. doi:10.1186/s12977-023-00616-9.
- 143 [6] J. D. Siliciano, R. F. Siliciano, Enhanced culture assay for detection and quantitation of
144 latently infected, resting CD4+ T-cells capable of producing infectious HIV-1, *Methods*
145 in Molecular Biology
- 1354 (2015) 3–15. doi:10.1007/978-1-4939-3067-2_1.
- 146 [7] D. Greenhalgh, G. Hay, Mathematical modelling of the spread of HIV/AIDS amongst
147 injecting drug users, *IMA Journal of Mathematics Applied in Medicine and Biology*
148 14 (1) (1997) 11–38.
- 149 [8] Y. Liang, D. Greenhalgh, X. Mao, A Stochastic Differential Equation Model for the
150 Spread of HIV amongst People Who Inject Drugs, *Computational and Mathematical*
151 *Methods in Medicine* 2016 (2016) 1–14. doi:10.1155/2016/6757928.
- 152 [9] I. Grant, J. H. Atkinson, J. R. Hesselink, C. J. Kennedy, D. D. Richman, S. A.
153 Spector, J. A. McCutchan, Evidence for Early Central Nervous System Involvement
154 in the Acquired Immunodeficiency Syndrome (AIDS) and Other Human Immunode-
155 ficiency Virus (HIV) Infections, *Annals of Internal Medicine* 107 (6) (1987) 828–836.
156 doi:10.7326/0003-4819-107-6-828.
- 157 [10] M. R. Tanner, J. G. O’Shea, K. M. Byrd, M. Johnston, G. G. Dumitru, J. N. Le, A. Lale,
158 K. K. Byrd, P. Cholli, E. Kamitani, W. Zhu, K. W. Hoover, A. P. Kourtis, *Antiretrovi-*

- ral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV – CDC recommendations, United States, 2025, MMWR Recomm Rep 74 (1) (2025) 1–56. doi:10.15585/mmwr.rr7401a1.
- [11] S. A. Strathdee, I. Kuo, N. El-Bassel, S. Hodder, L. R. Smith, S. A. Springer, Preventing HIV outbreaks among people who inject drugs in the United States: plus ça change, plus c'est la même chose, AIDS 34 (14) (2020) 1997–2005. doi:10.1097/QAD.0000000000002673.
- [12] T. R. Brown, A. Castillejo, Long-term follow-up of the London patient—the second adult to be cured of HIV-1 infection, Lancet HIV 6 (12) (2019) e821–e829. doi:10.1016/S2352-3018(19)30408-3.
- [13] G. Hutter, D. Nowak, M. Mossner, S. Ganepola, A. Müßig, B. Winter, et al., Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell-derived grafted dendritic cells, New England Journal of Medicine 360 (7) (2009) 692–698. doi:10.1056/NEJMoa0802905.
- [14] A. M. Anderson, L. Munro, B. Phipps, S. Spudich, V. Valcour, S. Nightingale, Neuroinflammation in HIV: The role of translocator protein, Journal of Neurovirology 26 (6) (2020) 768–786. doi:10.1007/s13365-020-00882-9.
- [15] J. Hellmuth, J. L. Fletcher, V. Valcour, S. Spudich, A. M. Anderson, M. Vinikoor, et al., Very early initiation of antiretroviral therapy during acute HIV infection is associated with normalized levels of immune activation markers in cerebrospinal fluid but not in plasma, Journal of Infectious Diseases 220 (2) (2018) 208–213. doi:10.1093/infdis/jiy348.
- [16] J. L. Taylor, A. Y. Walley, A. R. Bazzi, Stuck in the window with you: HIV exposure prophylaxis in the highest risk people who inject drugs, Substance Abuse 40 (4) (2019) 441–443. doi:10.1080/08897077.2019.1635551.
- [17] A. R. Baugher, C. Wejnert, D. Kanny, D. Broz, J. Feelemyer, R. B. Hershaw, et al., Are we ending the HIV epidemic among persons who inject drugs? Key findings from 19 US cities, AIDS 39 (12) (2025) 1813–1819. doi:10.1097/QAD.0000000000004249.

186 [18] F. J. J. Palella, K. M. Delaney, A. C. Moorman, M. O. Loveless, J. Fuhrman, G. A.
187 Satten, et al., Declining morbidity and mortality among patients with advanced human
188 immunodeficiency virus infection, New England Journal of Medicine 338 (13) (1998)
189 853–860. doi:10.1056/NEJM199803261381301.

190 Data Sharing

191 All model code, simulation outputs, and analysis scripts are available at <https://github.com/Nyx-Dynamics/Prevention-Theorem>. All model inputs derive from published literature
192 or synthetic populations; no individual-level data were used.
193

194 Declaration of Interests

195 The author reports prior employment with Gilead Sciences, Inc. from January 2020
196 through November 2024 and prior ownership of company stock, which was fully divested
197 in December 2024. Gilead Sciences, Inc. had no role in the conception, design, analysis,
198 interpretation, or writing of this study, and provided no funding, data, materials, or input
199 into any aspect of the work.

200 The author is the owner of Nyx Dynamics, LLC, a consulting company providing advisory
201 and fractional leadership services in healthcare, technology, and complex systems. This
202 research was conducted independently, released as open-source work, and was not produced
203 as part of, or in support of, any paid consulting engagement.

204 No other competing interests are declared.

205 Ethics Approval and Consent to Participate

206 This study did not involve human participants, human biological samples, or the collection
207 of identifiable private information. All analyses were conducted using publicly available,
208 aggregate data from published literature and guidelines. As such, institutional review board
209 (IRB) approval and informed consent were not required.

210 **Acknowledgments**

211 **Communities.** The author thanks the HIV prevention research community whose pub-
212 lished work informed model parameterization, and the people who inject drugs (PWID)
213 community advocates whose testimony informed characterization of structural barriers.

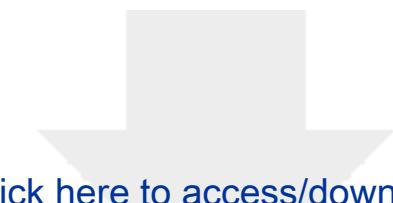
214 **Use of Artificial Intelligence and Assistive Technologies.** The author acknowledges
215 the use of artificial intelligence-assisted tools during manuscript preparation. Computational
216 analyses were conducted using Python with open-source packages including NumPy, Pandas,
217 SciPy, Matplotlib, and Seaborn. Large language models (Anthropic Claude and OpenAI
218 ChatGPT) were used to support literature search and improve readability of the manuscript.
219 JetBrains Junie was used for code correction, and Zotero AI was used for reference man-
220 agement. Manuscript preparation was conducted using the Overleaf L^AT_EX platform. All AI
221 tools were used as assistive technologies only. The author retains full responsibility for study
222 design, data analysis, interpretation of results, and all conclusions presented.



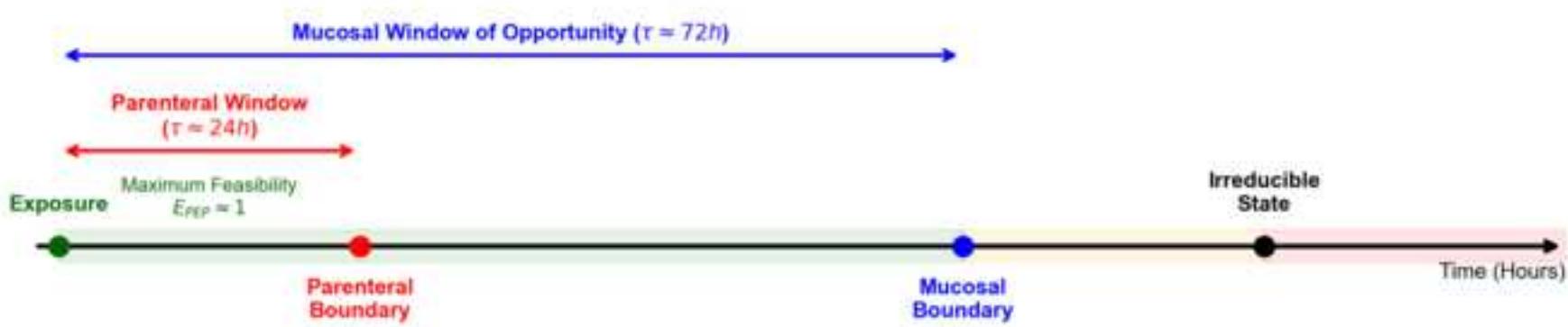
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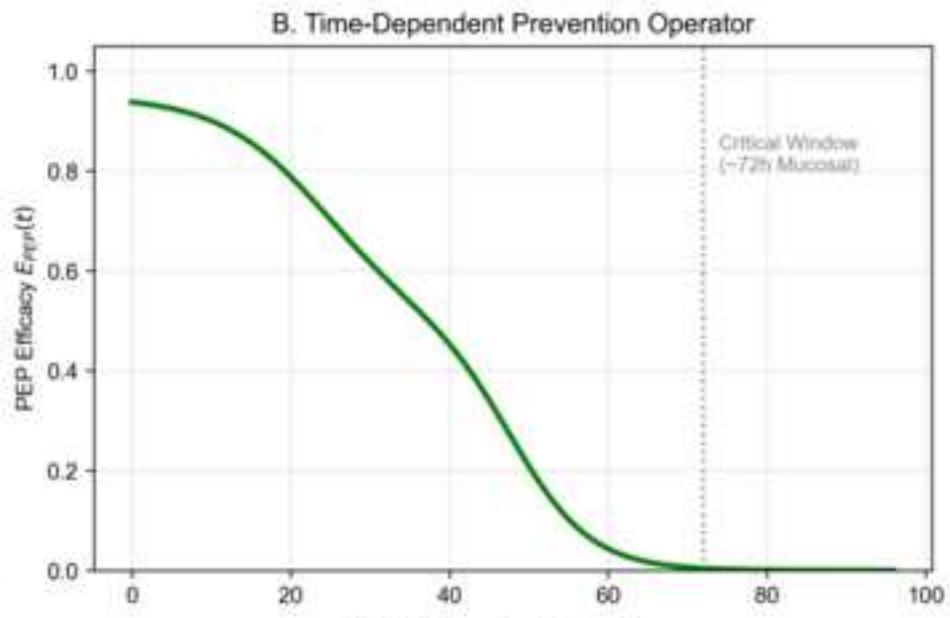
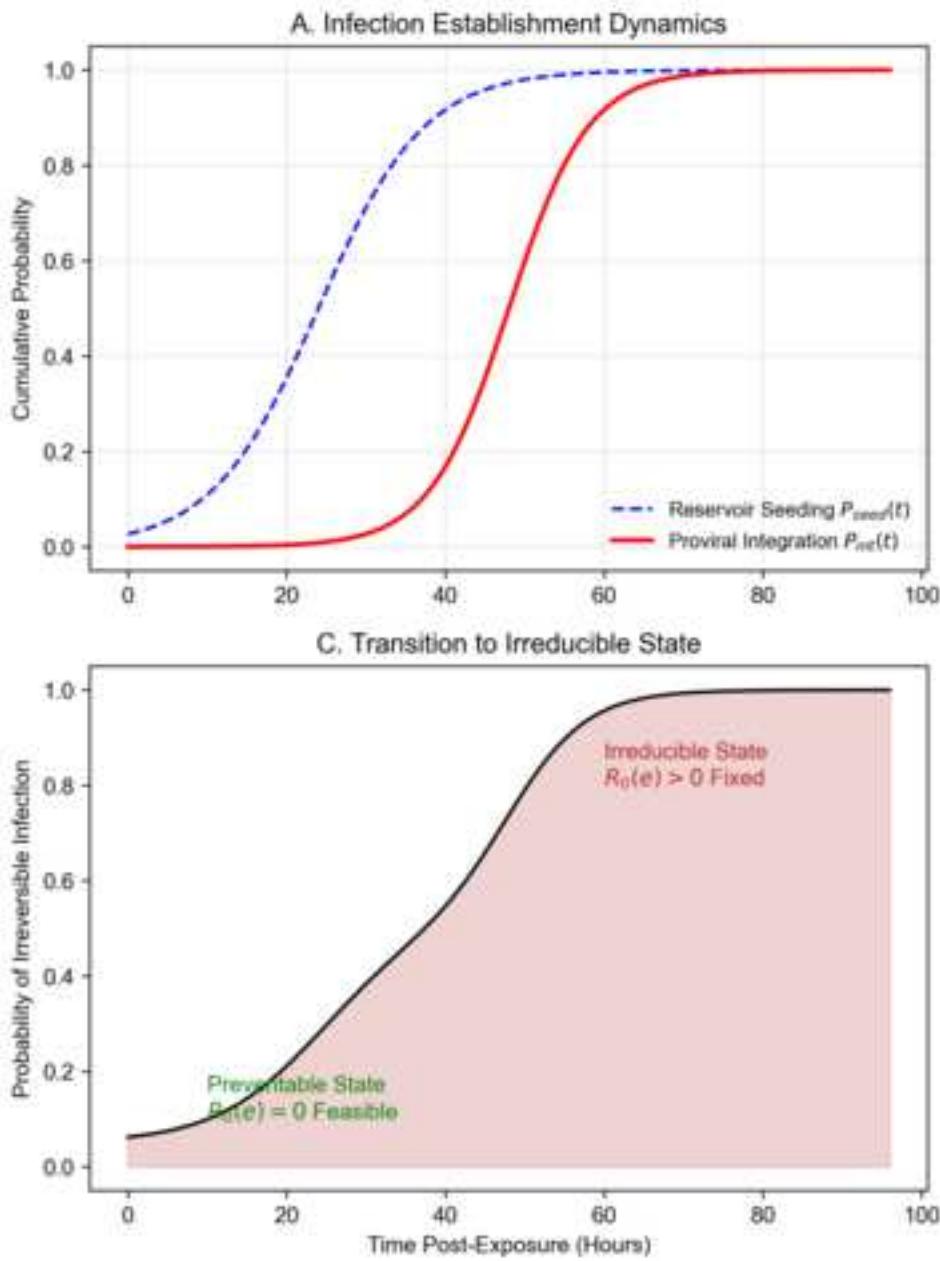


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**The Prevention Theorem**

$$R_0(e, t) = 1 - E_{PEP}(t)$$

Boundary: $E_{PEP}(t) \rightarrow 0$ as $P_{int}(t) \rightarrow 1$



The Prevention Theorem

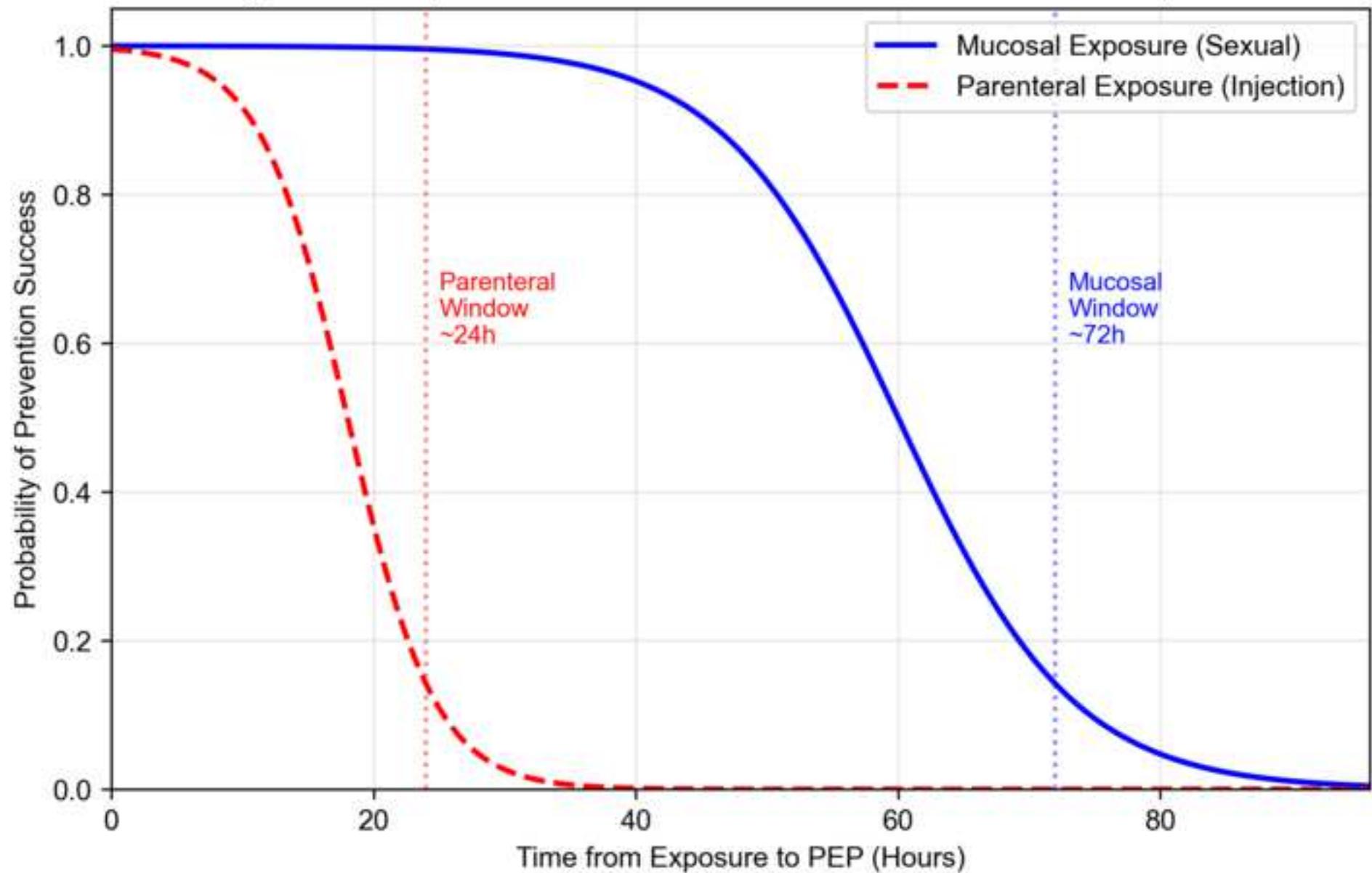
Prevention requires $R_0(e, t) = 0$.

$$R_0(e, t) = 1 - E_{PEP}(t)$$

As $t \rightarrow \infty$, $P_{int}(t) \rightarrow 1 \Rightarrow E_{PEP}(t) \rightarrow 0$.

∴ Prevention is only possible while $P_{int}(t) < 1$.

Figure 2: Compression of Prevention Window for Parenteral Exposure



Declaration of interests

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 authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

The corresponding author (ACD) reports prior employment with Gilead Sciences, Inc. from January 2020 through November 2024 and prior ownership of company stock, which was fully divested in December 2024. Gilead Sciences, Inc. had no role in the conception, design, analysis, interpretation, or writing of this study, and provided no funding, data, materials, or input into any aspect of the work.

The corresponding author (ACD) is the owner of Nyx Dynamics, LLC, a consulting company providing advisory and fractional leadership services in healthcare, technology, and complex systems. This research was conducted independently, released as open-source work, and was not produced as part of, or in support of, any paid consulting engagement.

No other competing interests are declared. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.