



Article

Generic Patterns in HIV Transmission Dynamics: Insights from a Phenomenological Risk-Stratified Modeling Approach

Susanne F. Awad and Diego F. Cuadros *

Digital Epidemiology Laboratory, Digital Futures, University of Cincinnati, Cincinnati, OH 45221, USA; suaw@lundbeck.com

* Correspondence: diego.cuadros@uc.edu; Tel.: +1-(513)-556-3423; Fax: +1-(513)-556-3370

Abstract: Background: Understanding the dynamics of HIV transmission in heterogeneous populations is crucial for effective prevention strategies. This study introduces the Risk Modulation Point (RMP), a novel threshold identifying where HIV transmission transitions from unsustainable spread to self-sustaining epidemic dynamics. **Methods:** Using a deterministic, risk-stratified compartmental model, we examined HIV transmission across populations stratified into 100–200 risk groups, each characterized by behavioral heterogeneity modeled through a power-law distribution. The model captures key features of HIV progression, with simulations conducted across high- (~20%), moderate- (~5%), and low (~0.2%)-prevalence regimes. **Results:** Our findings reveal universal patterns in HIV dynamics. The RMP marks a consistent threshold across scenarios, separating low-risk groups where transmission is minimal from higher-risk groups sustaining the epidemic. Logistic growth in HIV prevalence across risk groups, with sharp transitions near the RMP, was observed universally. The force of infection follows power-law scaling, directly reflecting the level and nature of risk behavior within each group. Importantly, the location of the RMP remains largely invariant to the underlying sexual risk distribution, population resolution, and mixing patterns, making it applicable across both generalized and concentrated epidemics. **Conclusion:** The RMP framework offers actionable public health insights. It identifies key populations and transition regions for targeted interventions such as antiretroviral therapy and pre-exposure prophylaxis. By tracking shifts in the RMP, it also serves as an early warning indicator for epidemic transitions, guiding resource allocation and monitoring. The focus of the model on intrinsic epidemic dynamics, excluding external interventions, highlights its utility in uncovering fundamental transmission patterns. This study bridges theoretical modeling and practical application, providing a flexible framework for understanding HIV and other stratified epidemics. The findings advance HIV modeling by revealing generic patterns that transcend specific contexts, supporting data-driven public health strategies.



Academic Editor: Alexandre G. De Brevern

Received: 19 December 2024

Revised: 7 February 2025

Accepted: 18 February 2025

Published: 26 February 2025

Citation: Awad, S.F.; Cuadros, D.F. Generic Patterns in HIV Transmission Dynamics: Insights from a Phenomenological Risk-Stratified Modeling Approach. *BioMedInformatics* **2025**, *5*, 11. <https://doi.org/10.3390/biomedinformatics5010011>

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Keywords: HIV transmission dynamics; risk modulation point (RMP); risk heterogeneity; deterministic compartmental model; epidemic thresholds

1. Introduction

The HIV-1 pandemic continues to pose a significant global health challenge, particularly in sub-Saharan Africa (SSA), where approximately 70% of the world's new HIV infections occur annually [1,2]. Despite decades of research and substantial public health efforts, the epidemic persists at high levels in many regions [3]. This enduring prevalence underscores the complexity of HIV transmission dynamics and the need for a deeper

understanding of the factors driving the epidemic in diverse populations. While HIV is often concentrated in high-risk groups, such as individuals with multiple sexual partners or those who inject drugs [4], it also exhibits significant spread within the general population in many SSA countries [5,6]. This duality highlights the critical need to examine the drivers of the epidemic across all segments of society.

HIV is predominantly transmitted through sexual contact, making sexual behavior a central determinant of transmission risk. Factors such as the number of sexual partners, concurrency of partnerships, and mixing patterns within sexual networks play key roles in shaping the epidemic [7,8]. For instance, individuals with multiple concurrent partners can act as epidemiological bridges, facilitating the spread of the virus across otherwise disconnected networks [9,10]. However, the complex, variable, and often private nature of human sexual behavior complicates efforts to accurately model and predict HIV transmission. Traditional models frequently rely on predefined risk categories, grouping individuals based on specific behavioral characteristics [11–14]. While informative, these approaches may oversimplify the continuous and overlapping spectrum of sexual behaviors observed in real-world settings.

To address these challenges, we adopted a novel, phenomenological modeling framework that accommodates an arbitrary number of risk groups, avoiding the rigid definitions often used in conventional models. This approach enables the exploration of a broad spectrum of behavioral heterogeneity and mixing patterns without imposing restrictive assumptions about population structure. By allowing intrinsic epidemic patterns to emerge naturally from the dynamics of the model, this method provides a powerful tool for identifying generic features of HIV transmission dynamics.

In this study, we aim to demonstrate that HIV epidemics exhibit consistent patterns of Risk Modulation Points (RMP), transition widths, and coupling strength across varying prevalence levels. RMP represents a critical threshold in HIV epidemic dynamics, marking the transition from limited, unsustainable transmission to self-sustaining epidemic spread. Below the RMP, transmission struggles to sustain itself and remains confined to low-risk groups. Above the RMP, transmission becomes sufficient to maintain ongoing spread, typically among higher-risk groups, but depending on mixing dynamics “spillover” to lower-risk groups (more in terms of acquisition) might occur. For example, in concentrated epidemics, HIV prevalence may be negligible in the general population but rise sharply among individuals with higher-risk behaviors, such as multiple concurrent partners.

The RMP defines the point where risk behaviors become sufficient to drive widespread transmission, causing some level of endemic status. This concept has significant public health implications. By identifying the RMP, we can target interventions to prevent individuals from crossing this threshold, thereby interrupting transmission before it becomes self-sustaining. Furthermore, the RMP provides insight into why some epidemics remain concentrated in high-risk groups while others spread more broadly, depending on where the RMP falls relative to the risk structure of the population. As a quantitative marker of a qualitative shift in epidemic behavior, the RMP offers a valuable framework for understanding and addressing the dynamics of HIV transmission.

The RMP represents a critical threshold in risk-stratified populations, marking the transition from localized, subcritical transmission ($R_0 < 1$) to sustained epidemic propagation ($R_0 > 1$). Similar threshold-based concepts are widely used in epidemiology. The concept of stratified R_0 has been extensively applied in sexually transmitted infections (STIs) [15,16], core group theory [17,18], and epidemic tipping point analysis [19,20]. For example, studies of gonorrhea transmission in high-risk populations in the United States (US) and targeted HIV hotspot interventions in sub-Saharan Africa have demonstrated that identifying and addressing risk-specific transmission thresholds is critical for epidemic

control [6,21]. Further, epidemic threshold concepts have been extensively applied in other infectious diseases, such as measles, COVID-19, and malaria, reinforcing the generalizability of the RMP as a tool for targeted prevention strategies [22–24]. By integrating these approaches, the RMP provides a unified framework to inform precision public health interventions and resource allocation strategies, particularly in HIV prevention efforts.

Our work is motivated by the need to enhance public health strategies through a better understanding of universal patterns in HIV transmission. By identifying the threshold behaviors, scaling properties, and stratification dynamics that are consistent across population structures, we provide insights into the fundamental mechanisms underlying the epidemic. These findings have significant implications for the design of targeted interventions, particularly in settings where traditional models may fall short in capturing the complexity of HIV transmission. By uncovering these generic patterns, we contribute to a deeper understanding of HIV epidemiology and provide a flexible modeling framework capable of informing more precise and effective public health interventions.

2. Methods

2.1. Model Structure

Building on previous models [25–27], we developed a deterministic compartmental model to explore, in a generalized manner, the influence of sexual behavior heterogeneity on HIV epidemiology. The model stratifies the sexually active population into compartments based on HIV status, stage of infection, and level of sexual risk behavior. HIV pathogenesis is described by three stages: acute, latent, and advanced.

2.2. Compartment Definitions

The population is divided into the following groups:

- Susceptible individuals (S_i): HIV-negative individuals in risk group k .
- Infected individuals: Individuals categorized into three stages of HIV pathogenesis:
 1. Acute stage ($I_{i,1}$): Initial phase of infection with high viral load and transmissibility.
 2. Latent stage ($I_{i,2}$): Chronic phase with lower viral load.
 3. Advanced stage ($I_{i,3}$): Final phase (AIDS) with high transmissibility and mortality.

Here, the subscript $i = 1, 2, \dots, n$ denotes the risk group, stratified by sexual behavior (e.g., partner acquisition rate).

2.2.1. Parameters and Notation

- $N_{0,i}$: Initial population size of risk group k .
- μ : Birth/death rate (per capita), assumed equal across groups.
- ω_1, ω_2 : Progression rates from acute to latent (ω_1) and latent to advanced (ω_2) stages.
- ω_3 : Disease-induced mortality rate in the advanced stage.
- Λ_i : Force of infection (FOI) for risk group k , defined as the hazard rate of acquiring HIV.

2.2.2. Transition Equations

With the compartments and parameters defined, the model is governed by the following differential equations:

Susceptible in risk group i :

$$\frac{dS_i}{dt} = \mu N_{0,i} - \mu S_i - \Lambda_i S_i \quad (1)$$

Acute-stage infection in risk group i :

$$\frac{dI_{i,1}}{dt} = \Lambda_i S_i - \mu I_{i,1} - \omega_1 I_{i,1} \quad (2)$$

Latent-stage infection in risk group i :

$$\frac{dI_{i,2}}{dt} = \omega_1 I_{i,1} - \mu I_{i,2} - \omega_2 I_{i,2} \quad (3)$$

Advanced-stage infection in risk group i :

$$\frac{dI_{i,3}}{dt} = \omega_2 I_{i,2} - \mu I_{i,3} - \omega_3 I_{i,3} \quad (4)$$

Here, the index i labels the i -risk group in the population, $S(i)$ is the HIV susceptible population in the i -risk group, and $I_\beta(i)$ is the HIV-infected population in the i -risk group. The index β marks the stage of HIV pathogenesis; $\beta = 1, 2, 3$ represent acute, latent, and advanced stages, respectively. $N_0(i)$ is the initial population size of each i -risk group. μ is the birth (and death) rate. The rate of progression from one HIV stage to another is described by $\omega_{I_{\beta=1,2}}$, and $\omega_{I_{\beta=3}}$ is the rate of HIV/AIDS disease mortality. The rates Λ_i are the HIV forces of infection (hazard rates of infection) experienced by the susceptible population. A detailed discussion of the model is described in the Supplementary Materials.

2.3. Equilibrium Solution

The role of sexual contact structure in HIV transmission dynamics was studied at the endemic equilibrium. The formal definition of the population variables at endemic equilibrium are given in Equations (S1.8)–(S1.11) in the Supplementary Materials. In addition to the analytical and computational tractability, this approach allows us to disentangle essential dynamical features of infection transmission from the transient effects of the temporal evolution. The equilibrium solution of the model was derived using a methodology of convergent successive approximations introduced by Abu Raddad et al. [28,29]. The methodology allows us to calculate the forces of infection from which all population and to derive epidemiologic measures.

2.4. Key Parameter Values

The parameters of the model were derived using the best available empirical data on HIV epidemiology and are listed in Table S1.1 in the Supplementary Materials. The HIV transmission probability per coital act for the acute stage was extracted from a re-analysis study of the Rakai data [30,31]. For latent and advanced infection, the transmission probabilities were extracted from Abu-Raddad et al. [32], which uses measurements from Wawer et al. [33]. The frequencies of coital acts per stage of infection were based on the measurements from Wawer et al. [33].

The durations of the acute, latent, and advanced stages were assumed to be 49 days (acute), 9 years (latent), and 2 years (advanced). These choices were based on the classification in Wawer et al. [33], the re-analysis of the Rakai data for the acute infection in Pinkerton [30], and the measured time from seroconversion to death in several cohort studies [34,35], and recent compilation of data by UNAIDS indicating that the average duration from HIV acquisition to death in absence of antiretroviral therapy is about 11 years [36,37]. The duration of the sexual activity lifespan was estimated at 35 years, since 15–49 years is the age group used to define the sexually active population in the literature and standard guidelines [32,38–40].

2.5. Sexual Contact Structure

The heterogeneity of sexual risk behavior in human populations was mapped by defining different forms of the sexual contact structure and variability within each sexual contact structure. Details of the sexual contact structure are included in the Supplementary Materials.

The level of variability in the effective sexual partner acquisition rate is described by the parameter α . To explore different heterogeneity patterns, we used a linear model ($\alpha = 1$) as well as nonlinear models ($\alpha = 2, 3, 4, 5$) to map the level of variability in the risk of exposure to HIV. The larger the value of α , the higher is the variability in risk behavior in the population as expressed in terms of the standard deviation in HIV risk of exposure (Figure S1.2B in Supplementary Materials).

The heterogeneity parameter (α) was varied between 1 and 5, reflecting a range of theoretical and empirical patterns:

- $\alpha = 1$ —Linear Case: Represents minimal heterogeneity, with nearly uniform risk distribution of risk among the risk groups. Serves as a baseline for comparisons. Observed in generalized epidemics, such as in rural settings in sub-Saharan Africa, where sexual behavior tends to be more homogeneous.
- $\alpha = 2, 3$ —Moderate Heterogeneity: Reflects typical risk patterns observed in many concentrated epidemics. Produces moderate differentiation between risk groups. Supported by studies showing moderate stratification in urban populations in sub-Saharan Africa or concentrated epidemics in Southeast Asia.
- $\alpha = 4, 5$ —High Heterogeneity: Models highly stratified populations, as observed in extreme cases of concentrated epidemics, where a small fraction of the population accounts for a disproportionately large share of partnerships and transmission events. Amplifies differences between risk groups, creating maximal separation. Reflective of concentrated epidemics in high-risk subpopulations, such as injection drug users or commercial sex workers, as observed in regions like Eastern Europe and parts of Asia.

The influence of α on risk group separation is evident in the widening divergence of force of infection curves and prevalence levels, as well as the enhanced threshold effects observed at higher α .

The pattern of sexual mixing between the different risk groups was represented through a mixing matrix that describes the likelihood that a member of one risk group will form a partnership with a member of another risk group [41]. The mixing matrix is formally defined in the Supplementary Materials, Equation (S1.3), with the degree of mixing represented by a parameter (e). This matrix illustrates a continuum of mixing between two extremes. At one end ($e = 1$), the mixing is fully assortative, meaning individuals within a specific risk group exclusively select partners from their own group. Conversely, at the opposite end ($e = 0$), the mixing is proportionate, where partnerships are formed based solely on the availability of partners across different risk groups, without any preferential bias in partner selection.

The force of infection (Λ_i) inherits the power-law behavior of the risk distribution (ρ_i) scaling approximately as $i\alpha$ at low prevalence levels. However, as prevalence increases, saturation effects alter this relationship, resulting in an exponential-like growth of Λ_i within higher-risk groups. This dynamic establishes a direct link between population heterogeneity and epidemic patterns.

2.6. Risk Modulation Point (RMP)

The basic reproductive number (R_0) was defined as the average number of secondary infections generated by one primary infection within an entirely susceptible population [15]. R_0 determines the sustainability of an infection upon entrance into a fully susceptible

population. If $R_0 > 1$, the infection is sustainable in the population. If $R_0 < 1$, the infection is not sustainable in the population.

In a population that consists of one sexual risk group, an expression for R_0 can be derived for our model using the second generation matrix methodology [42]:

$$R_0 = \frac{t_1 \rho}{(\mu + \omega_1)} + \frac{t_2 \rho \omega_1}{(\mu + \omega_1)(\mu + \omega_2)} + \frac{t_3 \rho \omega_1 \omega_2}{(\mu + \omega_1)(\mu + \omega_2)(\mu + \omega_3)} \quad (5)$$

This equation for $R_0 = 1$ defines the minimum threshold value of the effective partnership change rate $\rho_{\text{threshold}}$ at which HIV infection can be sustainable.

In a population where there is several of risk groups with variable levels of risk behavior and these groups are mixing with each other, the expression for R_0 is much more involved; HIV infection becomes sustainable even in the risk groups for which ρ are too small to sustain HIV infection in absence of mixing with other risk groups. However, for reasons discussed below, it is useful to still define an “ $R_{0,i}$ ” for each risk group in the population:

$$R_{0,i} = \frac{t_{1,i} \rho_i}{(\mu + \omega_1)} + \frac{t_{2,i} \rho_i \omega_1}{(\mu + \omega_1)(\mu + \omega_2)} + \frac{t_{3,i} \rho_i \omega_1 \omega_2}{(\mu + \omega_1)(\mu + \omega_2)(\mu + \omega_3)} \quad (6)$$

The RMP represents the risk group index (i) where the basic reproductive number (R_0) transitions from greater than 1 ($R_0 > 1$) to less than 1 ($R_0 < 1$). This threshold divides the population into two classes of risk groups: those above the RMP ($R_0 > 1$), which can sustain the epidemic independently, and those below the RMP ($R_0 < 1$), which rely on contributions from higher-risk groups via mixing to sustain transmission. Numerically, the RMP was determined by analyzing the prevalence distribution (y_i) across risk groups at equilibrium.

In summary, the RMP represents the critical threshold in a population’s risk hierarchy where HIV transmission transitions from unsustainable (confined to low-risk groups) to self-sustaining (spreading widely). It is the tipping point where the basic reproductive number (R_0) crosses 1:

- **Below the RMP** ($R_0 < 1$): Transmission cannot sustain itself without contributions from higher-risk groups.
- **Above the RMP** ($R_0 > 1$): Transmission becomes self-sustaining, driving epidemic growth or maintenance.

The RMP is identified numerically as the risk group where HIV prevalence begins to rise sharply, marking the boundary between these two regimes.

To identify the RMP, prevalence curves (y_i) generated from simulations were inspected to locate the point of sharp transition from negligible prevalence levels to substantial values. These prevalence curves exhibit logistic growth patterns, transitioning from near-zero values in low-risk groups to saturation in high-risk groups. The RMP was identified as the risk group index where prevalence begins to rise significantly, corresponding to the boundary where $R_0 \approx 1$. In practice, this transition was identified by numerically inspecting y_i curves and determining the risk group index where y_i exceeded 0.1 (10% prevalence), marking the transition from localized, unsustainable transmission to sustained epidemic spread. This threshold was chosen based on epidemic persistence principles, ensuring that the RMP represents the point at which prevalence is sufficiently high to sustain endemic transmission. Alternative methods, such as computing derivatives (dy_i/dt), were considered but were found to be less robust due to numerical instability, multiple inflection points in highly heterogeneous epidemics, and reduced interpretability in public health contexts.

To ensure the robustness of RMP identification, the process was repeated with varying parameter values, such as the heterogeneity parameter (α) and the resolution of risk group stratification (e.g., 100 vs. 200 groups). The identified RMPs were consistent across these

variations, confirming the reliability of this approach. This methodology links the RMP directly to the observed prevalence dynamics and the conceptual threshold of $R_0 = 1$, providing a clear basis for its determination.

2.7. HIV Prevalence Regimes

To systematically categorize the prevalence regimes used in our analysis, we define low, moderate, and high prevalence thresholds based on epidemiological benchmarks commonly used in HIV surveillance and public health interventions. These thresholds align with global classification frameworks, including UNAIDS guidelines that distinguish between low-level, concentrated, and generalized epidemics [43,44].

In our model, low prevalence is defined as HIV prevalence below 0.5%, where transmission remains largely confined to high-risk groups with minimal spillover into the general population. In this regime, epidemic sustainability depends entirely on high-risk individuals ($i > 90$ in a 100-group model), and the RMP occurs at very high-risk levels, reflecting the limited expansion of transmission networks.

Moderate prevalence is defined as HIV prevalence of about 5%, where bridging transmission expands beyond key populations, affecting moderate-risk groups. In this phase, localized transmission clusters become increasingly significant, and the RMP shifts downward, encompassing a broader subset of individuals. This regime represents a transition point between concentrated and generalized epidemics, where intervention strategies must target both high-risk individuals and emerging transmission hubs.

High prevalence is defined as HIV prevalence exceeding 20%, where transmission occurs widely across multiple risk strata, reaching endemic equilibrium. In this phase, the force of infection (Λ_i) becomes less sensitive to individual risk heterogeneity due to saturation effects, leading to a generalized epidemic. Empirical studies in sub-Saharan Africa support this threshold, as regions with >20% prevalence tend to exhibit sustained transmission across all risk groups.

2.8. Simulation Scenarios

We simulated the model under various prevalence levels and heterogeneity parameters to explore their influence on epidemic dynamics. The key scenarios included:

- **High Prevalence (~20%):** This represents generalized epidemics with widespread transmission. It is characteristic of generalized epidemics in southern Africa, where HIV transmission is widespread. It captures the dynamics of maximum sustainable prevalence, with minimal threshold effects due to saturation.
- **Moderate Prevalence (~5%):** This reflects intermediate transmission intensity. It also reflects concentrated epidemics in key populations, such as sex workers and men who have sex with men. It represents a transitional state between concentrated and generalized epidemics, with distinct threshold behavior.
- **Low Prevalence (~0.2%):** This represents concentrated epidemics in high-risk subpopulations. It is common in global settings with concentrated epidemics. It highlights the importance of risk stratification, with strong threshold effects and epidemic concentration in high-risk groups.

Each scenario was simulated under varying α values to evaluate the role of heterogeneity in shaping epidemic outcomes. These prevalence levels reflect real-world epidemiological diversity and demonstrate how varying transmission intensity influences threshold behaviors and risk stratification.

Simulations were conducted using two risk group resolutions (100 and 200 groups) to evaluate the impact of stratification on RMP scaling and transition widths. Doubling

the resolution allowed for finer delineation of risk groups, capturing subtle differences in transmission dynamics, especially in low-prevalence regimes.

The RMP was identified as the threshold risk group index (i) where prevalence transitions from negligible to high levels. This threshold was used to assess the sustainability of transmission and the concentration of the epidemic in high-risk groups. RMP locations were compared across prevalence levels, risk group resolutions ($n = 100$ vs. $n = 200$), and heterogeneity values.

2.9. Equilibrium Solution and Outcome Metrics

The equilibrium solution of the model was derived using the method of convergent successive approximations, allowing for calculation of the forces of infection (λ_i) and other epidemiological measures at steady state. Key metrics analyzed include:

- Force of Infection (λ_i): This measures the intensity of transmission in each risk group.
- Prevalence (y_i): This examines the distribution of HIV burden across risk groups.
- Threshold Behavior (RMP): This identifies the risk group index (i) where prevalence transitions from negligible to high levels.
- Transition width (Δ_i): This quantifies the sharpness of epidemic progression. It is defined as the difference in risk group indices where prevalence (y_i) increases from 20% to 80% of its maximum value. It quantifies the sharpness of the epidemic progression across risk groups and serves as a metric for stratification in the population. This metric captures the steepness of the logistic growth in prevalence across risk groups. A smaller Δ_i indicates a sharp and concentrated epidemic progression, characteristic of populations with higher stratification or greater heterogeneity in risk behavior (α). Conversely, a larger Δ_i reflects a more gradual transition, indicating less stratification and a wider distribution of transmission across risk groups.

2.10. Numerical Implementation

Simulations were performed using Matlab R2023a, version 9.14 [45]. The model's equilibrium solutions were validated for robustness under varying mixing patterns, prevalence levels, and heterogeneity. The MATLAB code used in our analysis is available at: GitHub (San Francisco, CA, USA)—diegofcudros/HIV_Model.

3. Results

The model simulations yielded critical insights into the interplay between risk heterogeneity, risk group resolution, and HIV epidemic dynamics across different prevalence levels. The results were analyzed to examine force of infection (λ_i), prevalence patterns (y_i), threshold behavior (RMP), and scaling properties under various scenarios.

3.1. Epidemic Dynamics at High Prevalence (~20%)

The high-prevalence scenario demonstrates how widespread transmission homogenizes epidemic dynamics across risk groups, reducing the influence of heterogeneity (α).

3.1.1. Force of Infection

Figure 1 (upper left panel) shows the force of infection (λ_i) across 100 risk groups. The force of infection exhibits an exponential increase, peaking at a high magnitude (~450), with sharp transitions occurring in early risk groups ($i < 20$). Variations in α values minimally affect the shape or magnitude of λ_i , indicating that transmission dynamics dominate over risk heterogeneity in this regime.

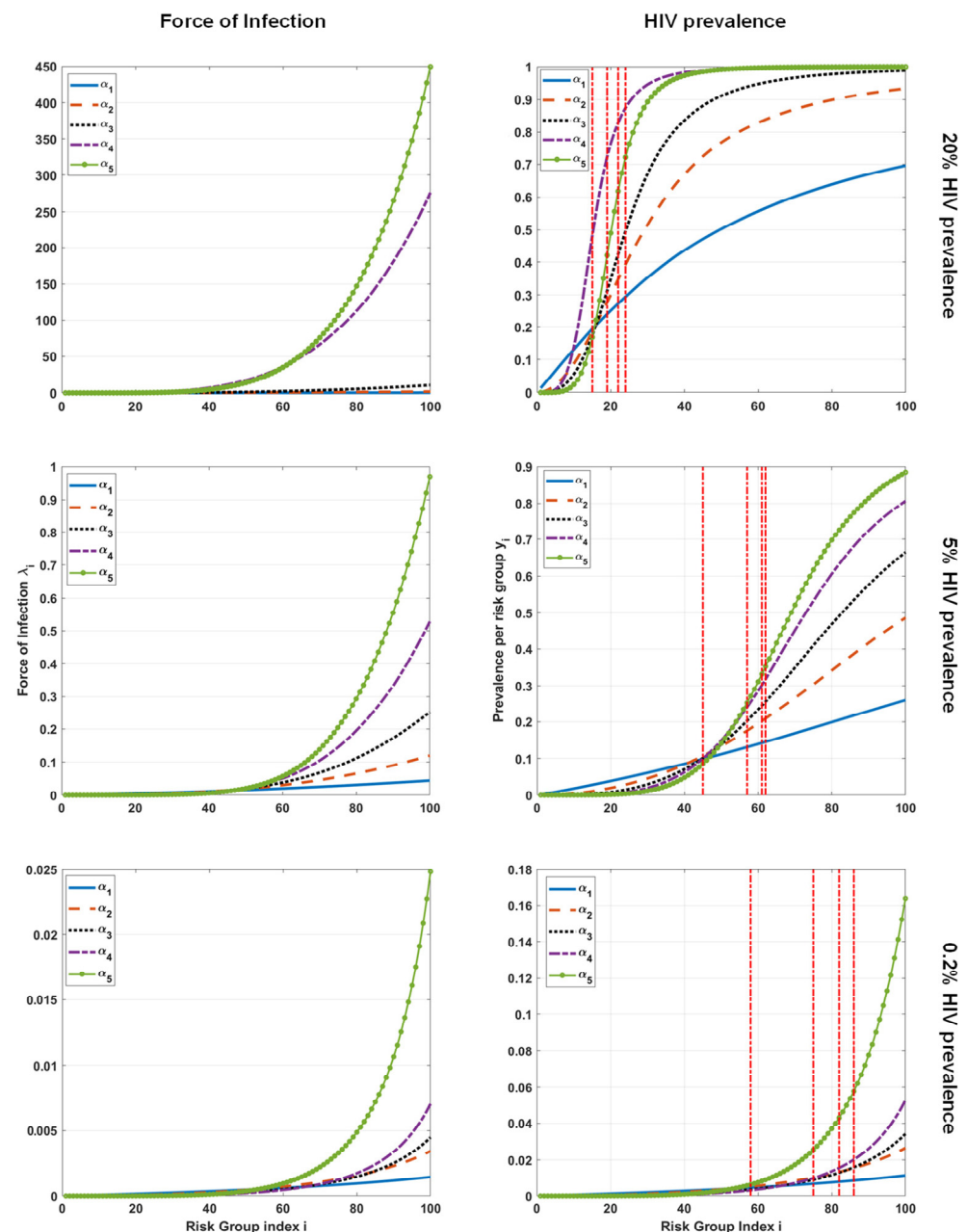


Figure 1. Force of infection (λ_i) and HIV prevalence (y_i) across risk groups under different prevalence regimes. Left panels show the force of infection and right panels show the corresponding HIV prevalence distributions across 100 risk groups, with different curves representing varying heterogeneity parameters (α_1 to α_5). Top row: High-prevalence scenario ($\sim 20\%$) showing a strong force of infection (reaching ~ 450) and prevalence saturation near 1.0 in high-risk groups. Middle row: Moderate-prevalence scenario ($\sim 5\%$) demonstrating an intermediate force of infection (~ 1.0) and more gradual prevalence increases. Bottom row: Low-prevalence scenario ($\sim 0.2\%$) showing a weak force of infection (~ 0.025) and concentrated prevalence in highest risk groups. The red vertical lines in the prevalence panels indicate Risk Modulation Points (RMPs) where prevalence transitions from negligible to high levels. Higher α values lead to sharper transitions and more concentrated epidemics in high-risk groups across all prevalence regimes.

3.1.2. Prevalence Patterns

Figure 1 (upper right panel) illustrates HIV prevalence (y_i) across risk groups. Prevalence follows a logistic growth curve, with early thresholds (RMPs at $i \approx 20$) and saturation occurring near 1.0 in high-risk groups. The RMPs are consistent across all α values, reflecting a robust threshold unaffected by heterogeneity.

3.1.3. Generic Patterns

- RMP Stability: The threshold location remains consistent, regardless of α , reflecting robust dynamics dominated by transmission intensity.
- High Saturation: Near-complete prevalence saturation (~ 1.0) occurs across all high-risk groups.

3.2. Dynamics at Moderate Prevalence ($\sim 5\%$)

The moderate-prevalence scenario highlights how risk heterogeneity influences epidemic dynamics more significantly than at high prevalence, as illustrated in Figure 1.

3.2.1. Force of Infection

Figure 1 (middle left panel) shows that Λ_i peaks at a lower magnitude (~ 0.9) compared to high prevalence, and exponential growth begins later ($i > 40$). Increased heterogeneity (α) sharpens the transitions in Λ_i , concentrating transmission in fewer high-risk groups.

3.2.2. Prevalence Patterns

Figure 1 (middle right panel) reveals a logistic growth pattern in y_i , with RMPs shifting to higher risk groups ($i \approx 50\text{--}60$). Increased α results in sharper transitions, whereas lower α spreads prevalence more evenly across risk groups.

3.2.3. Generic Patterns

Prevalence Saturation: Logistic growth remains consistent, with saturation near 0.9.

- RMP Sensitivity: The RMP shifts to higher risk groups compared to high-prevalence scenarios.
- Heterogeneity Amplification: Higher α values lead to sharper prevalence transitions and earlier RMPs.

3.3. Dynamics at Low Prevalence ($\sim 0.2\%$)

At low prevalence, the epidemic becomes highly stratified, with transmission and prevalence concentrated in the highest-risk groups.

3.3.1. Force of Infection

Figure 1 (lower left panel) demonstrates that Λ_i is negligible across most risk groups and peaks at a very low value (~ 0.12) only in the highest-risk groups ($i > 190$). Higher α sharpens the transitions, confining transmission to fewer groups.

3.3.2. Prevalence Patterns

Figure 1 (lower right panel) shows a logistic prevalence pattern, but with delayed transitions and RMPs occurring later ($i \approx 60\text{--}80$). Prevalence saturates at a lower ceiling (~ 0.5), with lower α leading to more gradual transitions.

3.3.3. Generic Patterns

- Threshold Scaling: RMP locations scale linearly with risk group resolution.
- Prevalence decay: Saturation is lower (~ 0.5) compared to higher-prevalence scenarios.
- Stratification: Transmission is confined to the top $\sim 10\%$ of risk groups ($i > 90$).

3.4. Impact of Risk Group Resolution

Doubling the risk group resolution to 200 reveals scaling properties of threshold behavior and preserves epidemic patterns, as shown in Figure 2.

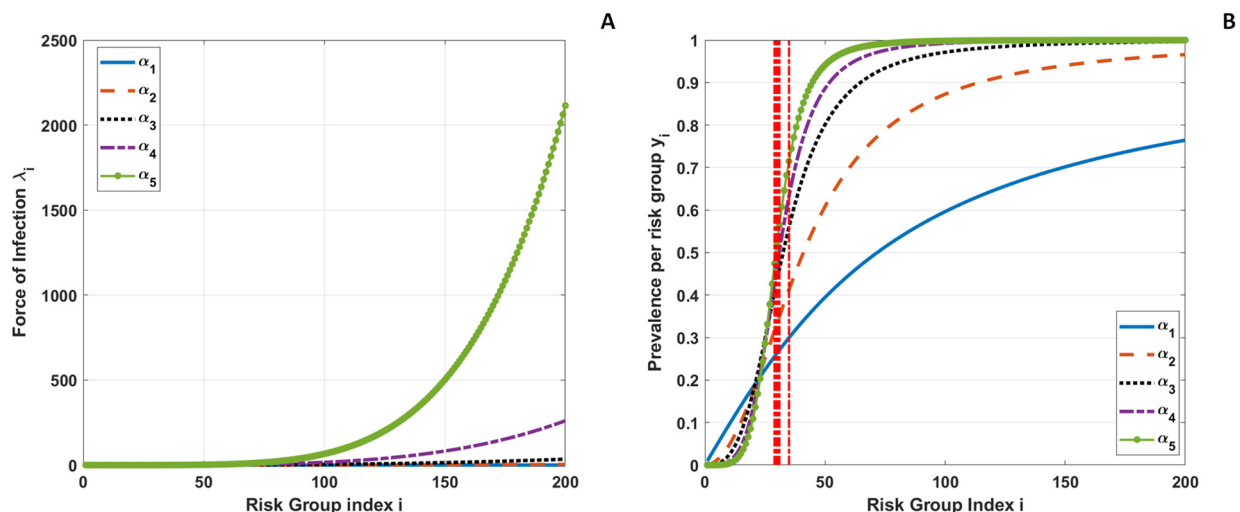


Figure 2. (A) Force of infection (Λ_i) and (B) HIV prevalence (y_i) across 200 risk groups with high prevalence. Panel A shows the force of infection (Y axis) exhibiting exponential growth with increasing risk group index (X-axis), reaching values up to ~ 2000 for the highest risk groups. Panel B shows the corresponding HIV prevalence distribution (Y axis) with increasing risk group index (X-axis), with red vertical lines indicating Risk Modulation Points (RMPs). Different curves represent varying heterogeneity parameters (α_1 to α_5). Higher α values lead to sharper transitions in prevalence and stronger concentration of force of infection in high-risk groups, while maintaining consistent RMP locations. The doubled resolution (200 vs. 100 risk groups) preserves the core patterns while providing finer granularity in the transition regions.

3.4.1. Force of Infection

Figure 2 (right panel) indicates that Λ_i remains consistent in shape but scales with resolution. Force of infection begins later and is distributed across more risk groups due to finer stratification.

3.4.2. Prevalence Patterns

Figure 2 (left panel) demonstrates that RMPs scale approximately linearly, shifting from $i \approx 20$ (100 groups) to $i \approx 40$ (200 groups). Logistic growth persists, with saturation confined to the top 20% of risk groups ($i > 60$).

3.4.3. Generic Patterns

- Linear RMP Scaling: Threshold locations double with resolution, confirming predictable scaling.
- Preserved dynamics: Prevalence and Λ_i patterns remain consistent.

3.5. Cross-Scenario Comparison

Across all prevalence scenarios, several universal patterns emerged, alongside unique behaviors specific to each regime. A consistent finding was the linear scaling of RMPs with risk group resolution, which demonstrates the robustness of threshold behavior under varying model resolutions. Exponential growth in the force of infection (Λ_i) was observed across all scenarios, with peak values determined by the prevalence level and heterogeneity (α). Similarly, logistic prevalence growth was a universal feature, although the saturation level and the sharpness of the transitions varied. At high prevalence ($\sim 20\%$), heterogeneity had minimal influence on epidemic dynamics, with early and consistent RMPs ($i \approx 20$) and near-uniform transmission and saturation across risk groups. In contrast, low prevalence ($\sim 0.2\%$) and scenario revealed significant sensitivity to heterogeneity, with transmission and prevalence highly concentrated in extreme high-risk groups ($i > 190$). These scenar-

ios also exhibited delayed RMPs, occurring later as α decreased. Moderate prevalence (~5%) represented an intermediate state, where heterogeneity played a noticeable but less dominant role, with RMPs occurring at $i \approx 50$ –60. Doubling the resolution from 100 to 200 risk groups preserved these core patterns while refining the thresholds and revealing more specific dynamics in low- prevalence scenarios, where finer stratification was critical to capturing the extreme concentration of transmission. These findings underscore the interplay between prevalence levels, risk heterogeneity, and model resolution in shaping epidemic dynamics.

3.5.1. Risk Modulation Point Characteristics

Table 1 summarizes the characteristics of the RMP across high (~20%), moderate (~5%), and low (~0.2%) prevalence regimes. Key metrics include the RMP location (i), variability in RMP position (Δ_i), prevalence growth near the threshold, force of infection (Λ_i) scaling, and transition width (Δ_i). The transition width (Δ_i) quantifies the sharpness of epidemic progression across risk groups by measuring the range of risk group indices over which prevalence increases from 20% to 80% of its maximum value. A narrower transition width indicates a sharper, more concentrated epidemic, typically observed in settings with high heterogeneity (α) or high prevalence levels, where transmission is dominated by a small subset of high-risk groups. In contrast, a broader transition width reflects a more gradual epidemic progression, characteristic of lower prevalence regimes where transmission spreads across a wider range of risk groups. This metric provides critical insights into the epidemic's dynamics, highlighting the interplay between risk heterogeneity and prevalence in shaping the steepness of the epidemic threshold.

Table 1. Characteristics of the Risk Modulation Point (RMP) across high (~20%), moderate (~5%), and low (~0.2%) prevalence regimes. The table includes the RMP location (i), variability in RMP position (Δ_i) across α , transition width (Δ_i), prevalence increases near the threshold, and force of infection (Λ_i) growth. High-prevalence regimes show consistent, sharp transitions, while low-prevalence regimes exhibit broader, more gradual transitions with significant sensitivity to α .

Prevalence Regime	RMP Location (i)	Variation in RMP (Δ_i)	Transition Width (Δ_i)	Prevalence Increase	Force of Infection Growth (Λ_i)
High (~20%)	$i \approx 20$	Minimal (<2)	Narrow: 5–10 (decreasing with α)	0.2 → 0.8 over 10 risk groups	$\Lambda_i \sim \exp(0.07i)$
Moderate (~5%)	$i \approx 50$ –60	Moderate ($\Delta_i \approx -5$)	Moderate: 15–30 (decreasing with α)	0.1 → 0.5 over 20 risk groups	$\Lambda_i \sim \exp(0.05i)$
Low (~0.2%)	$i \approx 60$ –80	Pronounced ($\Delta_i \approx -10$)	Broad: 25–35 (decreasing with α)	0.05 → 0.2 over 30 risk groups	$\Lambda_i \sim \exp(0.02i)$

At high prevalence, the RMP consistently occurs at $i \approx 20$ with minimal variation ($\Delta_i < 2$) across all α values. Transitions are sharp, with prevalence increasing from 0.2 to 0.8 over ~10 risk groups, and the force of infection shows exponential growth ($\Lambda_i \sim \exp(0.1i)$) near the threshold. Transition widths decrease with α , narrowing from $\Delta_i \approx 10$ for $\alpha = 1$ to $\Delta_i \approx 5$ for $\alpha = 5$.

In the moderate prevalence regime, the RMP shifts to $i \approx 50$ –60 and shows moderate α -dependent variability ($\Delta_i \approx -5$ per unit increase in α). Transitions are broader than in high-prevalence settings, with prevalence increasing from 0.1 to 0.5 over ~20 risk groups and a slower force of infection growth ($\Lambda_i \sim \exp(0.05i)$). Transition widths also vary significantly, spanning $\Delta_i \approx 25$ risk groups for $\alpha = 1$ and narrowing to $\Delta_i \approx 15$ for $\alpha = 5$.

At low prevalence, the RMP appears later, at $i \approx 60$ –80, with strong α -dependent shifts ($\Delta_i \approx -10$ per unit increase in α). Transitions are gradual, with prevalence increasing

from 0.05 to 0.2 over ~30 risk groups and weak force of infection growth ($\Lambda_i \sim \exp(0.02i)$). Transition widths are broad, spanning $\Delta_i \approx 35$ risk groups for $\alpha = 1$ and narrowing to $\Delta_i \approx 25$ for $\alpha = 5$.

3.5.2. RMP Position vs. Prevalence

The location of the RMP (*i*RMP) scales systematically with prevalence, as described by the relation: $iRMP \approx 20 + 40 \log(P/P_{\max})$, where $P_{\max} = 0.4$ is the maximum prevalence observed in the high-prevalence regime, and P is the actual prevalence level. This equation highlights the logarithmic dependence of the RMP on prevalence, with higher prevalence resulting in earlier thresholds (lower *i*RMP) and lower prevalence shifting the RMP to later risk groups.

3.5.3. Risk Modulation Point and Resolution Scaling

Observed RMP Locations Across Prevalence Levels

Figure 3A illustrates the observed Risk Modulation Point (RMP) locations (*i*RMP) across different prevalence levels (20%, 5%, and 0.2%). The RMP shifts systematically as prevalence decreases, reflecting delayed transitions to higher-risk groups: At high prevalence (20%), the RMP occurs early in the risk group distribution at $iRMP \approx 20$, indicating concentrated transmission in lower-risk groups. At moderate prevalence (5%), the RMP shifts to $iRMP \approx 55$, highlighting a more dispersed transmission pattern across risk groups. At low prevalence (0.2%), the RMP appears even later at $iRMP \approx 70$, showing a concentration of transmission in the highest-risk groups. This progression confirms the scaling relationship between prevalence and RMP location, with the RMP shifting logarithmically to higher risk groups as prevalence decreases.

It is distinctive to see that the incidence rate follows a power law ($f(i) = ai^b$) as confirmed by fitting the curves with a power law with adjusted R-square at nearly 1.00 for all forms of sexual risk distribution (Table S2.1 in Supplementary Materials). The exponents exactly match the exponent of the distribution of partner change rate. We also explored the results for non-power-law distributions for sexual risk behavior, such as exponential and sinusoidal forms, and the growth of the incidence rate is consistent and fitted with a power law distribution.

Likewise, the growth in prevalence follows a logistic function, as confirmed by fitting the curves with this function with 200 risk groups as an example (Figure S2.2 and Table S2.2 in Supplementary Materials). The curves show a distinctive pattern of a modulated threshold effect. The inflection points (points of dynamical transition) are occurring within roughly the same risk group irrespective of sexual risk distribution. On further examination of this effect, we found that this transition reflects a modulated form of the $R_0 = 1$ sustainability threshold.

Transition Width Scaling with Resolution

Figure 3B visualizes how the width of the transitions (Δ_i) varies across resolutions (100 vs. 200 risk groups) and prevalence regimes. The results indicate linear scaling of Δ_i with resolution, preserving regime-specific patterns: At high prevalence (20%), the transition widths are narrow, with $\Delta_i \approx 10$ for 100 groups and $\Delta_i \approx 20$ for 200 groups. At moderate prevalence (5%), the transitions broaden, with $\Delta_i \approx 20$ for 100 groups and $\Delta_i \approx 40$ for 200 groups. At low prevalence (0.2%), the transitions are the broadest, with $\Delta_i \approx 30$ for 100 groups and $\Delta_i \approx 60$ for 200 groups.

The results confirm that doubling the resolution doubles the transition widths, maintaining proportional scaling across prevalence levels. This scaling underscores the importance of higher resolution for accurately capturing dynamics in low-prevalence regimes, where transitions are more gradual.

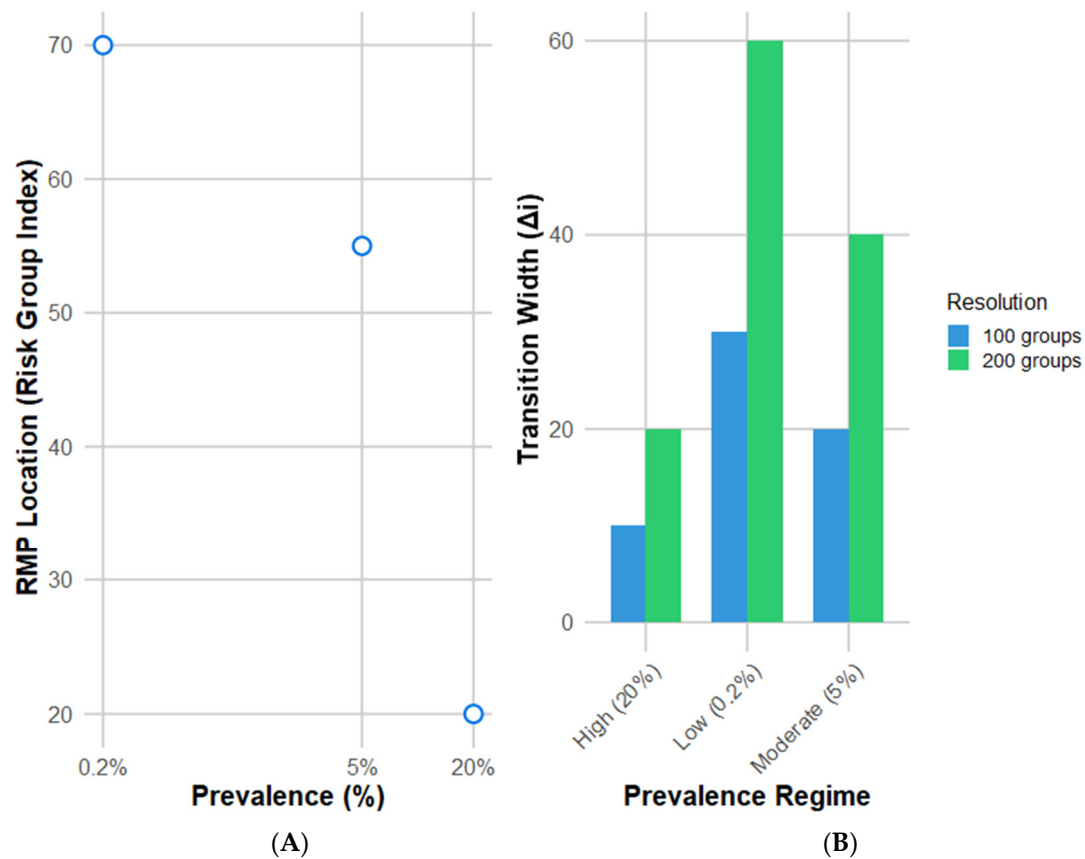


Figure 3. (A) RMP locations across prevalence levels and (B) Resolution scaling of transition widths. (A) Shows the observed Risk Modulation Point (RMP) locations shifting systematically as prevalence decreases from 20% (RMP $\approx$ 20) to 0.2% (RMP $\approx$ 70), reflecting delayed epidemic transitions at lower prevalence levels. (B) Demonstrates how transition widths (Δ_i) scale with risk group resolution, comparing 100 groups (blue) versus 200 groups (green) across different prevalence regimes. The doubling of resolution leads to proportional increases in transition widths while maintaining the relative patterns across prevalence levels.

RMP Locations Across Prevalence Regimes

The RMP, defined as the risk group index (i RMP) at which prevalence begins to increase sharply, exhibits strong dependence on both prevalence levels and the heterogeneity parameter (α) (Figure 4, left panels). At high prevalence (20%), the RMP remains stable across all α values, located consistently at i RMP $\approx$ 20. This stability reflects the homogenization of transmission dynamics due to saturation effects, where high prevalence minimizes the role of heterogeneity.

In contrast, at medium prevalence (5%), the RMP systematically shifts to higher risk group indices with increasing α . Specifically, i RMP = 50, 55, and 60 for $\alpha = 1, 3, 5$, respectively. This shift is attributed to the increasing concentration of transmission in higher-risk groups as heterogeneity intensifies. For low prevalence (0.2%), the RMP shifts even further, with i RMP = 70, 75, and 80 for $\alpha = 1, 3, 5$. These results indicate that as prevalence decreases, the epidemic threshold is increasingly delayed, and transmission becomes confined to very high-risk groups.

Transition Widths Across Prevalence Regimes

At high prevalence (20%), the transition width is narrow ($\Delta_i \approx 5$) across all α values, reflecting rapid epidemic progression due to saturation (Figure 4, right panels). The RMP remains constant at $i \approx 20$ regardless of α , demonstrating the robustness of the threshold in saturated epidemics. This stability reflects the homogenization of transmission dynamics

due to saturation effects, where high prevalence minimizes the role of heterogeneity. In the medium prevalence regime (5%), Δ_i narrows with increasing α , decreasing from 25 for $\alpha = 1$ to 10 for $\alpha = 5$. This narrowing indicates sharper transitions at higher heterogeneity levels, where transmission is concentrated in fewer groups. RMP shifts systematically from $i = 50$ to $i = 60$ as α increases, showing increased stratification. This reflects the increasing influence of heterogeneity in shaping transmission patterns at intermediate prevalence levels. At low prevalence (0.2%), the transition width is significantly broader, with $\Delta_i = 35, 30, 25$ for $\alpha = 1, 3, 5$, respectively. This reflects a more gradual epidemic progression as the population becomes more stratified and transmission dynamics are dominated by high-risk groups. RMP ranges from $i = 70$ to $i = 80$, indicating maximum stratification effect.

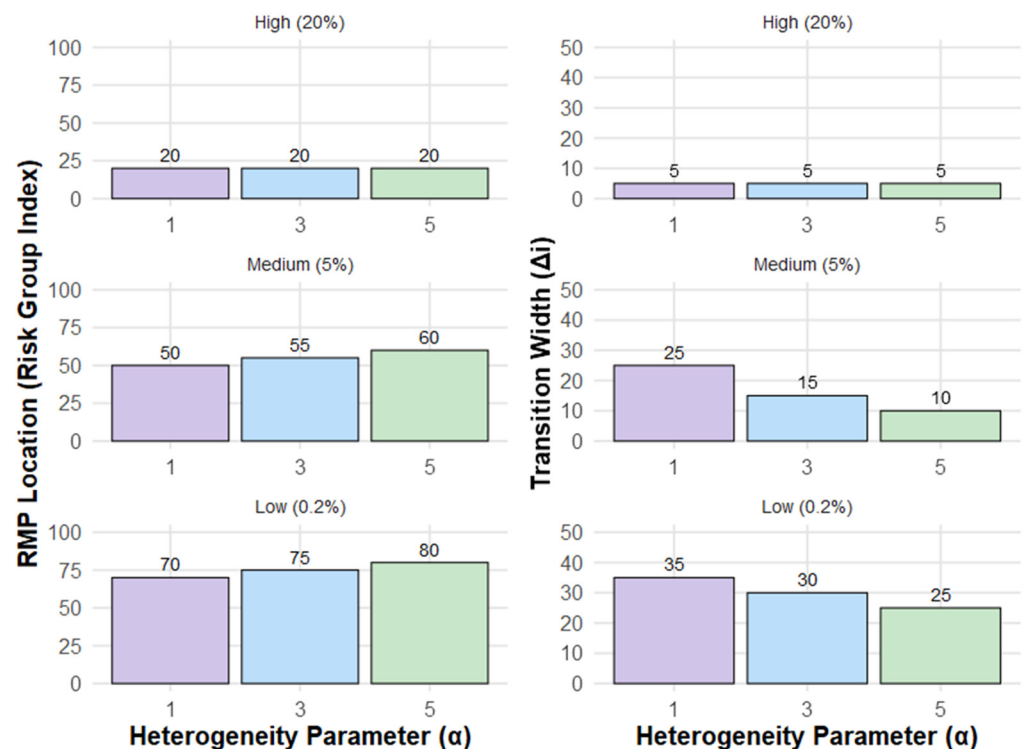


Figure 4. RMP Locations and Transition Widths Across Prevalence Regimes. Comparison of Risk Modulation Point (RMP) locations (left panels) and transition widths (Δ_i , right panels) across high- (20%), medium- (5%), and low (0.2%)-prevalence regimes, stratified by heterogeneity parameter ($\alpha = 1, 3, 5$). Left panels: RMP locations shift systematically with prevalence levels. At high prevalence, RMP remains constant at $iRMP \approx 20$ regardless of α , while at medium and low prevalence, RMP shifts to higher risk groups, reaching $iRMP = 50, 55, 60$ (medium) and $iRMP = 70, 75, 80$ (low) for $\alpha = 1, 3, 5$, respectively. Right panels: Transition widths (Δ_i) narrow with increasing α and decrease as prevalence increases. High prevalence exhibits consistently narrow transitions ($\Delta_i = 5$ across all α), while at medium prevalence, Δ_i reduces from 25 ($\alpha = 1$) to 10 ($\alpha = 5$). At low prevalence, broader transitions ($\Delta_i = 35, 30, 25$) reflect stronger stratification effects.

The Impact of Saturation Effects on the Force of Infection at Different Prevalence Levels

The relationship between force of infection (Λ_i) and risk behavior (ρ_i) exhibits distinct saturation effects depending on prevalence levels. At low prevalence ($\sim 0.2\%$), transmission is highly concentrated in the highest-risk groups ($i > 90$ in a 100-group model), where Λ_i follows a steep power-law scaling. In this regime, small increases in behavioral risk led to disproportionately high infection risks, emphasizing the critical role of superspreaders in sustaining the epidemic. The strong nonlinear scaling observed in this phase aligns with empirical findings that HIV epidemics in early or concentrated stages remain confined to specific high-risk subpopulations, such as sex workers or people who inject drugs (PWID).

In contrast, at moderate prevalence (~5%), the power-law scaling remains evident but exhibits broader transmission across risk groups. The saturation effect begins to flatten the FOI curve, meaning that lower-risk groups start contributing meaningfully to transmission. This marks the transition from a concentrated epidemic to a more generalized one, where interventions targeted at a broader range of risk groups become necessary. The RMP shifts toward lower-risk groups, reflecting a more diffuse transmission pattern as prevalence increases.

At high prevalence (~20%), transmission dynamics become more homogeneous, and the force of infection exhibits saturation at lower risk levels. The power-law effect is still present but less steep, as high levels of HIV prevalence create network-level immunity effects. In this regime, heterogeneity plays a diminished role, and broad, population-wide interventions (e.g., universal antiretroviral therapy (ART), mass pre-exposure prophylaxis (PrEP) distribution) are required to further curb transmission. The flattening of the FOI curve at high prevalence reinforces the idea that high-risk interventions remain crucial at earlier epidemic stages, whereas a generalized approach is more effective in mature epidemics.

4. Discussion

This study introduces the concept of the RMP as a critical threshold in HIV transmission dynamics, marking the transition from limited, unsustainable transmission to self-sustaining epidemic spread. The RMP distinguishes two distinct epidemic behaviors: below it, transmission remains confined to low-risk groups and cannot sustain itself; above it, transmission becomes self-sustaining, often concentrated among higher-risk groups. By quantifying this threshold, we provide a framework for understanding how epidemics shift in response to population risk structures, prevalence levels, and heterogeneity.

A central finding of our study is the systematic relationship between risk heterogeneity (α) and prevalence levels, which together determine the sharpness and concentration of epidemic progression. As the heterogeneity parameter increases, indicating greater variability in individual risk behaviors, transmission becomes increasingly concentrated in fewer, higher-risk groups. This concentration sharpens epidemic transitions and narrows the range of risk groups involved in the spread of HIV. Notably, this effect is most pronounced at lower prevalence levels, where the epidemic is largely confined to the highest risk populations. In contrast, at high prevalence levels, heterogeneity plays a diminished role, widespread transmission homogenizes epidemic dynamics across risk groups, diluting the impact of individual behavioral differences.

Our simulations reveal several universal patterns across different epidemic regimes, regardless of the specific prevalence or heterogeneity levels. The logistic growth of HIV prevalence across risk groups consistently emerges as a robust feature, characterized by sharp transitions around the RMP and eventual saturation in higher-risk groups. This pattern underscores the inherent saturation dynamics of HIV epidemics, where transmission rates plateau due to factors like behavioral limits or biological constraints. Additionally, the RMP exhibits linear scaling with risk group resolution, ensuring consistency in threshold behavior as population stratification becomes more refined. Doubling the number of risk groups results in a proportional shift in the RMP, highlighting the predictability of epidemic thresholds relative to the granularity of risk stratification. Furthermore, the force of infection demonstrates exponential growth across risk groups, with peak values determined by the overall prevalence and modulated by heterogeneity. This exponential increase reflects the amplification effect of higher-risk behaviors on transmission dynamics. These intrinsic mathematical features provide a unified framework for understanding

diverse epidemic behaviors and offer valuable insights into the fundamental mechanisms driving HIV transmission.

The concept of the RMP offers critical insights into the distinction between concentrated and generalized HIV epidemics, revealing how transmission dynamics shift across different population structures. In regions like Eastern Europe, where HIV transmission is predominantly confined to high-risk groups such as individuals with multiple concurrent partners or injection drug users [46–48], the RMP occurs late in the risk hierarchy. This reflects the epidemic's reliance on these groups for sustainability, with transmission remaining limited in the general population and the epidemic not becoming self-sustaining beyond these key populations. In contrast, in sub-Saharan Africa, where some countries are experiencing high-HIV-prevalence epidemics, substantial transmission occurs within the general population [6,49], and the RMP shifts earlier in the risk distribution. This indicates that transmission is not solely dependent on high-risk groups but is sustained across a broader population base. This shift highlights how the RMP serves as a quantitative marker for the progression of the epidemic and provides a framework for understanding the epidemiological diversity observed globally.

Population structure and heterogeneity play central roles in shaping epidemic trajectories. Increased heterogeneity leads to more stratified epidemics, with transmission concentrated in higher-risk groups and the RMP delayed. This stratification means that interventions targeting high-risk groups can be particularly effective in preventing the epidemic from becoming generalized. Prevalence levels further modulate this interplay. At low prevalence, the RMP is delayed, and epidemic transitions occur gradually over a broader range of risk groups, emphasizing the importance of interventions targeting the highest-risk populations. At high prevalence, the RMP occurs earlier, transitions are sharper, and transmission extends beyond high-risk groups, necessitating broad-based interventions. Our findings underscore the importance of considering both individual risk behaviors and population-level factors when assessing epidemic potential and designing interventions. By capturing the intrinsic dynamics of HIV transmission through the lens of the RMP, we can better understand the conditions under which an epidemic may shift from concentrated to generalized, informing more effective public health responses.

A particularly striking result is the invariance of RMP location to the nature of risk group distribution, sexual risk heterogeneity, and mixing patterns. Despite variations in these parameters, the RMP consistently defines the critical threshold where self-sustaining transmission begins. This robustness highlights the fundamental role of the RMP as a universal feature of HIV transmission dynamics, providing a reliable marker for threshold behavior across diverse epidemiological contexts. These mathematical insights not only simplify modeling efforts but also deepen our understanding of the structural principles underlying HIV epidemics. By identifying and focusing on universal patterns such as power-law growth of incidence and logistic growth of prevalence, this study provides a streamlined yet comprehensive approach to modeling. These features emphasize that epidemic outcomes are governed by intrinsic properties of transmission dynamics rather than the finer details of population structure, offering a framework that is both flexible and widely applicable to diverse HIV epidemic scenarios.

The RMP identifies the threshold in a risk-stratified population where HIV transmission transitions from localized, unsustainable spread (subcritical, $R_0 < 1$) to self-sustaining epidemic propagation (supercritical, $R_0 > 1$). Calculating the RMP is critical because it pinpoints intervention targets by identifying groups near the RMP, which represent “tipping points”, among which modest reductions in transmission can shift the epidemic from growth to decline. This also explains epidemic transitions by distinguishing concentrated epidemics, which remain confined to high-risk groups, from generalized epidemics that

spread across broader populations. Furthermore, it serves as a guide for resource allocation, ensuring that prioritizing groups near the RMP maximizes the efficiency of interventions such as PrEP and ART, particularly in resource-limited settings.

While the term “RMP” is novel, its principles align with foundational epidemiological theories and applications. The RMP builds on the concept of the basic reproductive number (R_0) [15,16], which defines the sustainability of transmission. However, the RMP extends this by stratifying R_0 across risk groups ($R_{0,i}$), identifying the critical group where $R_{0,i} \approx 1$, and integrating behavioral heterogeneity, akin to core group [17,18], where high-risk subgroups sustain transmission, as observed in sex workers in STI epidemics.

The importance of the RMP is supported by various epidemiological studies. For example, research on core groups in STI transmission has shown that targeting high-risk groups where $R_0 > 1$ effectively reduced gonorrhea prevalence in the US [50]. Similarly, identifying HIV “hotspots” and prioritizing geographic clusters with elevated transmission potential ($R_0 > 1$) significantly improved epidemic control in sub-Saharan Africa [51]. Furthermore, the RMP aligns with targeted intervention frameworks in precision public health. For instance, targeted PrEP interventions for high-risk populations have been shown to reduce HIV incidence in men who have sex with men [52], while malaria focal interventions aimed at high-risk transmission hotspots successfully reduced transmission in Kenya [53]. By monitoring shifts in the RMP over time, public health officials can anticipate epidemic transitions and adjust intervention strategies before HIV spreads beyond high-risk populations. These refinements strengthen our understanding of epidemic dynamics and offer practical guidance for prevention policies.

The RMP also holds promise as an early warning indicator for changes in epidemic dynamics. Monitoring shifts in the RMP over time allows public health authorities to detect emerging trends, such as increasing transmission among lower-risk groups that may signal the transition from a concentrated to a generalized epidemic. This surveillance can inform timely adjustments in intervention strategies, enabling more proactive and effective responses to evolving epidemic conditions.

4.1. Superspreading as a Robust Feature of Power-Law Transmission Models

Our findings demonstrate that universal patterns of epidemic growth, specifically power-law scaling of the force of infection and logistic prevalence growth, strongly support the concept of the RMP as an epidemic threshold. The force of infection (λ_i) follows a power-law relationship with risk behavior, meaning that higher-risk groups experience exponentially greater transmission rates. This scaling effect reinforces the idea that once the RMP is crossed, sustained transmission becomes inevitable, aligning with theoretical threshold concepts in infectious disease modeling.

Additionally, HIV prevalence across risk groups exhibits logistic growth, with a sharp transition at the RMP. This sigmoid pattern indicates that transmission remains low in lower-risk groups until the epidemic reaches a critical tipping point, where prevalence accelerates rapidly. The steepness of this transition, particularly in highly heterogeneous populations, provides further evidence that the RMP marks a fundamental shift in epidemic dynamics, distinguishing self-limiting from self-sustaining transmission.

Across all prevalence levels, our model consistently shows that a small fraction of high-risk individuals contributes disproportionately to transmission, a hallmark of superspreading behavior. Specifically, in low-to-moderate prevalence settings, we find that the top 10% of risk groups ($i > 90$) account for more than 70% of new infections when $\alpha \geq 3$. This pattern is highly consistent with empirical studies of HIV epidemics in key populations, including sex workers in Kenya [54], MSM in Thailand, where network-driven superspreading events sustain transmission in urban centers [55], and HIV clusters in

South Africa, where community-level viral load disproportionately concentrates among high-contact individuals [56].

The persistence of superspreading dynamics in our model, even under varying levels of prevalence and heterogeneity, underscores its robustness as a fundamental feature of HIV transmission. Unlike traditional models that assume homogeneous mixing, our power-law framework naturally captures the emergence of high-transmission hubs, reinforcing the need for risk-based intervention strategies. Moreover, the interaction between superspreading and the RMP provides an epidemiological basis for targeted intervention thresholds. As the epidemic progresses and the RMP shifts, interventions must be dynamically adjusted to account for changes in superspreading potential. This finding highlights the need for adaptive public health strategies that use real-time surveillance data to target emerging transmission hotspots.

4.2. Public Health Applications of the RMP for Epidemic Control

The identification of the RMP has significant implications for public health strategies aimed at controlling HIV transmission. By pinpointing the threshold where transmission becomes self-sustaining, we can prioritize interventions targeting specific risk groups that are critical in driving the epidemic. In settings where the RMP occurs among higher-risk groups, targeted interventions, such as condom distribution, PrEP, needle exchange programs, and harm reduction initiatives, can effectively disrupt transmission before it cascades into lower-risk populations [57–59]. Focusing on individuals and groups near the RMP is especially impactful. These transition regions represent tipping points in epidemic dynamics, where timely and focused prevention efforts can prevent the epidemic from becoming self-sustaining and spreading more widely. Behavioral interventions to reduce high-risk behaviors and expanding HIV testing with rapid initiation of ART for newly diagnosed individuals can significantly reduce transmission [60,61].

Building on the insights from this study, several paths for future research can enhance the RMP framework. Extending the model to incorporate dynamic risk behaviors and evolving sexual networks over time would provide a more realistic representation of epidemic trajectories. This includes accounting for changes in behavior, partnership patterns, and social norms that influence transmission dynamics. Integrating the effects of interventions such as ART, PrEP, condom distribution, and behavioral change campaigns would enable evaluation of how they shift the RMP or modify transition widths, offering actionable insights into optimizing prevention and treatment strategies. Applying the framework to other infectious diseases with stratified transmission patterns, such as other sexually transmitted infections or hepatitis C among injection drug users, could uncover universal principles governing stratified epidemics. Incorporating empirical data on risk group distributions, contact patterns, intervention coverage, and behavioral trends would enhance the model's accuracy and reliability. Applying the model to diverse geographic regions with varying epidemic characteristics and simulating real-world intervention scenarios can provide insights into how the RMP shifts in response to demographic or behavioral transformations.

Tracking shifts in the RMP over time can provide a real-time indicator of changing epidemic dynamics, offering a valuable tool for adaptive public health responses. As the RMP moves downward (i.e., affecting lower-risk groups), it signals that HIV transmission is expanding beyond high-risk populations, necessitating broader intervention strategies such as population-wide ART scale-up, increased HIV testing, and expanded PrEP access. In contrast, if the RMP remains stable or shifts upward, transmission remains concentrated in high-risk groups, suggesting that targeted interventions, such as outreach programs for sex workers, MSM, or people who inject drugs, remain the most effective strategy.

By integrating routine surveillance data with dynamic RMP estimation, public health agencies could develop early warning systems to detect epidemic shifts before widespread transmission occurs. This approach aligns with precision public health principles, where data-driven interventions are adapted in real time to maximize impact. As seen in other infectious disease models, threshold-based monitoring frameworks can help guide timely policy adjustments, ensuring that intervention resources are deployed efficiently based on the evolving epidemic landscape. These findings highlight the potential of RMP tracking as an operational tool for real-time epidemic control, bridging the gap between theoretical modeling and practical intervention planning. Future research should explore integration with national HIV surveillance systems, evaluating how RMP-based insights can enhance decision-making for resource allocation, outbreak preparedness, and long-term epidemic mitigation.

The RMP framework, while developed in the context of HIV transmission dynamics, has the potential to be adapted to other infectious diseases characterized by heterogeneous transmission patterns. Many infectious diseases exhibit risk-stratified dynamics, where a subset of the population drives the majority of transmission. Identifying thresholds similar to the RMP could provide insights into epidemic control strategies beyond HIV.

For instance, in vector-borne diseases such as malaria or dengue, transmission is highly dependent on environmental and behavioral factors, such as mosquito breeding sites and human mobility. An RMP-like approach could help pinpoint critical intervention thresholds, such as the minimum vector control coverage needed to prevent sustained transmission. Similarly, in air-borne infections like tuberculosis or COVID-19, network-driven transmission and superspreading events play a major role in epidemic propagation. Applying the RMP concept to these diseases could help define thresholds where outbreaks become self-sustaining, guiding strategies like targeted vaccination, isolation policies, or environmental controls.

These extensions highlight the flexibility of the RMP framework in epidemic modeling and public health intervention planning. While this study focuses on HIV, future research should explore how RMP-based methodologies can be adapted to other infectious diseases, broadening its applicability to diverse epidemic contexts.

4.3. Practical Implementation and Methodological Considerations

While the RMP offers a novel framework for prioritizing interventions, its real-world application requires careful consideration of two key challenges: (1) the feasibility of dynamically calculating the RMP in resource-limited settings, and (2) the operational definition of “high-risk groups” identified post-RMP. Calculating the RMP demands granular behavioral and prevalence data stratified by risk, which may not be available in real time in many settings. For example, in rural Malawi, limited surveillance infrastructure delayed the identification of shifting thresholds during a recent HIV resurgence, underscoring the need for strengthened data systems [62]. Additionally, translating model-derived risk indices into actionable subgroups (e.g., sex workers, mobile populations) requires contextual adaptation. In Kampala, Uganda, mapping theoretical thresholds to geographic hotspots enabled targeted PrEP distribution [63]. However, such successes hinge on partnerships between modelers and local stakeholders to align risk criteria with cultural and epidemiological realities. A critical limitation of our methodology is its reliance on static risk stratification, which may not capture behavioral fluidity or hidden populations (e.g., stigmatized groups). Future work should integrate machine learning and dynamic network models to refine RMP estimation and adapt to evolving risk landscapes. These steps, while resource-intensive, are essential to bridge the gap between theoretical thresholds and impactful public health action.

4.4. The Limitations of the Study

While this study provides valuable insights, several limitations must be acknowledged. The model incorporates simplifications that may not fully capture the complexities of real-world transmission. Parameters like the transmission probability (β) and mixing patterns (Φ) are treated as static, not accounting for temporal changes due to behavioral shifts, interventions, or evolving social networks. The absence of dynamic feedback mechanisms, such as behavior changes in response to rising prevalence or prevention campaigns, may oversimplify transmission dynamics. Estimating parameters such as heterogeneity (α) and risk group distributions is challenging, particularly in settings with limited behavioral data.

A key limitation of this methodology is its reliance on static risk stratification, which may not capture behavioral fluidity or unmeasured risk factors (e.g., migration, stigma-driven hidden populations). Future work should integrate dynamic risk assessments and machine learning to refine real-time RMP estimation. However, in practical applications, the feasibility of instantaneously calculating the RMP in real-world settings should be considered. The identification of the RMP relies on numerical prevalence analysis, which requires reliable surveillance data to assess epidemic transitions dynamically. This dependency on high-resolution data may pose challenges in settings where data availability is limited. Moreover, defining what constitutes a ‘high-risk group’ remains a critical consideration when implementing interventions based on the RMP. In mathematical models, high-risk groups are typically stratified based on behavioral factors such as contact rates and partner concurrency, but in public health practice, these groups are often categorized by demographic, occupational, or geographic factors. Thus, operationalizing RMP-based interventions requires context-specific definitions of high-risk populations that align with epidemiological evidence and available public health resources.

While this methodology provides a valuable framework for guiding interventions, its reliance on dynamic surveillance data and precise group classification presents a potential limitation that should be addressed in future research and policy applications. Furthermore, as shown in Figure 1 (right panel), estimates of the RMP were not feasible due to the near-uniform transmission distribution in low-heterogeneity settings. At this level, prevalence increased gradually across all risk groups, preventing the identification of a distinct epidemic transition point.

The assumed risk group distributions and mixing patterns are generalized approximations and may not capture the distinctions among specific populations, such as cultural practices or regional variations in sexual networks. The abstraction of the model from empirical data and the exclusion of external interventions (e.g., ART, condom use) limit the applicability of our findings to settings where such interventions are influencing epidemic trajectories. Including these factors would enhance the realism of the model but also increase its complexity. Additionally, the model does not account for other influences on HIV transmission, such as co-infections with other sexually transmitted infections, variations in viral strain virulence, or differences in access to healthcare services. This decision was made to isolate intrinsic epidemic features without the confounding effects of external disturbances. While this approach provides a clear view of the fundamental drivers of HIV transmission, it limits the applicability of the findings to settings where such interventions are actively shaping epidemic trajectories.

5. Conclusions

In conclusion, our study advances our understanding of HIV transmission dynamics by identifying the RMP as a universal threshold that governs epidemic progression across diverse contexts. The consistent patterns observed, such as the logistic growth of prevalence, the exponential increase in the force of infection, and linear scaling of the RMP with risk

group resolution, highlight intrinsic features of HIV epidemics that are robust to variations in population structure and heterogeneity. By providing a unified framework that links mathematical insights with epidemiological significance, the RMP concept offers valuable guidance for public health interventions and future research. Our findings underscore the importance of considering both individual risk behaviors and broader population dynamics when addressing HIV epidemics. The RMP serves not only as a theoretical construct but also as a practical tool for informing targeted interventions, resource allocation, and surveillance efforts. Ultimately, the insights gained from this study contribute to more effective strategies in the global fight against HIV. By expanding our understanding of the fundamental mechanisms driving HIV transmission and epidemic progression, we can develop interventions that are both efficient and impactful, reducing the burden of HIV on individuals and societies worldwide.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/biomedinformatics5010011/s1>, Supplementary Methods and Results [64–81]. Figure S1.1: Compartmental structure of the HIV population level model; Figure S1.2: Clustering coefficient distribution and the standard deviation in HIV risk of exposure as a function of the distribution of sexual risk behavior; Figure S2.1: The distribution of HIV prevalence at different distributions of sexual risk behavior with 200 risk groups; Table S1.1: Model assumptions in terms of parameter values; Table S2.1: Power law model fit for the incidence rate at six different distributions of risk behavior; Table S2.2: HIV prevalence fitted with logistic functions at different distributions of risk behavior for 20% prevalence with 200 risk group.

Author Contributions: Conceptualization, S.F.A. and D.F.C.; methodology, S.F.A. and D.F.C.; software, S.F.A.; validation, S.F.A.; formal analysis, S.F.A.; investigation, S.F.A. and D.F.C.; resources, S.F.A. and D.F.C.; data curation, S.F.A.; writing—original draft preparation, S.F.A. and D.F.C.; writing—review and editing, S.F.A. and D.F.C.; visualization, S.F.A.; supervision, D.F.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The MATLAB code used in our analysis is available at: GitHub—diegofcuadros/HIV_Model.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Kharsany, A.B.M.; Karim, Q.A. HIV Infection and AIDS in Sub-Saharan Africa: Current Status, Challenges and Opportunities. *Open AIDS J.* **2016**, *10*, 34–48. [[CrossRef](#)] [[PubMed](#)]
2. Amuche, N.J.; Emmanuel, E.I.; Innocent, N.E. HIV/AIDS in sub-Saharan Africa: Current status, challenges and prospects. *Asian Pac. J. Trop. Dis.* **2017**, *7*, 239–256. [[CrossRef](#)]
3. Frank, T.D.; Carter, A.; Jahagirdar, D.; Biehl, M.H.; Douwes-Schultz, D.; Larson, S.L.; Arora, M.; Dwyer-Lindgren, L.; Steuben, K.M.; Abbastabar, H. Global, regional, and national incidence, prevalence, and mortality of HIV, 1980–2017, and forecasts to 2030, for 195 countries and territories: A systematic analysis for the Global Burden of Diseases, Injuries, and Risk Factors Study 2017. *Lancet HIV* **2019**, *6*, e831–e859. [[CrossRef](#)]
4. Alipour, A.; Haghdoust, A.A.; Sajadi, L.; Zolala, F. HIV prevalence and related risk behaviours among female partners of male injecting drugs users in Iran: Results of a bio-behavioural survey, 2010. *Sex. Transm. Infect.* **2013**, *89*, iii41–iii44. [[CrossRef](#)]
5. Tanser, F.C.; de Oliveira, T.; Maheu-Giroux, M.; Bärnighausen, T.W. Concentrated HIV subepidemics in generalized epidemic settings. *Curr. Opin. HIV AIDS* **2014**, *9*, 115–125. [[CrossRef](#)]
6. Bulstra, C.A.; Hontelez, J.A.C.; Giardina, F.; Steen, R.; Nagelkerke, N.J.D.; Bärnighausen, T.W.; de Vlas, S.J. Mapping and characterising areas with high levels of HIV transmission in sub-Saharan Africa: A geospatial analysis of national survey data. *PLoS Med.* **2020**, *17*, e1003042. [[CrossRef](#)] [[PubMed](#)]

7. Anderson, R.M.; Gupta, S.; Ng, W. The significance of sexual partner contact networks for the transmission dynamics of HIV. *J. Acquir. Immune Defic. Syndr.* **1990**, *3*, 417–429.
8. Garnett, G.P.; Johnson, A.M. Coining a new term in epidemiology: Concurrency and HIV. *AIDS* **1997**, *11*, 681–683. [[CrossRef](#)] [[PubMed](#)]
9. Morris, M.; Kretzschmar, M.E.E. Concurrent partnerships and the spread of HIV. *AIDS* **1997**, *11*, 641–648. [[CrossRef](#)]
10. Zhong, L.; Zhang, Q.; Li, X. Modeling the Intervention of HIV Transmission across Intertwined Key Populations. *Sci. Rep.* **2018**, *8*, 2432. [[CrossRef](#)] [[PubMed](#)]
11. Tully, S.P.; Cojocaru, M.-G.; Bauch, C.T. Coevolution of risk perception, sexual behaviour, and HIV transmission in an agent-based model. *J. Theor. Biol.* **2013**, *337*, 125–132. [[CrossRef](#)]
12. Nagoski, E.; Janssen, E.; Lohrmann, D.K.; Nichols, E. Risk, Individual Differences, and Environment: An Agent-Based Modeling Approach to Sexual Risk-Taking. *Arch. Sex. Behav.* **2011**, *41*, 849–860. [[CrossRef](#)]
13. Romero-Severson, E.O.; Volz, E.M.; Koopman, J.S.; Leitner, T.; Ionides, E.L. Dynamic Variation in Sexual Contact Rates in a Cohort of HIV-Negative Gay Men. *Am. J. Epidemiol.* **2015**, *182*, 255–262. [[CrossRef](#)]
14. Huebner, D.M.; Perry, N.S. Do Behavioral Scientists Really Understand HIV-Related Sexual Risk Behavior? A Systematic Review of Longitudinal and Experimental Studies Predicting Sexual Behavior. *Arch. Sex. Behav.* **2015**, *44*, 1915–1936. [[CrossRef](#)] [[PubMed](#)]
15. Anderson, R.M.; May, R.M. *Infectious Diseases of Humans: Dynamics and Control*; Oxford University Press: Oxford, UK, 1991; p. 757.
16. Diekmann, O.; Heesterbeek, J.A.P. *Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation*; John Wiley & Sons: Hoboken, NJ, USA, 2000; Volume 5.
17. Hethcote, H.W.; Yorke, J.A. *Gonorrhea Transmission Dynamics and Control*; Springer: Berlin/Heidelberg, Germany, 2014; Volume 56.
18. Woolhouse, M.E.; Dye, C.; Etard, J.-F.; Smith, T.; Charlwood, J.; Garnett, G.; Hagan, P.; Hii, J.x.; Ndhlovu, P.; Quinnell, R. Heterogeneities in the transmission of infectious agents: Implications for the design of control programs. *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 338–342. [[CrossRef](#)] [[PubMed](#)]
19. Lim, S.; Shin, J.; Kwak, N.; Jung, K. Phase transitions for information diffusion in random clustered networks. *Eur. Phys. J. B* **2016**, *89*, 188. [[CrossRef](#)]
20. Ansari, S.; Anvari, M.; Pfeffer, O.; Molkenthin, N.; Moosavi, M.R.; Hellmann, F.; Heitzig, J.; Kurths, J. Moving the epidemic tipping point through topologically targeted social distancing. *Eur. Phys. J. Spec. Top.* **2021**, *230*, 3273–3280. [[CrossRef](#)] [[PubMed](#)]
21. Buve, A.; Weiss, H.A.; Laga, M.; Van Dyck, E.; Musonda, R.; Zekeng, L.; Kahindo, M.; Anagonou, S.; Morison, L.; Robinson, N. The epidemiology of gonorrhoea, chlamydial infection and syphilis in four African cities. *AIDS* **2001**, *15*, S79–S88. [[CrossRef](#)]
22. Han, H.; Wu, B.; Jia, J.; Song, Y. Summary of global surveillance data of infectious diseases in June 2020. *Dis. Surveill.* **2020**, *35*, 568–570.
23. Puls, A.; Bracke, S. COVID-19 pandemic risk analytics: Data mining with reliability engineering methods for analyzing spreading behavior and comparison with infectious diseases. In *Reliability Engineering and Computational Intelligence. Studies in Computational Intelligence*; Springer: Cham, Switzerland, 2020.
24. Ajayi, I.O.; Ajumobi, O.; Falade, C.O. Malaria and COVID-19: Commonalities, intersections and implications for sustaining malaria control. *Pan Afr. Med. J.* **2020**, *37*, 1. [[CrossRef](#)]
25. Awad, S.F.; Abu-Raddad, L.J. Could there have been substantial declines in sexual risk behavior across sub-Saharan Africa in the mid-1990s? *Epidemics* **2014**, *8*, 9–17. [[CrossRef](#)] [[PubMed](#)]
26. Awad, S.F.; Sgaier, S.K.; Lau, F.K.; Mohamoud, Y.A.; Tambatamba, B.C.; Kripke, K.E.; Thomas, A.G.; Bock, N.; Reed, J.B.; Njeuhmeli, E. Could circumcision of HIV-positive males benefit voluntary medical male circumcision programs in Africa? Mathematical modeling analysis. *PLoS ONE* **2017**, *12*, e0170641. [[CrossRef](#)] [[PubMed](#)]
27. Awad, S.; Cuadros, D.; Abu-Raddad, L. Characterizing HIV prevalence distribution across sub-populations at variable levels of sexual behavior. *Int. J. Infect. Dis.* **2012**, *16*, e180–e181. [[CrossRef](#)]
28. Abu-Raddad, L.J.; Ferguson, N.M. Characterizing the symmetric equilibrium of multi-strain host-pathogen systems in the presence of cross immunity. *J. Math. Biol.* **2005**, *50*, 531–558. [[CrossRef](#)]
29. Abu-Raddad, L.J.; Boily, M.C.; Self, S.; Longini, I.M., Jr. Analytic insights into the population level impact of imperfect prophylactic HIV vaccines. *J. Acquir. Immune Defic. Syndr.* **2007**, *45*, 454–467. [[CrossRef](#)]
30. Pinkerton, S.D. Probability of HIV transmission during acute infection in Rakai, Uganda. *AIDS Behav.* **2008**, *12*, 677–684. [[CrossRef](#)]
31. Hollingsworth, T.D.; Anderson, R.M.; Fraser, C. HIV-1 transmission, by stage of infection. *J. Infect. Dis.* **2008**, *198*, 687–693. [[CrossRef](#)]
32. Abu-Raddad, L.J.; Longini, I.M., Jr. No HIV stage is dominant in driving the HIV epidemic in sub-Saharan Africa. *AIDS* **2008**, *22*, 1055–1061. [[CrossRef](#)]
33. Wawer, M.J.; Gray, R.H.; Sewankambo, N.K.; Serwadda, D.; Li, X.; Laeyendecker, O.; Kiwanuka, N.; Kigozi, G.; Kiddugavu, M.; Lutalo, T.; et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J. Infect. Dis.* **2005**, *191*, 1403–1409. [[CrossRef](#)]

34. Morgan, D.; Whitworth, J. The natural history of HIV-1 infection in Africa. *Nat. Med.* **2001**, *7*, 143–145. [CrossRef] [PubMed]
35. Baeten, J.M.; Richardson, B.A.; Lavreys, L.; Rakwar, J.P.; Mandalika, K.; Bwayo, J.J.; Kreiss, J.K. Female-to-male infectivity of HIV-1 among circumcised and uncircumcised Kenyan men. *J. Infect. Dis.* **2005**, *191*, 546–553. [CrossRef] [PubMed]
36. UNAIDS. *UNAIDS Reference Group on Estimates, Modelling and Projections*; UNAIDS: Geneva, Switzerland, 2007.
37. UNAIDS; WHO. *AIDS Epidemic Update 2007*; WHO: Geneva, Switzerland, 2007. Available online: https://www.unaids.org/en/resources/documents/2007/20071130_2007_epiupdate_en.pdf (accessed on 17 February 2025).
38. Buve, A.; Carael, M.; Hayes, R.J.; Auvert, B.; Ferry, B.; Robinson, N.J.; Anagonou, S.; Kanhonou, L.; Laourou, M.; Abega, S.; et al. Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: Methods and prevalence of HIV infection. *AIDS* **2001**, *15* (Suppl. 4), S5–S14. [CrossRef] [PubMed]
39. UNAIDS. *UNAIDS Report on the Global AIDS Epidemic 2010*; UNAIDS: Geneva, Switzerland, 2010.
40. Dunkle, K.L.; Stephenson, R.; Karita, E.; Chomba, E.; Kayitenkore, K.; Vwalika, C.; Greenberg, L.; Allen, S. New heterosexually transmitted HIV infections in married or cohabiting couples in urban Zambia and Rwanda: An analysis of survey and clinical data. *Lancet* **2008**, *371*, 2183–2191. [CrossRef]
41. Garnett, G.P.; Anderson, R.M. Factors controlling the spread of HIV in heterosexual communities in developing countries: Patterns of mixing between different age and sexual activity classes. *Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci.* **1993**, *342*, 137–159. [CrossRef]
42. Heffernan, J.M.; Smith, R.J.; Wahl, L.M. Perspectives on the basic reproductive ratio. *J. R. Soc. Interface/R. Soc.* **2005**, *2*, 281–293. [CrossRef] [PubMed]
43. Larmarange, J. HIV prevalence in sub-Saharan Africa: Background of an estimation. *Med. Sci. M/S* **2009**, *25*, 87–92.
44. Brown, T.; Bao, L.; Raftery, A.E.; Salomon, J.A.; Baggailey, R.F.; Stover, J.; Gerland, P. Modelling HIV epidemics in the antiretroviral era: The UNAIDS Estimation and Projection package 2009. *Sex. Transm. Infect.* **2010**, *86*, ii3–ii10. [CrossRef]
45. *Matlab*, version 2023a. 9.14; The MathWorks, Inc.: Natick, MA, USA, 2023.
46. Hamers, F.F.; Downs, A.M. HIV in central and eastern Europe. *Lancet* **2003**, *361*, 1035–1044. [CrossRef]
47. Altice, F.L.; Azbel, L.; Stone, J.; Brooks-Pollock, E.; Smyrnov, P.; Dvoriak, S.; Taxman, F.S.; El-Bassel, N.; Martin, N.K.; Booth, R.E.; et al. The perfect storm: Incarceration and the high-risk environment perpetuating transmission of HIV, hepatitis C virus, and tuberculosis in Eastern Europe and Central Asia. *Lancet* **2016**, *388*, 1228–1248. [CrossRef] [PubMed]
48. Jolley, E.; Rhodes, T.; Platt, L.; Hope, V.D.; Latypov, A.; Donoghoe, M.C.; Wilson, D. HIV among people who inject drugs in Central and Eastern Europe and Central Asia: A systematic review with implications for policy. *BMJ Open* **2012**, *2*, e001465. [CrossRef]
49. Okano, J.T.; Sharp, K.; Valdano, E.; Palk, L.; Blower, S.M. HIV transmission and source-sink dynamics in sub-Saharan Africa. *Lancet HIV* **2020**, *7*, e209–e214. [CrossRef] [PubMed]
50. Garnett, G.P.; Anderson, R.M. Contact Tracing and the Estimation of Sexual Mixing Patterns: The Epidemiology of Gonococcal Infections. *Sex. Transm. Dis.* **1993**, *20*, 181–191. [CrossRef]
51. Cuadros, D.F.; Awad, S.F.; Abu-Raddad, L.J. Mapping HIV clustering: A strategy for identifying populations at high risk of HIV infection in sub-Saharan Africa. *Int. J. Health Geogr.* **2013**, *12*, 28. [CrossRef] [PubMed]
52. Wong, N.S.; Kwan, T.H.; Tsang, O.T.-Y.; Lee, M.P.; Yam, W.C.; Lam, W.; Leung, W.-S.; Chan, J.M.-c.; Ho, K.M.; Lee, S.-S. Pre-exposure prophylaxis (PrEP) for MSM in low HIV incidence places: Should high risk individuals be targeted? *Sci. Rep.* **2018**, *8*, 11641. [CrossRef]
53. Bousema, T.; Stresman, G.; Baidjoe, A.; Bradley, J.; Knight, P.; Stone, W.; Osoti, V.; Makori, E.; Owaga, C.O.; Odongo, W.; et al. The Impact of Hotspot-Targeted Interventions on Malaria Transmission in Rachuonyo South District in the Western Kenyan Highlands: A Cluster-Randomized Controlled Trial. *PLoS Med.* **2016**, *13*, e1001993. [CrossRef]
54. Okal, J.; Geibel, S.; Muraguri, N.; Musyoki, H.; Tun, W.; Broz, D.; Kuria, D.; Kim, A.; Oluoch, T.; Raymond, H.F. Estimates of the size of key populations at risk for HIV infection: Men who have sex with men, female sex workers and injecting drug users in Nairobi, Kenya. *Sex. Transm. Infect.* **2013**, *89*, 366–371. [CrossRef] [PubMed]
55. Tee, K.K.; Kantor, R.; Sungkanuparph, S.; Takebe, Y.; Li, P.C.K.; Ditangco, R.A.; Phanuphak, P.; Sirisanthana, T.; Sim, B.L.H.; Ratanasuwan, W.; et al. Transmission Networks of HIV-1 Among Men Who Have Sex with Men in East and Southeast Asia. *J. Acquir. Immune Defic. Syndr.* **2015**, *70*, e28–e30. [CrossRef] [PubMed]
56. Tanser, F.C.; Vandormael, A.; Cuadros, D.F.; Phillips, A.N.; de Oliveira, T.; Tomita, A.M.; Bärnighausen, T.W.; Pillay, D. Effect of population viral load on prospective HIV incidence in a hyperendemic rural African community. *Sci. Transl. Med.* **2017**, *9*, eaam8012. [CrossRef]
57. Kurth, A.E.; Celum, C.L.; Baeten, J.M.; Vermund, S.H.; Wasserheit, J.N. Combination HIV Prevention: Significance, Challenges, and Opportunities. *Curr. HIV/AIDS Rep.* **2011**, *8*, 62–72. [CrossRef] [PubMed]
58. Wyk, J.V.; Ajana, F.; Bisshop, F.; Wit, S.d.; Osiyemi, O.; Portilla, J.; Routy, J.P.; Wyen, C.; Ait-Khaled, M.; Nascimento, M.C.; et al. High prevalence of sexually transmitted infections, homelessness and drug use among street-based sex workers in London: Results from a pilot intervention of mobile outreach testing and treatment. *HIV Med.* **2021**, *22*, 116.

59. Copenhaver, M.M.; Johnson, B.T.; Lee, I.-C.; Harman, J.J.; Carey, M.P. Behavioral HIV risk reduction among people who inject drugs: Meta-analytic evidence of efficacy. *J. Subst. Abus. Treat.* **2006**, *31*, 163–171. [\[CrossRef\]](#) [\[PubMed\]](#)
60. Benidir, B.; Ali, T.; Sanchez, L.P.; Salunkhe, V.; Gootee, S.; Arnold, F.W. 1272. Impact of Rapid Initiation of Antiretroviral Therapy on Retention in Care in the Southern United States. *Open Forum Infect. Dis.* **2022**, *9*, ofac492. [\[CrossRef\]](#)
61. Kalichman, S.C.; Cherry, C.; Kalichman, M.O.; Amaral, C.M.; White, D.; Pope, H.L.; Swetzes, C.; Eaton, L.A.; Macy, R.; Cain, D. Integrated behavioral intervention to improve HIV/AIDS treatment adherence and reduce HIV transmission. *Am. J. Public Health* **2011**, *101*, 531–538. [\[CrossRef\]](#) [\[PubMed\]](#)
62. Dasgupta, A.N.Z.; Wringe, A.; Crampin, A.C.; Chisambo, C.; Koole, O.; Makombe, S.D.; Sungani, C.; Todd, J.; Church, K. HIV policy and implementation: A national policy review and an implementation case study of a rural area of northern Malawi. *AIDS Care* **2016**, *28*, 1097–1109. [\[CrossRef\]](#)
63. Doshi, R.H.; Sande, E.; Ogwal, M.; Kiyangi, H.; McIntyre, A.F.; Kusiima, J.; Musinguzi, G.; Serwadda, D.; Hladik, W. Progress toward UNAIDS 90-90-90 targets: A respondent-driven survey among female sex workers in Kampala, Uganda. *PLoS ONE* **2018**, *13*, e0201352. [\[CrossRef\]](#) [\[PubMed\]](#)
64. Wawer, M.J.; Reynolds, S.J.; Serwadda, D.; Kigozi, G.; Kiwanuka, N.; Gray, R.H. Might male circumcision be more protective against HIV in the highly exposed? An immunological hypothesis. *AIDS* **2005**, *19*, 2181–2182. [\[CrossRef\]](#)
65. UNAIDS; WHO. *AIDS Epidemic Update 2024*; UNAIDS: Geneva, Switzerland, 2024. Available online: <https://www.unaids.org/en/resources/documents/2024/global-aids-update-2024> (accessed on 17 February 2025).
66. Newman, M.E.J. Properties of highly clustered networks. *Phys. Rev. E* **2003**, *68*, 026121. [\[CrossRef\]](#) [\[PubMed\]](#)
67. Newman, M.E.J.; Park, J. Why social networks are different from other types of networks. *Phys. Rev. E* **2003**, *68*, 036122. [\[CrossRef\]](#) [\[PubMed\]](#)
68. Keeling, M. The implications of network structure for epidemic dynamics. *Theor. Popul. Biol.* **2005**, *67*, 1–8. [\[CrossRef\]](#)
69. Cuadros, D.F.; Crowley, P.H.; Augustine, B.; Stewart, S.L.; Garcia-Ramos, G. Effect of variable transmission rate on the dynamics of HIV in sub-Saharan Africa. *BMC Infect. Dis.* **2011**, *11*, 216. [\[CrossRef\]](#)
70. Handcock, M.S.; Jones, J.H. Likelihood-based inference for stochastic models of sexual network formation. *Theor. Popul. Biol.* **2004**, *65*, 413–422. [\[CrossRef\]](#)
71. Hamilton, D.T.; Handcock, M.S.; Morris, M. Degree distributions in sexual networks: A framework for evaluating evidence. *Sex. Transm. Dis.* **2008**, *35*, 30–40. [\[CrossRef\]](#) [\[PubMed\]](#)
72. Bansal, S.; Grenfell, B.T.; Meyers, L.A. When individual behaviour matters: Homogeneous and network models in epidemiology. *J. R. Soc. Interface/R. Soc.* **2007**, *4*, 879–891. [\[CrossRef\]](#)
73. Abu-Raddad, L.J.; Patnaik, P.; Kublin, J.G. Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. *Science* **2006**, *314*, 1603–1606. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Kretzschmar, M.; Morris, M. Measures of concurrency in networks and the spread of infectious disease. *Math. Biosci.* **1996**, *133*, 165–195. [\[CrossRef\]](#) [\[PubMed\]](#)
75. Morris, M. Sexual networks and HIV. *AIDS* **1997**, *11* (Suppl. A), S209–S216. [\[PubMed\]](#)
76. Watts, C.H.; May, R.M. The influence of concurrent partnerships on the dynamics of HIV/AIDS. *Math. Biosci.* **1992**, *108*, 89–104. [\[CrossRef\]](#) [\[PubMed\]](#)
77. May, R.M.; Anderson, R.M. The transmission dynamics of human immunodeficiency virus (HIV). *Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci.* **1988**, *321*, 565–607.
78. Watts, D.J.; Strogatz, S.H. Collective dynamics of ‘small-world’ networks. *Nature* **1998**, *393*, 440–442. [\[CrossRef\]](#) [\[PubMed\]](#)
79. Barrat, A.; Barthelemy, M.; Pastor-Satorras, R.; Vespignani, A. The architecture of complex weighted networks. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 3747–3752. [\[CrossRef\]](#)
80. Boccaletti, S.; Latora, V.; Moreno, Y.; Chavez, M.; Hwang, D.U. Complex networks: Structure and dynamics. *Phys. Rep.* **2006**, *424*, 175–308. [\[CrossRef\]](#)
81. Barabási, A.L. *Linked: How Everything Is Connected to Everything Else and What It Means for Business, Science and Everyday Life*; First Plume Printing: London, UK, 2003.

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.