Mathematical Biosciences and Engineering

MBE, 23(8): 2307–2322.
DOI: 10.3934/mbe.2026084
Received: 10 March 2026
Revised: 17 June 2026
Accepted: 07 July 2026
Published: 22 July 2026

https://www.aimspress.com/journal/MBE

Research article

Why accurate risk stratification matters in HIV population modeling

Dobromir Dimitrov[1,2,*], Laura Matrajt[1,2], Xinze Ren[2], Sarah E. Stansfield[1] and Mia Moore[1]

[1] Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center, Seattle, WA 98109, USA
[2] Department of Applied Mathematics, University of Washington, Seattle, WA 98109, USA

* **Correspondence:** Email: ddimitro@fredhutch.org; Tel: +4258948537.

Abstract: Accurate representation of behavioral risk heterogeneity significantly influences the projections of Human Immunodeficiency Virus transmission models without receiving the deserved attention when models are structured. As a result, models widely vary in how they stratify risk and how individuals progress through risk groups. We systematically evaluated how these two structural features—the number of risk groups and assumptions about risk progression (comparing three mechanisms of fixed, age-based, or mixed risk)—shape epidemic projections. Using deterministic HIV models stratified by HIV stage and behavioral risk, we simulated populations over 250 years under standardized initial conditions. Our results show that risk-progression mechanisms strongly influence long-term epidemic behavior. Fixed-risk models gradually shift the population toward lower-risk groups, thus reducing HIV incidence over time. In contrast, age-based progression sustains a larger high-risk population and produces a substantially higher long-term incidence, while mixed progression yields intermediate outcomes. The granularity of risk stratification further modifies the projections: models with more risk groups generate significantly different incidence trajectories and equilibrium population sizes under age-based and mixed progression, whereas fixed-risk models produce similar long-term results with a different number of risk groups. These findings highlight that both risk-progression assumptions and the level of stratification can meaningfully alter HIV forecasts. Therefore, the careful treatment of population risk heterogeneity is essential to generate reliable projections and to guide intervention strategies.

Keywords: mathematical modeling; heterogeneity; HIV prevention

1. Introduction

Mathematical models have long been used to investigate problems in ecology and epidemiology [1–4]. Particularly, they have been essential tools when simulating Human Immunodeficiency Virus (HIV) epidemics, the cause of Acquired Immunodeficiency Syndrome (AIDS), across diverse settings and projecting the impact of prevention and treatment interventions [5–10]. These models are particularly valuable to evaluate policy options, anticipate future epidemic trajectories, and understand the mechanisms that shape transmission dynamics.

A central feature of many HIV transmission models is the representation of *risk heterogeneity*, that is, the variation across individuals in their likelihood of acquiring HIV. Models that incorporate such heterogeneity through differences in sexual activity, partner selection, or behavioral patterns are better positioned to capture the skewed distribution of infection risk that characterizes HIV and other sexually transmitted infections.

Despite its importance, risk heterogeneity is often simplified in large-scale epidemic estimation tools or national modeling frameworks. Many estimates rely on unstratified general-epidemic models that fit HIV prevalence curves without explicit subgroup structure [11] or on models that only use a few broad risk categories [12–14]. Typical implementations classify individuals into two to four groups representing gradients of sexual activity or behavioral risk—commonly distinguishing a small, disproportionately high-risk subgroup. However, previous studies indicate that such simplifications can meaningfully affect epidemic projections [15,16]. Models that only differ in the definition or number of risk groups may produce qualitatively distinct epidemic behaviors even when calibrated to similar average levels of risk. Prior work, including collaborative studies with Dr. Yang Kuang, has also shown that seemingly minor modeling choices—whether demographic assumptions not directly tied to HIV transmission [17,18], or the selection of evaluation metrics [19]—can meaningfully alter model predictions and, consequently, the public health conclusions drawn from them.

Published models exhibit substantial variations in the level of detail used to represent risk heterogeneity. For example, a recent review of 154 agent-based HIV modeling studies found wide variations in the number of risk groups adopted: most models used four to six groups, some only used two or three, and others used seven or more [20]. Yet, while HIV transmission models are typically calibrated to epidemiologic outcomes such as HIV prevalence, incidence, or demographic characteristics, the parameters defining risk heterogeneity are rarely included as calibration targets. As a result, the realized distribution of risk—such as the proportion of individuals in each risk group or the magnitude of risk differences between groups—may shift during calibration or long-term simulations, and such shift may remain unnoticed if the evolution of risk distribution is not explicitly examined or reported. A separate review of models that evaluated HIV prevention interventions similarly concluded that population subgroups related to sexual risk or demographic characteristics are frequently underrepresented, despite their potential to substantially influence model outcomes [21].

These structural choices have far-reaching implications. Previous analyses have shown that the number of modeled risk strata can influence the basic reproduction number, shift model behavior across threshold regimes, or alter projections of treatment or prevention effectiveness—even when an average risk behavior is held constant across scenarios [15,16]. Another study demonstrated that employing a model with less granular risk assessment significantly underestimates the infectivity associated with symptomatic HIV [22]. Although the majority of population models are used for short- to medium-term projections (up to 50 years), many are run to quasi-equilibrium during calibration or

initiated at the hypothetical start of the HIV epidemic, which results in simulations that extend well beyond a century [23–25]. A recently published model comparison analysis evaluated expansions of pre-exposure prophylaxis (PrEP) use in South Africa over 20 years, which was obtained with 3 highly respected models [26]. Despite good alignment in HIV prevalence, HIV incidence, HIV care cascade and key intervention characteristics (coverage, efficacy and retention), models came up with substantially different impact projections. It was demonstrated that discrepancies are driven by the HIV risk distribution employed by each model. These examples underscore the need to understand how both the *granularity* of risk stratification and the *assumptions governing risk progression* across the life course influence long-term epidemic outcomes.

In this study, we extend prior efforts by evaluating the dynamic behavior of HIV transmission models across a range of risk structure assumptions. We examine not only differences in the number of risk groups but also how individuals enter and move between these groups over time. By comparing models that vary in both granularity and progression rules, we assess how these structural decisions influence the HIV incidence, equilibrium population distributions, and overall epidemic burden. Through this systematic examination, we aim to clarify the conditions under which simplified models may mischaracterize HIV dynamics and to highlight the importance of accurately representing risk heterogeneity in HIV modeling structure assumptions.

2. Materials and methods

2.1. Model description

We developed a set of deterministic, compartmental HIV transmission models to simulate HIV acquisition, transmission, and HIV-related mortality in a sexually active population. Individuals were assumed to be sexually active for an average of 30 years (Figure 1). Each model stratified the population by both HIV status—HIV-negative (susceptible, S), HIV-positive (infected, I), and AIDS (A)—and by behavioral risk, with individuals assigned to one of n ordered risk groups ranging from lowest (group 1) to highest (group n). The model equations are:

$$\begin{aligned}
\frac{dS_1}{dt} &= \Lambda_1^n + \tau_2^n S_2 - (\lambda_1^n + \mu_1^n)S_1, \\
\frac{dI_1}{dt} &= \lambda_1^n S_1 + \tau_2^n I_2 - (\mu_1^n + \gamma)I_1, \\
\frac{dA_1}{dt} &= \gamma I_1 + \tau_2^n A_2 - (\mu_1^n + \delta)A_1, \\
\frac{dS_i}{dt} &= \Lambda_i^n + \tau_{i+1}^n S_{i+1} - (\lambda_i^n + \tau_i^n + \mu_i^n)S_i, \qquad i = 2 \,..\, n-1, \\
\frac{dI_i}{dt} &= \lambda_i^n S_i + \tau_{i+1}^n I_{i+1} - (\tau_i^n + \mu_i^n + \gamma)I_i, \\
\frac{dA_i}{dt} &= \gamma I_i + \tau_{i+1}^n A_{i+1} - (\tau_i^n + \quad \mu_i^n + \delta)A_i, \\
\frac{dS_n}{dt} &= \Lambda_n^n - (\lambda_n^n + \tau_n^n + \mu_n^n)S_n, \\
\frac{dI_n}{dt} &= \lambda_n^n S_n - (\tau_n^n + \mu_n^n + \gamma)I_n,
\end{aligned}$$

$$\frac{dA_n}{dt} = \gamma I_n - (\tau_n^n + \mu_n^n + \delta)A_n,$$

where Λ_i^n is the number of individuals who annually reach sexual activity age in risk group i, τ_i^n is the rate at which individuals in risk group i transition to risk group i-1 as a result of risk reduction (no transition occurs into the group with highest risk and from the group with lowest risk), μ_i^n is the departure rate at which individuals age out of the population (assumed 30 -years of sexual activity), γ is the rate at which HIV positive individuals develop AIDS, and δ is the HIV-related mortality among individuals with AIDS.

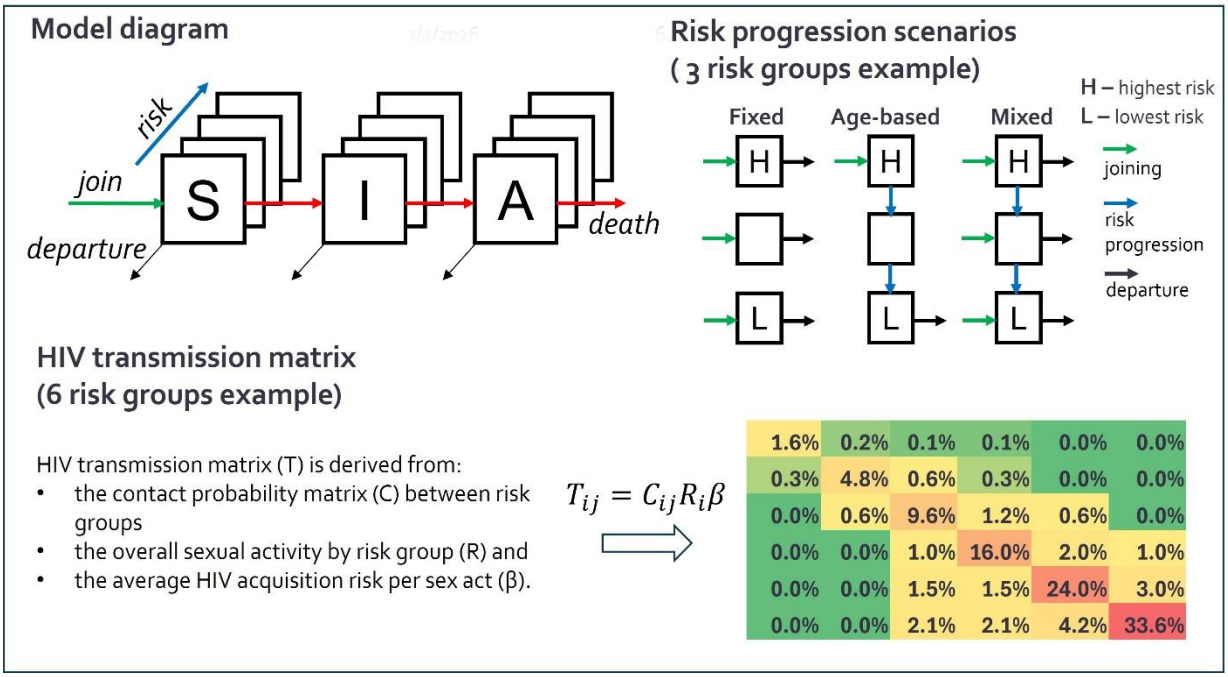

Figure 1. Model schematics.

The total number of adolescents reaching annually is chosen to generate realistic long-term population growth in the absence of HIV. The rate of acquiring HIV for individuals from risk group i is given by the force of infection as follows:

$$\lambda_i^n = \left(\sum_{j=1}^{n} \frac{T_{ij}^n I_j}{S_j + I_j} \right).$$

Here, the transmission matrix T^n is derived from the diagonally dominant sexual-mixing matrix (C^n), which represents the likelihood of creating partnerships between different risk groups, the overall sexual activity that individuals from different risk groups have (R^n), and the average HIV acquisition risk per sex act (β) as follows:

$$T_{ij}^n = C_{ij}^n R_i^n \beta$$

where C_{ij}^n is the probability of a sexual partner of an individual from risk group i to be from risk group

j and satisfying $\sum_{j=1}^{n} C_{ij}^{n} = 1$, R_i^n is the weighted sexual activity that individuals from risk group i have, accounting for the number of sex acts, the prevalence of anal sex, and proportion of acts in which protection is used. Finally, β is the probability of HIV acquisition per a single unprotected exposure through vaginal sex.

All simulations were initialized with 1% of the population living with HIV and were run for 200 years under standardized initial conditions in order to reach long-term equilibrium.

2.2. Model parameterization

Table 1. Model parameters.

Symbol	Description	Value	Comment
N_0	Initial population size	*1000*	Assumed
n	Number of risk groups	*1–6*	Scenarios
Λ_i^n	Annual recruitment, representing the number of individuals becoming sexually active annually	Fixed risk: $\Lambda_i^n = 36/n$ for all i Age-based risk: $\Lambda_i^n = 0$, $i = 1 \ldots n\text{-}1$, $\Lambda_n^n = 36$ Mixed risk*: $\Lambda^2 = [8\ 28]$, $\Lambda^3 = [4\ 8\ 24]$, $\Lambda^6 = [2\ 2\ 4\ 4\ 6\ 18]$	Fixed total, see Supplement for details
μ_i^n	Annual departure rate at which individuals in risk group i age out of the population	Fixed risk: $\mu_i^n = 1/30$ for all i Age-based risk: $\mu_1^n = n/30$, $\mu_i^n = 0$, $i = 2 \ldots n$ Mixed risk*: $\mu^2 = \left[\frac{13}{270}\ \frac{1}{54}\right]$, $\mu^3 = \left[\frac{11}{180}\ \frac{1}{45}\ \frac{1}{60}\right]$, $\mu^6 = \left[\frac{1}{9}\ \frac{1}{90}\ \frac{1}{45}\ \frac{1}{45}\ \frac{1}{30}\ 0\right]$	Fixed total [5], see Supplement for details
γ	Annual rate at which HIV positive individuals develop AIDS	*0.1*	[27]
β	Probability of HIV acquisition per unprotected vaginal sex	*0.002*	[28]
δ	Annual HIV-related mortality rate among individuals with AIDS	*0.1*	Adjusted** from [27]
τ_i^n	Risk progression rate, the rate at which individuals in risk group i transition to risk group i-1 as a result of risk reduction	Fixed risk: $\tau_i^n = 0$ for all i Age-based risk: $\tau_i^n = n/30$, $i = 2 \ldots n$ Mixed risk: $\tau_i^n = n/60$, $i = 2 \ldots n$	Scenarios

*Recruitment and departure rates for the mixed risk scenario are calculated to satisfy 2 conditions: i) constant annual recruitment and ii) all risk groups being equally represented in the equilibrium population in absence of HIV. Details on the parameter estimation are presented in the Supplement.

2.3. Simulated scenarios

To evaluate how assumptions about risk heterogeneity influence model projections, we simulated populations stratified in 1, 2, 3, and 6 risk groups with individuals equally distributed across groups at

model start. The contact matrix C and sexual-activity vector R were first specified for a 6-group population and then appropriately aggregated for models with fewer groups. Aggregation preserved the overall initial force of infection by averaging the matrix rows and columns and the corresponding activity levels (see Supplement). We explored two commonly used risk progression mechanisms:

(i) *fixed risk*, in which individuals who enter the population are equally distributed across risk groups and remain in the same group throughout life. All groups share identical departure (aging out) rates. This approach is widely used in models that include multiple risk strata and assume risk is a static trait, [21] although some such models allow for transition between groups [29];

(ii) a*ge-based risk*, in which all individuals join the highest risk group at sexual debut and progress to lower-risk groups as they aged. Aging-out only occurred from the lowest-risk group. This scenario reflects modeling approaches that use age as a proxy for risk or adopt risk strata without explicit transition rates [30,31].

Generally speaking, in the *fixed risk* scenario, 100% of the individuals leave their risk group by aging out (population departures) and 0% by decreasing risk. In contrast, in the *age-based* scenario, 0% of individuals leave their risk groups (except the lowest risk group) by aging out and 100% by decreasing risk. Additionally, we explored a *mixed risk* scenario in which individuals progressed toward lower-risk groups at half the rate of the age-based scenario with recruitment and departure rates specified so that all risk groups were equally represented in the long-term HIV-free equilibrium (see Figure 1). This scenario represents the rollout of possible prevention interventions such as initiating a large proportion of individuals on PrEP. All three progression mechanisms were calibrated to generate broadly comparable population dynamics and long-term risk distributions when simulated in the absence of HIV. (see Figure 2A,B and Supplement for details). A complete description of sexual mixing assumptions and simulation scenarios is provided in the Supplement.

2.4. Metrics of interest

The following metrics were used to assess the influence of risk-structure assumptions: i) *annual HIV incidence rate*, defined as the percentage of HIV-negative individuals acquiring HIV each year; ii) *population risk distribution*, tracking the proportion of the population in each behavioral risk group over time; iii) *population attributable fraction of HIV incidence (PAFi)* associated with each risk group, calculated as the percentage of the annual new HIV occurring in each group, and iv) *population attributable fraction* of HIV transmission *(PAFt)* associated with each risk group, calculated as the percentage of new infections attributable to transmission from individuals in each risk group. These metrics were further synthesized to construct a population risk profile, defined as the cumulative fraction of total HIV acquisition risk borne by the riskiest α proportion of the population ($\alpha \in [0,1]$). This representation allowed us to quantify how risk concentration evolves under different model structures and behavioral progression assumptions.

3. Results

3.1. Population dynamics under different risk-progression assumptions

First, we compared the population dynamics projected by models with six behavioral risk groups to those produced by an unstratified model, evaluating outcomes both in the absence and presence of

HIV. Across all scenarios without HIV, simulations stabilized at the same long-term population size and maintained the initial uniform distribution of individuals across risk groups, confirming that the scenarios were structurally comparable (Figure 2A,B). Notably, the *fixed-risk* scenario, which includes no transitions between risk groups, produced identical population trajectories to the unstratified model. In contrast, the age-based and mixed-risk scenarios, which allow transitions, generated more rapid population growth toward equilibrium.

Introducing HIV into the system led to substantial reductions in the overall population size (Figure 2C). The magnitude of this decline varied across scenarios: approximately 20% under *fixed risk*, 25% under *age-based* progression, and nearly 35% under the *mixed risk* mechanism. Notably, the unstratified model projected a larger population reduction (~30%) than the *fixed* and *age-based* six-group models, but a smaller reduction than the *mixed* model. These results highlight the strong influence of risk concentration and sexual-mixing structure on the long-term demographic outcomes.

3.2. Short-term epidemic dynamics (up to 50 years)

During the first 25–30 years, all risk-stratified models exhibited broadly similar population trajectories (even up to 50 years) as well as HIV incidence and HIV prevalence patterns (Figure 2C–F), with differences emerging afterwards. Models incorporating risk heterogeneity produced higher HIV-related mortality over the initial decades, thereby reducing population size more rapidly than the unstratified model.

Among the risk-progression mechanisms, the *age-based* scenario initially produced lower HIV incidence than the *fixed* or *mixed* scenarios. This pattern reversed after approximately 20–30 years, because the *age-based* model's incidence continued to rise and eventually stabilized at a substantially higher long-term level (Figure 2D). These early dynamics reflect the combined influence of the initial population structure, patterns of risk depletion, and the inflow of high-risk individuals at sexual debut.

3.3. Long-term epidemic dynamics

Simulated scenarios generated highly diverse long-term HIV incidence patterns, with as much as a five-fold difference between the lowest and highest projections (Figure 2D). These differences underscore the importance of risk-progression assumptions. The *fixed risk* scenario produced a population with progressive preference for low-risk groups, which became noticeable after 20 years. This could be attributed to the depletion of high-risk groups under epidemic pressure, causing the population to shift over time toward lower-risk categories (see Figure S2). This phenomenon, also reported in other studies [32], produced a steady decline in the overall population risk and, consequently, a substantial long-term reduction in HIV incidence. In contrast, the *age-based* scenario maintained a large high-risk population because all new recruits entered the highest-risk group and many died before progressing to lower-risk categories. This produced a sustained concentration of high-risk individuals and generated persistently high long-term HIV incidence. This pattern is consistent with observed demographic shifts in high-burden African settings, where HIV has reshaped the population age structure [33–35]. The *mixed risk* scenario produced intermediate behavior. Allowing for both risk reduction and aging-out generated a more balanced long-term distribution of risk groups. and resulted in HIV incidence which increased less dramatically than in the age-based model but remained substantially higher than in the unstratified model.

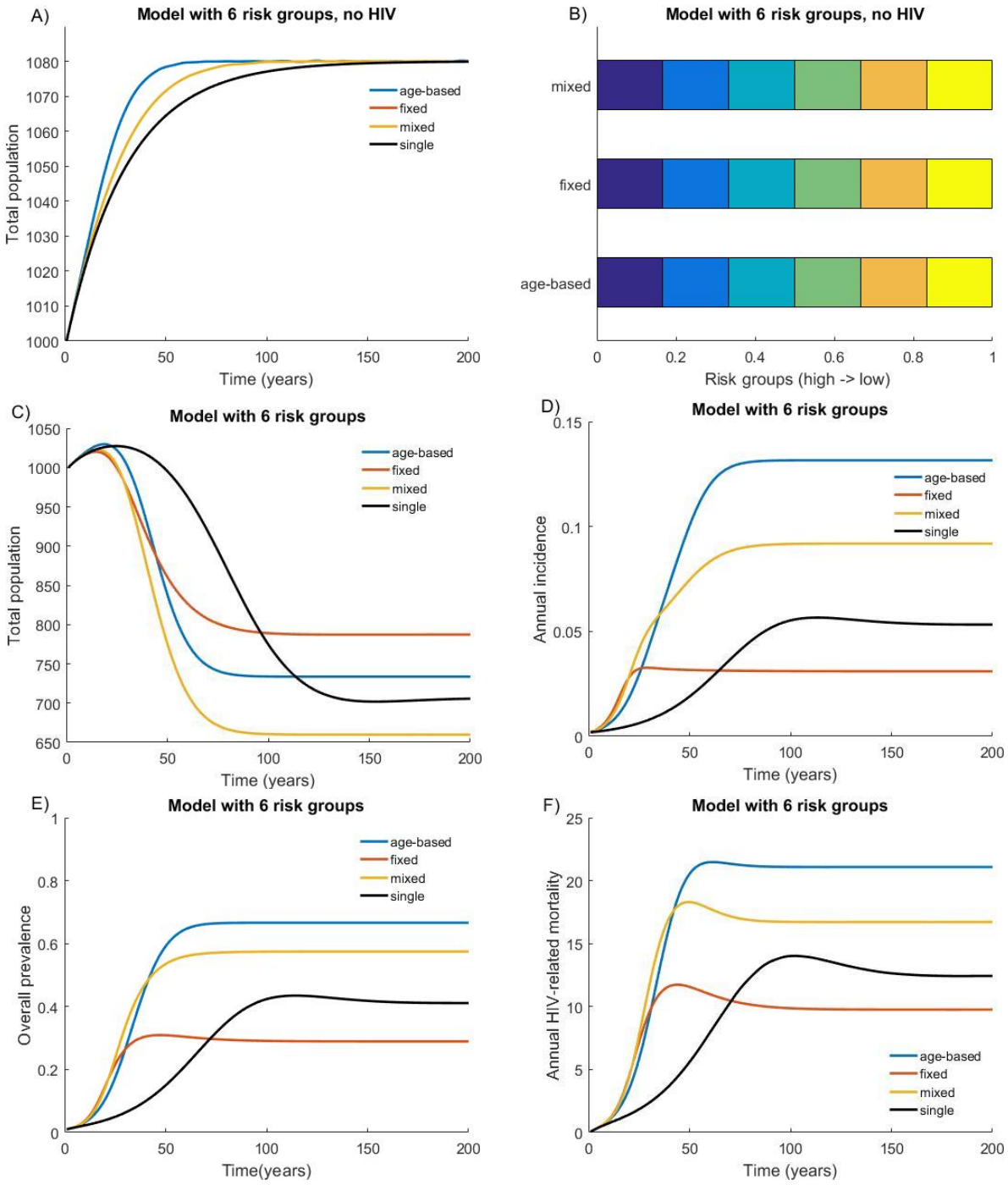

Figure 2. Population dynamics in the presence and absence of HIV for a model with six risk groups. A) Total population size over time in the absence of HIV; B) Equilibrium risk group distribution in absence of HIV; C) Total population size over time in the presence of HIV and D) Annual HIV incidence over time; E) HIV prevalence over time; F) Annual HIV-related deaths over time.

Long-term prevalence and mortality trends broadly mirrored the incidence across all three mechanisms (Figure 2E,F). Interestingly, the age-based model—with the highest HIV incidence—did not experience the largest population decline because the population became younger over time,

offsetting some of the increased HIV-related mortality.

3.4. Evolution of risk distribution and incidence concentration

Figure 3 illustrates how the behavioral risk distribution and the concentration of HIV incidence evolve over time under each risk-progression mechanism. Risk-progression assumptions strongly shaped both the population-level distribution of individuals across behavioral risk groups and the fraction of incident infections attributable to each group.

In the *fixed-risk* scenario, the depletion of high-risk groups caused the population to shift increasingly toward lower-risk categories. As a result, HIV incidence became more concentrated among a shrinking population subgroup, thereby steepening the slope of the risk-profile curves and moving them farther from the diagonal, representing equal risk across the population. Conversely, in the *age-based* scenario, high-risk groups expanded over time due to continual recruitment into the highest-risk category. This produced a more uniform long-term distribution of behavioral risk and risk-profile curves that approached the diagonal, indicating a more even distribution of HIV acquisition risk. Notably, the *mixed-risk* scenario largely preserved its initial risk structure over time. Although some increase in the risk concentration occurred, the effect was less pronounced than in the fixed-risk model.

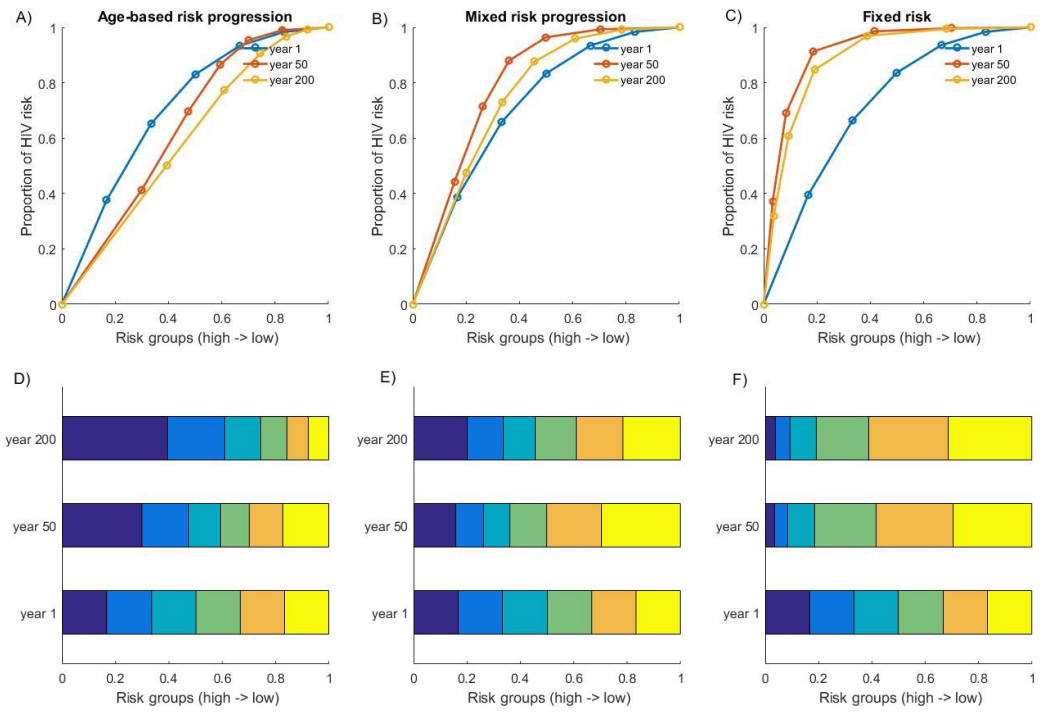

Figure 3. Evolution of risk distribution over time for a model with six risk groups. A)–C) Proportion of the HIV incidence which occurs among the riskiest fraction of the population (on x-axis) under different risk progression scenarios at different time points. Circles delineate risk groups in decreasing order of riskiness; D)–F) Population composition by risk groups at different time points.

3.5. Effects of increasing risk granularity

Next, we evaluated how the number of behavioral risk groups (1, 2, 3, or 6) affected epidemic projections under each risk-progression mechanism (Figure 4). Several patterns emerged: i) in the short term (first 20–30 years), the population size projections were similar across all models, regardless of the number of risk groups, even when incidence differed; ii) in the following intermediate period (up to 75 years), models incorporating risk stratification projected sharper population declines than the unstratified model, reflecting elevated HIV-related mortality within higher-risk groups, and iii) in the long term (100 + years) models with more granular risk assessment (more risk groups) maintained larger long-term population size when using the *age-based* risk progression mechanism but resulted in smaller long-term population size when *mixed* risk progression is employed. Increasing the number of risk groups significantly elevated long term HIV incidence under *age-based* and *mixed* scenarios, with the largest differences observed with *age-based* progression. (Figure 4D,E). This confirms the importance of the proper risk assessment when either risk mechanism is used. Interestingly, in the *fixed risk* scenario, long-term incidence and equilibrium population size were nearly identical for models with 2, 3, or 6 groups (Figure 4C,F). This suggests that two risk groups may be sufficient when using a fixed-risk structure, as higher resolutions have little influence on the model projections.

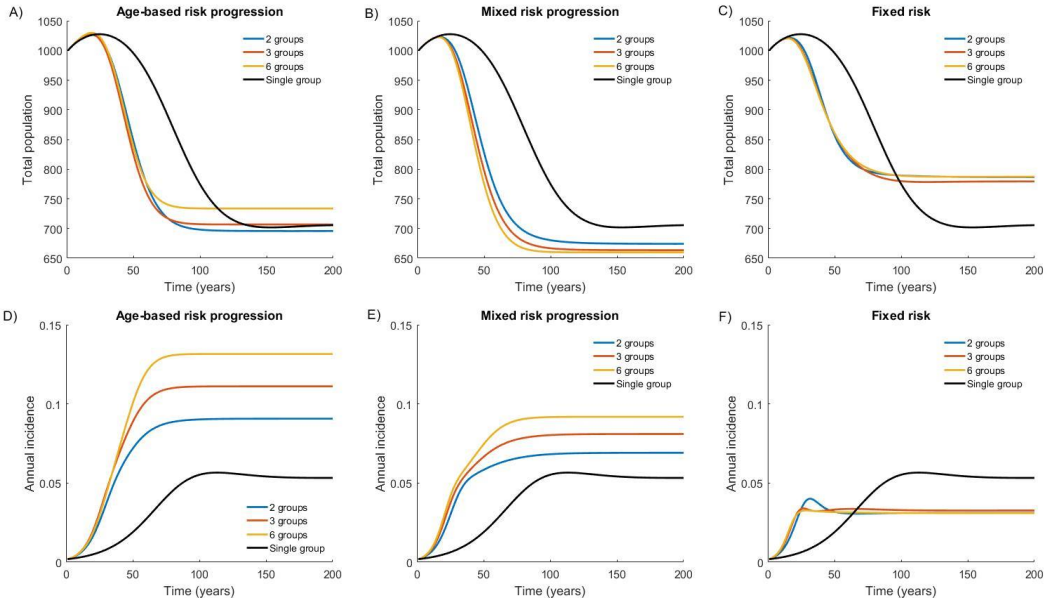

Figure 4. Population dynamics in presence of HIV for models with different number of risk groups. A)–C) Total population size over time for different risk progression scenarios; D)–F) Annual HIV incidence over time for different risk progression scenarios.

Additionally, we examined the equilibrium distribution of HIV risk across populations stratified by 1, 2, 3, or 6 risk groups (Figure 5). Overall, we did not find significant impact of risk group resolution on the projected population risk profile in the long-term, especially under *fixed* risk and *mixed* risk scenarios (Figure 5B,C). In the *age-based* scenario, increasing the number of risk groups is associated with a higher but more uniformly distributed HIV burden (Figure 4D vs. Figure 5A). In the *mixed risk* scenario, adding more risk groups increased the HIV burden without affecting the risk

concentration (Figure 4E vs. Figure 5B). All risk-stratified scenarios are associated with some level of risk concentration compared to a homogeneous risk assumption (single risk group).

Analyses of the population attributable fraction of HIV incidence (PAFi) and HIV transmission (PAFt) showed that high-risk groups consistently contributed disproportionately to new infections (Figures S2 and S3). However, in the *fixed risk* scenario, the PAFi contribution of the riskiest group substantially decreased over time compared to models with risk progression (age based and mixed) due to the fast depletion of this group (see Figure S2I, light blue).

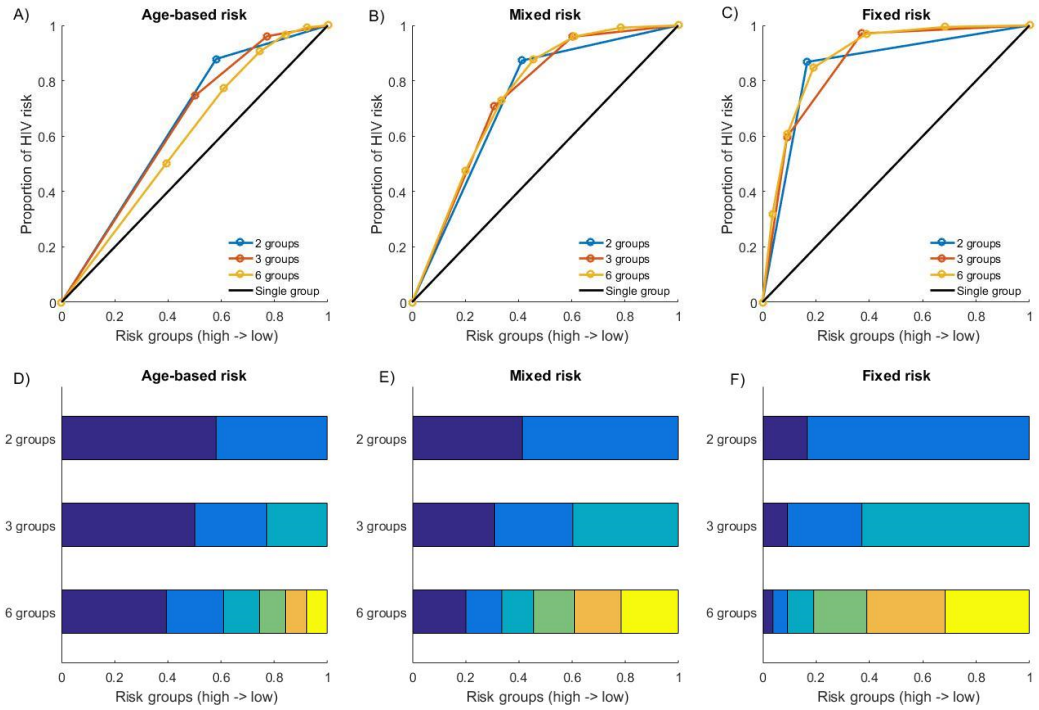

Figure 5. Equilibrium risk distribution for models with different number of risk groups. A)–C) Proportion of the HIV incidence which occurs among the riskiest subpopulation under different risk progression scenarios. Circles delineate risk groups in decreasing order of riskiness; D)–F) Equilibrium population distribution by risk groups.

4. Discussion

Our analysis demonstrates that assumptions about behavioral risk heterogeneity—both in terms of how individuals move through risk strata over their lifetimes and how finely risk groups are represented—can substantially alter epidemic projections. Even when models share identical initial conditions, different risk-progression mechanisms (fixed, age-based, or mixed) generate distinct long-term patterns of HIV incidence, mortality, and population structure. These findings highlight that the representation of behavioral risk is not a minor modeling choice but a core structural assumption that can meaningfully influence the conclusions drawn from HIV transmission models.

Across scenarios, we observed that the mechanism governing risk progression strongly shapes the distribution of population risk and the concentration of HIV burden. Models with fixed risk, which allow no downward risk transitions, produced long-term declines in the overall population risk because

high-risk groups were progressively depleted by HIV. As a result, HIV incidence became increasingly concentrated among a shrinking fraction of the population. In contrast, models that employed age-based risk progression generated a larger and more persistent high-risk population by placing all new entrants into the highest-risk group. This produced more uniform distributions of both population risk and incidence across risk groups, leading to substantially higher long-term HIV burden. Mixed-risk models fell between these extremes, thereby maintaining a balanced risk distribution over time and producing intermediate epidemic trends.

We demonstrated that the number of risk groups in the model structure can influence epidemic trajectories as strongly as the choice of risk-progression mechanism. Even when using the same behavioral-progression assumptions, models with fewer risk groups tended to underrepresent the distribution of risk and mischaracterize the long-term population structure compared with more granular models. Increasing the number of risk groups generally amplified differences in incidence and equilibrium population size—particularly under age-based and mixed risk progression—because finer stratification allows for stronger differentiation in sexual activity and mixing patterns. Notably, fixed-risk models were comparatively insensitive to the number of groups; in these scenarios, models with two, three, or six groups produced similar long-term outcomes, suggesting that highly granular stratification may offer limited benefits when risk is assumed to remain constant throughout life.

These findings have implications for public-health decision making. Under certain risk-progression assumptions, models with different levels of granularity can produce divergent assessments of which population subgroups contribute most to transmission and, consequently, where interventions should be targeted. Models with only a few risk groups may suggest prioritizing the highest-risk individuals, whereas more detailed models reveal that moderate-risk groups can also substantially contribute to new infections and may offer important opportunities for intervention impact. Such discrepancies could lead to different conclusions about the allocation and expected effectiveness of prevention strategies, particularly in settings where the behavioral risk is heterogeneous and dynamic.

This study has several limitations. We did not explicitly include the full HIV care continuum, such as stages of linkage to care, antiretroviral therapy (ART) initiation, viral suppression, or treatment interruptions. As a result, the modeled dynamics most closely resemble early-epidemic conditions [36,37]. We also did not incorporate explicit prevention interventions (e.g., PrEP) or calibrate the model to a specific epidemic setting. Nonetheless, the annual AIDS mortality rate predicted by our simulations is considerably lower than that observed at the peak of the epidemic and only about twice the rate reported in the United States over the past decade [38], suggesting that existing prevention and treatment effects are indirectly reflected in our parameterization. Finally, the projected impact of risk heterogeneity in our analysis depends on the specific assumptions on between-group risk differences and sexual mixing. Our goal was to provide a conceptual demonstration of how risk-related assumptions influence epidemic projections; future work will extend these analyses using more realistic, setting-specific models and explicitly evaluate the implications for modern HIV prevention strategies.

5. Conclusions

Overall, our results underscore that accurate projections of HIV burden require both sufficiently detailed risk stratification and realistic assumptions about how behavioral risk evolves over time. Models that overlook these structural dimensions risk misrepresenting epidemic potential and drawing misleading conclusions about intervention priorities. At the same time, parameterizing models with multiple risk groups can be challenging and may not always be feasible. By systematically evaluating the interplay between model granularity and risk progression, this study highlights the importance of thoughtfully representing behavioral heterogeneity in HIV transmission models and provides a foundation for future work aimed at improving the fidelity and policy relevance of such models.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Acknowledgments

This work was partially supported by two National Institute of Allergy and Infectious Diseases (NIAID) grants - UM1 068617 and R01 AI79417. NIAID had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Conflict of interest

The authors declare there is no conflict of interest.

References

1. M. Kot, *Elements of Mathematical Ecology*, Cambridge University Press, 2001.
2. Y. Kuang, Basic properties of mathematical population models, *J. Biomath.*, **17** (2002), 129–142.
3. F. Brauer, C. Castillo-Chavez, Z. Feng, *Mathematical Models in Epidemiology*, New York: Springer, 2019.
4. D. T. Dimitrov, H. V. Kojouharov, Analysis and numerical simulation of phytoplankton-nutrient systems with nutrient loss, *Math. Comput. Simul.*, **70** (2005), 33–43. https://doi.org/10.1016/j.matcom.2005.03.001
5. J. W. Eaton, N. Bacaer, A. Bershteyn, V. Cambiano, A. Cori, R. E. Dorrington, et al., Assessment of epidemic projections using recent HIV survey data in South Africa: a validation analysis of ten mathematical models of HIV epidemiology in the antiretroviral therapy era, *Lancet Glob. Health*, **3** (2015), e598–e608.
6. D. Dimitrov, M. C. Boily, B. R. Mâsse, E. R. Brown, Impact of pill sharing on drug resistance due to a wide-scale oral prep intervention in generalized epidemics, *J AIDS Clinic Res.*, (2012), S5–004. https://doi.org/10.4172/2155-6113.S5-004

7. R. Silhol, R. L. Anderson, O. Stevens, J. Stannah, R. D. Booton, S. Baral, et al., Measuring HIV acquisitions among partners of key populations: estimates from HIV transmission dynamic models, *JAIDS, J. Acquired Immune Defic. Syndr.*, **95** (2024), e59–e69. https://doi.org/10.1097/QAI.0000000000003334
8. O. Stevens, R. Anderson, J. Stover, Y. Teng, J. Stannah, R. Silhol, et al., Comparison of empirically derived and model-based estimates of key population HIV incidence and the distribution of new infections by population group in sub-Saharan Africa, *JAIDS, J. Acquired Immune Defic. Syndr.*, **95** (2024), e46–e58. https://doi.org/10.1097/QAI.0000000000003321
9. S. E. Stansfield, J. Heitner, K. M. Mitchell,, C. M. Doyle, R. M. Milwid, M. Moore, et al., Population-level impact of expanding PrEP coverage by offering long-acting injectable PrEP to MSM in three high-resource settings: a model comparison analysis, *J. Int. AIDS Soc.*, **26** (2023), e26109. https://doi.org/10.1002/jia2.26109
10. S. de Montigny, B. J. S. Adamson, B. R. Masse, L. P. Garrison, J. G. Kublin, P. B. Gilbert, et al., Projected effectiveness and added value of HIV vaccination campaigns in South Africa: A modeling study, *Sci. Rep*., **8** (2018), 6066. https://doi.org/10.1038/s41598-018-24268-4
11. C. van Schalkwyk, M. Mahy, L. F. Johnson, J. W. Imai-Eaton, Updated data and methods for the 2023 UNAIDS HIV estimates, *JAIDS, J. Acquired Immune Defic. Syndr.*, **95** (2024), e1–e4. https://doi.org/10.1097/QAI.0000000000003344
12. B. Adamson, L. Garrison, R. V. Barnabas, J. J. Carlson, J. Kublin, D. Dimitrov, Competing biomedical HIV prevention strategies: potential cost-effectiveness of HIV vaccines and PrEP in Seattle, WA, *J. Int. AIDS Soc.*, **22** (2019), e25373. https://doi.org/10.1002/jia2.25373
13. K. M. Mitchell, B. Hoots, D. Dimitrov, D. German, C. Flynn, J. E. Farley, et al., Improvements in the HIV care continuum needed to meaningfully reduce HIV incidence among men who have sex with men in Baltimore, US: a modelling study for HPTN 078, *J. Int. AIDS Soc.*, **22** (2019), e25246. https://doi.org/10.1002/jia2.25246
14. P. Vickerman, F. Terris-Prestholt, S. Delany, L. Kumaranayake, H. Rees, C. Watts, Are targeted HIV prevention activities cost-effective in high prevalence settings? Results from a sexually transmitted infection treatment project for sex workers in Johannesburg, South Africa, *Sex. Transm. Dis.*, **33** (2006), S122–S32. https://doi.org/10.1097/01.olq.0000221351.55097.36
15. M. Kot, D. T. Dimitrov, The dynamics of a simple, risk-structured HIV model, *Math. Biosci. Eng.*, **17** (2020), 4184–4209. https://doi.org/10.3934/mbe.2020232.
16. B. Wallace, D. Dimitrov, L. Hébert-Dufresne, A. M. Berdahl, Hotspot model shows how location-based superspreading accelerates and reshapes epidemics, *PNAS Nexus*, **4** (2025), pgaf299. https://doi.org/10.1093/pnasnexus/pgaf299.
17. Y. Zhao, D. T. Wood, H. V. Kojouharov, Y. Kuang, D. T. Dimitrov, Impact of population recruitment on the HIV epidemics and the effectiveness of HIV prevention interventions, *Bull. Math. Biol.*, **78** (2016) 2057–2090. https://doi.org/10.1007/s11538-016-0211-z.
18. D. T. Dimitrov, Y. Kuang, B. R. Masse, Assessing the public health impact of HIV interventions: The critical role of demographics, *JAIDS, J. Acquired Immune Defic. Syndr.*, **66** (2014), e60–e62. https://doi.org/10.1097/QAI.0000000000000133
19. Y. Q. Zhao, D. T. Dimitrov, H. Liu, Y. Kuang, Mathematical insights in evaluating state dependent effectiveness of HIV prevention interventions, *Bull. Math. Biol.*, **75** (2013), 649–675. https://doi.org/10.1007/s11538-013-9824-7

20. R. V. Anderle, R. B. de Oliveira, F. A. Rubio, J. Macinko, I. Dourado, D. Rasella, Modelling HIV/AIDS epidemiological complexity: a scoping review of agent-based models and their application, *PLoS One*, **19** (2024), e0297247. https://doi.org/10.1371/journal.pone.0297247
21. R. Giddings, P. Indravudh, G. F. Medley, F. Bozzani, M. Gafos, S. Malhotra, et al., Infectious disease modelling of HIV prevention interventions: a systematic review and narrative synthesis of compartmental models, *Pharmacoeconomics*, **41** (2023), 693–707. https://doi.org/10.1007/s40273-023-01260-z
22. B. L. Rapatski, F. Suppe, J. A. Yorke, HIV epidemics driven by late disease stage transmission, *JAIDS, J. Acquired Immune Defic. Syndr.*, **38** (2005), 241–253. https://doi.org/10.1097/01.qai.0000146596.21084.02
23. A. Bershteyn, J. Gerardin, D. Bridenbecker, C. W. Lorton, J. Bloedow, R. S. Baker, et al., IImplementation and applications of EMOD, an individual-based multi-disease modeling platform, *Pathog Dis.*, **76** (2018), fty059. https://doi.org/10.1093/femspd/fty059
24. C. C. Kerr, R. M. Stuart, R. T. Gray, A. J. Shattock, N. Fraser-Hurt, C. Benedikt, et al., Optima: a model for HIV epidemic analysis, program prioritization, and resource optimization, *JAIDS, J. Acquired Immune Defic. Syndr.*, **69** (2015), 365–376. https://doi.org/10.1097/QAI.0000000000000605
25. C. Selinger, A. Bershteyn, D. T. Dimitrov, B. J. S. Adamson, P. Revill, T. B. Hallett, et al., Targeting and vaccine durability are key for population-level impact and cost-effectiveness of a pox-protein HIV vaccine regimen in South Africa, *Vaccine*, **37** (2019), 2258–2267. https://doi.org/10.1016/j.vaccine.2019.02.073
26. S. E. Stansfield, M. Moore, L. Jamieson, G. Meyer-Rath, L. F. Johnson, D. Kaftan, et al., Estimated impact of long-acting injectable PrEP in South Africa: a model comparison analysis, *J. Int. AIDS Soc.*, **28** (2025), e26453. https://doi.org/10.1002/jia2.26453
27. T. D. Hollingsworth, R. M. Anderson, C. Fraser, HIV-1 transmission, by stage of infection, *J. Infect. Dis*., **198** (2008), 687–693. https://doi.org/10.1086/590501
28. M. C. Boily, R. F. Baggaley, L. Wang, B. Masse, R. G. White, R. J. Hayes, et al., Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies, *Lancet Infect. Dis.*, **9** (2009), 118–129. https://doi.org/10.1016/S1473-3099(09)70021-0
29. G. Akudibillah, A. Pandey, J. Medlock, Maximizing the benefits of ART and PrEP in resource-limited settings, *Epidemiol. Infect.*, **145** (2017), 942–956. https://doi.org/10.1017/S0950268816002958
30. R. A. Alsallaq, J. Buttolph, C. M. Cleland, T. Hallett, I. Inwani, K. Agot, et al., The potential impact and cost of focusing HIV prevention on young women and men: A modeling analysis in western Kenya, *PLOS One*, **12** (2017), e0175447. https://doi.org/10.1371/journal.pone.0175447
31. K. M. Mitchell, D. Dimitrov, R. Silhol, L. Geidelberg, M. Moore, A. Liu, et al., The potential effect of COVID-19-related disruptions on HIV incidence and HIV-related mortality among men who have sex with men in the USA: a modelling study, *Lancet HIV*, **8** (2021), e206–e215. https://doi.org/10.1016/S2352-3018(21)00022-9
32. M. Moore, M. C. Boily, D. J. Donnell, D. Dimitrov, *Reducing the Global HIV Burden: The Importance of Uneven Exposure to the Results of HIV Prevention Trials*, Infectious Diseases and Our Planet. Cham: Springer International Publishing, (2020), 217–239. https://doi.org/10.1007/978-3-030-50826-5_8

33. K. A. Risher, A. Cori, G. Reniers, M. Marston, C. Calvert, A. Crampin, et al., Age patterns of HIV incidence in eastern and southern Africa: a modelling analysis of observational population-based cohort studies, *Lancet HIV*, **8** (2021), e429–e439. https://doi.org/10.1016/S2352-3018(21)00069-2
34. K. Zuma, L. Simbayi, N. Zungu, S. Moyo, E. Marinda, S. Jooste, et al., The HIV epidemic in South Africa: key findings from 2017 national population-based survey, *Int. J. Environ. Res. Public Health*, **19** (2022), 8125. https://doi.org/10.3390/ijerph19138125
35. P. Heuveline, Impact of the HIV epidemic on population and household structure: the dynamics and evidence to date, *Aids*, **18** (2004), S45–S53. https://doi.org/10.1097/00002030-200406002-00006
36. J. M. Hyman, J. Li, E. A. Stanley, The differential infectivity and staged progression models for the transmission of HIV, *Math. Biosci.*, **155** (1999), 77–109. https://doi.org/10.1016/S0025-5564(98)10057-3
37. L. J. Abu-Raddad, I. A. Longini, No HIV stage is dominant in driving the HIV epidemic in sub-Saharan Africa, *Aids*, **22** (2008), 1055–1061. https://doi.org/10.1097/QAD.0b013e3282f8af84
38. *CDC*. AtlasPlus-Charts, 2026. Available from: https://gis.cdc.gov/grasp/nchhstpatlas/charts.html.

AIMS Press