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Metapopulation Modeling of Human Immunodeficiency Virus Spread Under Spatially Heterogeneous Pre-Exposure Prophylaxis Uptake

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Abstract:
The human immunodeficiency virus remains a persistent global public health challenge despite significant advancements in biomedical prevention strategies. Among these interventions, pre-exposure prophylaxis has demonstrated remarkable efficacy in preventing viral acquisition among high-risk populations. However, the population-level impact of pre-exposure prophylaxis is frequently undermined by spatial heterogeneities in healthcare access, medication adherence, and underlying epidemic dynamics. Traditional epidemiological models often rely on the assumption of homogeneous population mixing, which fails to capture the complex spatial distribution of communities and the critical role of human mobility in disease transmission. This paper presents a comprehensive metapopulation modeling framework designed to evaluate the spread of the human immunodeficiency virus under varying conditions of spatially heterogeneous pre-exposure prophylaxis uptake. By dividing the broader population into distinct interacting geographical patches such as urban cores, suburban rings, and rural peripheries, the proposed model incorporates explicit mobility matrices to simulate daily commuting and long-term migration patterns. Through extensive scenario-based simulations, this research demonstrates that uniform scale-up of preventive medication is less efficient than spatially targeted interventions that prioritize localized transmission hotspots. The findings reveal that high human mobility can significantly dilute the protective benefits of localized prophylactic interventions, transforming neighboring low-uptake regions into epidemiological reservoirs. The insights derived from this study underscore the necessity for geographically tailored public health strategies and provide a robust analytical foundation for optimizing resource allocation in the ongoing effort to eliminate the transmission of the human immunodeficiency virus.

1. INTRODUCTION

The transmission of the human immunodeficiency virus continues to command substantial attention from public health authorities and academic researchers worldwide. Despite decades of intensive scientific investigation and the successful development of antiretroviral therapies, the pathogen persists in causing significant morbidity and mortality, particularly among vulnerable demographic groups [1]. The epidemiological landscape of the human immunodeficiency virus has fundamentally transformed over the past decade, driven primarily by the introduction and widespread approval of pre-exposure prophylaxis [2]. This biomedical intervention, which typically involves the daily administration of antiretroviral medications to uninfected individuals, has been proven to reduce the risk of sexual acquisition of the virus by over ninety percent when taken with strict adherence [3]. Consequently, pre-exposure prophylaxis has become a cornerstone of global strategies aimed at ending the epidemic.

Despite the clinical efficacy of this preventive regimen, translating individual-level protection into population-level epidemic control has proven exceptionally complex. Real-world implementation is frequently hampered by structural barriers, socioeconomic disparities, and behavioral variability, leading to highly uneven uptake across different geographical regions [4]. In numerous public health jurisdictions, urban centers with robust healthcare infrastructure report high levels of prescription and adherence, whereas suburban and rural areas exhibit significant deficits in both awareness and accessibility. This spatial heterogeneity in preventive coverage creates a fragmented landscape of population immunity, thereby complicating efforts to forecast long-term epidemiological trends.

The inherent limitations of standard epidemiological models further exacerbate the challenge of understanding this complex spatial dynamic. Conventional compartmental models traditionally operate under the assumption of a well-mixed population, meaning that every individual has an equal probability of encountering every other individual within the defined system [5]. While this assumption facilitates mathematical tractability, it fundamentally ignores the spatial clustering of human populations and the structured nature of human contact networks. In reality, individuals reside in distinct geographic areas and their interactions are heavily dictated by local environments, daily commuting patterns, and regional socio-economic structures.

To address the limitations of homogeneous mixing models, researchers have increasingly turned to metapopulation frameworks. A metapopulation model conceptualizes a large, heterogeneous population as a network of distinct, localized subpopulations, often referred to as patches. Within each patch, individuals mix relatively homogeneously, but the patches themselves are connected through defined mobility networks representing human movement. By integrating these spatial and mobility components, metapopulation models provide a highly granular and realistic mechanism for exploring how localized interventions, such as the targeted rollout of pre-exposure prophylaxis, influence the broader regional spread of the human immunodeficiency virus.

The primary objective of this paper is to develop and analyze a comprehensive metapopulation model that captures the intricate interplay between spatially heterogeneous pre-exposure

prophylaxis uptake and human mobility networks. By systematically disaggregating the population into distinct urban, suburban, and rural patches, this research aims to elucidate how local variations in prophylactic coverage impact systemic epidemic trajectories. Furthermore, this study seeks to identify the optimal spatial allocation of public health resources under budget constraints, testing the hypothesis that targeted interventions in highly connected mobility hubs yield superior epidemiological outcomes compared to a uniform distribution of resources.

2. Literature Review and Background

2.1 Historical Perspectives on Human Immunodeficiency Virus Modeling

The mathematical modeling of infectious diseases has a rich history that has continuously evolved to meet the specific biological and social complexities of different pathogens. Early efforts to model the human immunodeficiency virus in the late twentieth century primarily utilized deterministic compartmental structures [6]. These foundational models divided populations into basic epidemiological states, such as susceptible, infected, and deceased, and governed the transitions between these states using ordinary differential equations. While these early frameworks provided critical insights into the basic reproduction number and the long-term endemic potential of the virus, they were severely constrained by their inability to account for behavioral heterogeneity.

As the epidemic progressed, researchers recognized that the assumption of uniform risk was fundamentally flawed. The transmission dynamics of the human immunodeficiency virus are heavily concentrated within specific key populations, including men who have sex with men, people who inject drugs, and commercial sex workers. To reflect this reality, second-generation mathematical models introduced risk-stratified compartments [7]. These models allowed researchers to simulate the disproportionate burden of the disease on specific demographic groups and evaluate the impact of targeted behavioral interventions, such as condom distribution programs and needle exchange initiatives. However, even these advanced models largely ignored the spatial dimension of transmission, treating entire cities or countries as single, cohesive entities without geographic internal structure.

The advent of network theory in the early two-thousands provided a paradigm shift in epidemiological modeling. Network-based models conceptualized populations as complex webs of individual nodes connected by specific types of relationships [8]. This approach allowed for the explicit representation of sexual concurrency and the structure of sexual networks, which are critical determinants of human immunodeficiency virus transmission. Despite their unparalleled granularity, network models remain computationally intensive and frequently require vast amounts of highly sensitive behavioral data that are difficult to collect and validate. Consequently, while network models are exceptional for exploring micro-level transmission dynamics, they often face scalability challenges when applied to macro-level public health planning across large geographic regions.

2.2 The Evolution of Pre-Exposure Prophylaxis Modeling

The introduction of pre-exposure prophylaxis necessitated a further evolution in epidemiological modeling techniques. Initial models designed to evaluate the impact of this biomedical intervention primarily focused on clinical trial settings and individual-level cost-effectiveness [9]. These early analyses were instrumental in securing regulatory approval and establishing baseline public health guidelines. They incorporated complex behavioral parameters, such as the potential for risk compensation, which is the phenomenon where individuals might increase their sexual risk behaviors due to the perceived protection afforded by the medication.

As the rollout of the prophylactic medication expanded into real-world settings, the modeling focus shifted toward population-level impact and the cascade of care. Researchers developed dynamic transmission models that explicitly tracked individuals through the various stages of preventive care, including awareness, initial prescription, routine adherence, and potential discontinuation [10]. These models revealed that the population-level effectiveness of the intervention was highly sensitive to medication adherence and the retention of individuals within the healthcare system. However, these models continued to assume that prophylactic resources and healthcare infrastructure were uniformly distributed across the modeled populations, failing to account for the spatial realities of healthcare access.

2.3 Spatial Dynamics and Metapopulation Theory

The recognition that geographical space plays a fundamental role in infectious disease transmission has driven the adoption of spatial epidemiological techniques. Metapopulation theory, originally developed in the field of population ecology to study fragmented animal habitats, has been successfully adapted for infectious disease modeling [11]. In the context of epidemiology, a metapopulation model defines a landscape of discrete patches, representing cities, neighborhoods, or administrative districts. The dynamics within each patch are governed by local biological and behavioral parameters, while the patches interact through matrices of human movement.

The application of metapopulation models has been particularly successful in the study of rapidly spreading respiratory pathogens, such as influenza and severe acute respiratory syndrome [12]. In these contexts, air travel and daily commuting networks serve as the primary conduits for disease dissemination. However, the application of metapopulation theory to sexually transmitted infections, and specifically the human immunodeficiency virus, has been relatively limited. This gap in the literature is largely due to the differing timescales of transmission; while respiratory diseases spread over days or weeks, the human immunodeficiency virus epidemic evolves over years and decades.

Recent advancements in the availability of human mobility data, derived from mobile phone tracking and detailed census commuting surveys, have made it feasible to construct long-term metapopulation models for sexually transmitted infections [13]. These datasets allow researchers to quantify not only permanent migration but also the short-term, recurrent movements that

facilitate the spatial bridging of sexual networks. By integrating these detailed mobility matrices with the complex clinical pathways of pre-exposure prophylaxis, researchers can now simulate how an intervention implemented in a resource-rich urban core might indirectly suppress transmission in interconnected, resource-limited suburban and rural areas.

2.4 Identifying the Research Gap

Despite the growing sophistication of both spatial modeling and biomedical intervention analysis, there remains a critical synthesis gap in the current literature. Most existing studies either analyze pre-exposure prophylaxis uptake within a spatially homogeneous framework or examine the spatial dynamics of the human immunodeficiency virus without adequately incorporating the nuanced clinical cascade of preventive medications. There is a profound need for a unified modeling approach that explicitly links localized healthcare infrastructure disparities, variable adherence rates to prophylactic regimens, and empirically grounded human mobility networks. This paper addresses this specific gap by constructing a robust metapopulation framework capable of evaluating complex, spatially differentiated intervention strategies over extended temporal horizons.

3. Methodology and Analysis

3.1 Conceptual Metapopulation Framework

The methodology of this study is grounded in a deterministic, continuous-time metapopulation framework. The entire geographical region of interest is partitioned into a finite number of distinct, non-overlapping patches. To capture the socioeconomic and infrastructural diversity typical of regional public health jurisdictions, the model specifically defines three archetypal patch categories: the high-density urban core, the surrounding suburban commuter rings, and the low-density rural periphery. Each patch maintains its own internal epidemiological dynamics, driven by localized demographic profiles, behavioral risk characteristics, and specific healthcare capacities.

Within every spatial patch, the local population is systematically stratified into mutually exclusive epidemiological compartments [14]. The primary state is the susceptible compartment, representing individuals who are uninfected and not currently utilizing any biomedical prevention. From the susceptible state, individuals may transition into the pre-exposure prophylaxis compartment. This transition is governed by a patch-specific uptake rate, which serves as a proxy for local healthcare access, community awareness, and public health funding. Individuals within the prophylactic compartment experience a significantly reduced hazard of acquiring the virus, contingent upon a secondary parameter representing local medication adherence levels.

If a susceptible individual acquires the virus, they transition into an acute infection state. This phase is characterized by an exceptionally high viral load and a correspondingly elevated probability of transmitting the pathogen during risk events [15]. Following the acute phase,

individuals progress to a chronic infection state. From the chronic state, individuals may be diagnosed and initiated on antiretroviral therapy. Successful adherence to therapeutic regimens transitions the individual to a virally suppressed state, wherein their physical health stabilizes and their probability of transmitting the virus is effectively reduced to zero. Throughout all stages, the model accounts for natural demographic processes, including background mortality and the continuous entry of newly sexually active individuals into the susceptible pool.

3.2 Demographic and Mobility Parameterization

A defining feature of the metapopulation approach is the explicit mathematical representation of human movement between the defined geographic patches. Rather than relying on simple diffusion processes, this model utilizes an origin-destination mobility matrix to govern inter-patch interactions. The mobility matrix represents the probability or frequency that an individual residing in a specific home patch will travel to and engage in localized interactions within a specific destination patch.

This model primarily focuses on short-term mobility, such as regular commuting for employment or social engagement, rather than permanent demographic relocation. When individuals from a suburban patch commute to the urban core, they temporarily mix with the resident population of the urban core, as well as with other commuters who have traveled to the same destination [16]. Consequently, the effective population present within any given patch at a specific time is a dynamic aggregate of permanent residents and temporary visitors.

The force of infection, which dictates the rate at which susceptible individuals acquire the virus, is calculated based on this dynamic, mobility-adjusted population structure [17]. For a resident of a specific patch, the overall risk of infection is a weighted sum of the transmission risks encountered in their home patch and the risks encountered in all other patches they visit. The weights are determined by the proportional time spent in each location, as defined by the mobility matrix. This formulation ensures that an outbreak originating in a high-prevalence urban center can effectively seed secondary transmission chains in rural communities through the bridging behavior of mobile individuals.

Table 1 Baseline Demographic and Epidemiological Parameters

Parameter Category	Description	Assumed Baseline Value
Transmission Probability	Base risk of transmission per unsprotected interaction	Zero point zero one five
Intervention Efficacy	Reduction in acquisition risk under strict prophylactic adherence	Ninety-five percent

Urban Contact Rate	Average number of relevant interactions per month in urban core	Four point two
Rural Contact Rate	Average number of relevant interactions per month in rural patches	Two point eight
Viral Suppression Rate	Annual rate of achieving undetectable status post-diagnosis	Sixty-five percent
Demographic Turnover	Annual entry and exit rate of the sexually active population	Two point five percent

To parameterize the model, baseline values were derived from an extensive synthesis of global epidemiological surveillance reports and socio-behavioral surveys. The transmission probabilities and intervention efficacies were calibrated using standardized clinical trial outcomes [18]. The contact rates, representing the frequency of behavioral risk events, were intentionally varied across patch types to reflect higher structural density and distinct social network architectures typical of urban environments.

Figure 1: Metapopulation Network Schematic

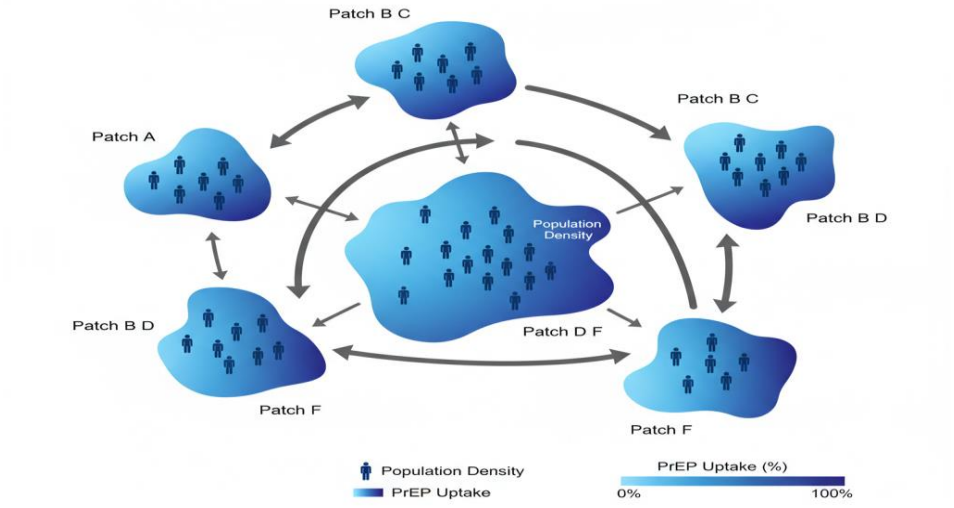


Figure 1 Metapopulation Network Schematic

3.3 Intervention Scenarios and Simulation Design

To rigorously evaluate the impact of spatial heterogeneities, the simulation framework was designed to analyze several distinct intervention scenarios over a projected twenty-year time

horizon. The foundational scenario is the baseline trajectory, which assumes the complete absence of pre-exposure prophylaxis. This baseline serves as the epidemiological counterfactual against which all subsequent preventive interventions are measured.

The second scenario models a uniform scale-up strategy. In this configuration, public health resources are distributed equally across all geographic patches, resulting in identical rates of prophylactic uptake and adherence regardless of the underlying local prevalence or demographic density [19]. While administratively straightforward, this scenario often represents an unrealistic assumption regarding real-world healthcare delivery.

The third scenario implements a spatially targeted resource allocation strategy. In this highly optimized configuration, pre-exposure prophylaxis resources are disproportionately directed toward the urban core and specific high-mobility suburban corridors. The rural peripheries, which exhibit lower baseline prevalence and contact rates, receive a correspondingly smaller allocation of the preventive intervention [20]. This scenario mimics a pragmatic public health strategy designed to maximize the interruption of transmission networks within densely populated hubs.

The mathematical simulations were executed using advanced numerical integration techniques to solve the large system of coupled differential equations governing the patch dynamics. To ensure the robustness of the findings, extensive sensitivity analyses were conducted on the mobility matrices. By systematically scaling the intensity of inter-patch commuting from zero, representing completely isolated communities, to extremely high levels of integration, the research team was able to isolate the specific mechanisms through which human movement facilitates or hinders localized epidemic control.

4. Results and Discussion

4.1 Baseline Epidemic Trajectories and Spatial Stratification

The simulation results under the baseline counterfactual scenario demonstrate a distinctly stratified epidemic trajectory across the metapopulation landscape. In the absence of prophylactic interventions, the human immunodeficiency virus exhibits a rapid initial expansion within the highly connected urban core, driven by elevated contact rates and dense network structures [21]. Following this urban explosion, the incidence curves for the suburban and rural patches exhibit a delayed but persistent rise. This sequential pattern clearly illustrates the classic core-periphery dynamic, wherein the urban center acts as an epidemiological source, continuously seeding new infections into the surrounding geographic regions through the daily movement of commuters.

By the end of the twenty-year baseline projection, the prevalence stabilizes into an endemic equilibrium, but the spatial disparities remain stark. The urban core sustains an infection burden nearly three times higher than that of the remote rural patches [22]. These baseline findings validate the necessity of the metapopulation approach; treating this modeled region as a single, homogeneously mixed entity would have grossly underestimated the severe concentration of the

disease within the central hubs, while simultaneously overestimating the immediate risk to the peripheral populations.

4.2 Impact of Uniform Versus Targeted Prophylactic Uptake

The introduction of pre-exposure prophylaxis profoundly alters the transmission landscape, but the magnitude of the impact is highly dependent on the spatial allocation strategy. Under the uniform scale-up scenario, where uptake rates are held constant across all patches, the overall regional incidence experiences a substantial decline. However, a detailed patch-level analysis reveals underlying inefficiencies in this approach. Because rural patches inherently possess lower transmission momentum, uniformly applying resources to these areas yields diminishing marginal returns [23]. Meanwhile, the uniform allocation fails to supply sufficient preventive coverage to the urban core to completely collapse the concentrated transmission networks located there.

Conversely, the spatially targeted scenario yields significantly superior systemic outcomes. By aggressively concentrating prophylactic coverage within the urban core and key suburban commuter transit hubs, the model projects a steep and sustained reduction in the overall regional incidence. Table 2 provides a comparative breakdown of these projections.

Table 2 Projected Incidence Reduction Across Metapopulation Patches Under Various Pre-Exposure Prophylaxis Scenarios

Metapopulation Patch	Scenario A Uniform Scale	Scenario B Targeted Scale
Central Urban Core	Thirty-five percent reduction	Sixty-two percent reduction
Inner Suburban Ring	Forty-two percent reduction	Fifty-eight percent reduction
Outer Rural Periphery	Fifty-one percent reduction	Forty-seven percent reduction

The data presented in Table 2 highlights a critical counter-intuitive finding of metapopulation dynamics. Although the rural periphery receives significantly less direct intervention under the targeted strategy, its incidence reduction is only marginally lower than under the uniform strategy. This phenomenon occurs because the rural regions benefit immensely from the indirect protection afforded by the aggressive suppression of the virus in the urban core [24]. By neutralizing the epidemiological source, the targeted intervention effectively cuts off the primary supply of new infections flowing into the peripheral patches. This systemic protective effect underscores the immense value of prioritizing highly connected geographical hubs when public health resources are constrained.

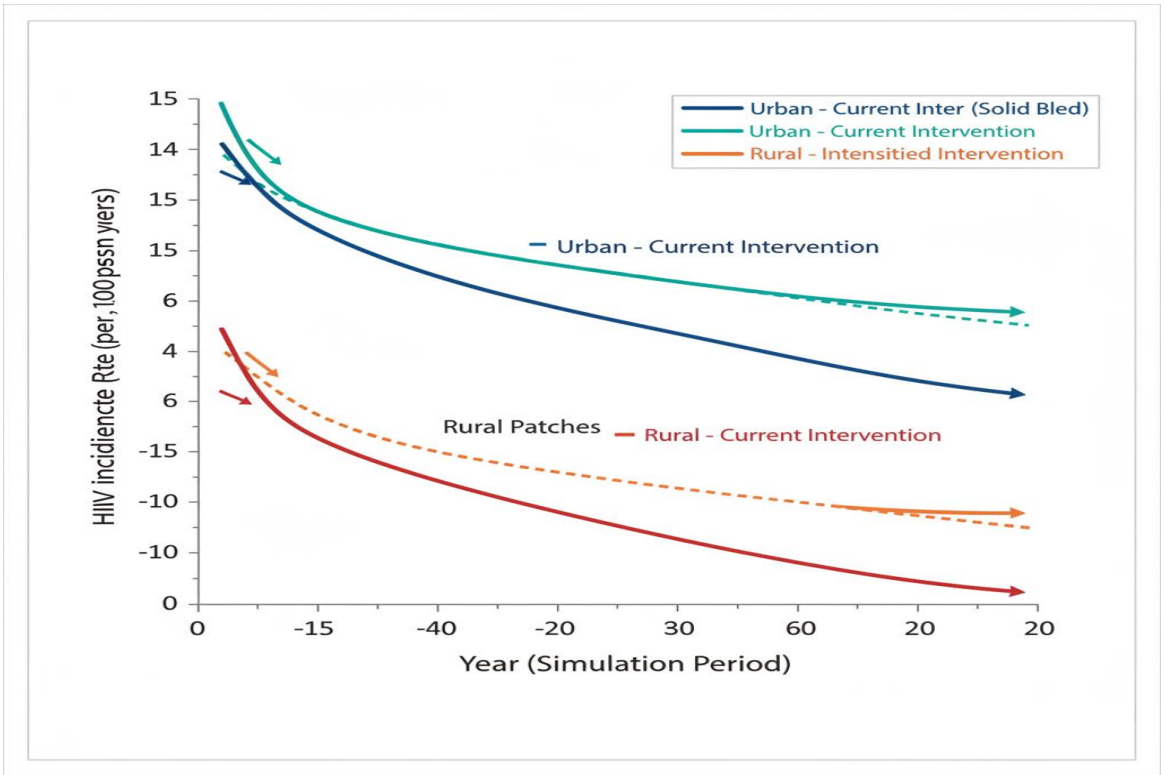


Figure 2 Epidemiological Projection Trajectories

4.3 The Modulating Role of Inter-Patch Mobility

The most complex and revealing insights from the modeling analysis emerge when examining the interaction between pre-exposure prophylaxis uptake and the intensity of human mobility. The sensitivity analysis demonstrated that high rates of inter-patch commuting can significantly dilute the localized benefits of high prophylactic coverage.

In sub-scenarios where an isolated urban patch achieves exceptionally high medication uptake, local elimination of the virus appears feasible. However, when the mobility matrix is adjusted to simulate heavy daily commuting from adjacent low-uptake suburban areas, the local incidence in the urban core rebounds [25]. The influx of susceptible and acutely infected individuals from the under-resourced suburbs continuously reintroduces the pathogen into the urban environment, circumventing the protective barrier established by the localized intervention.

This dynamic illustrates a fundamental vulnerability in fragmented public health systems. If adjacent municipalities or administrative districts implement uncoordinated prevention policies, the regions with robust healthcare infrastructure will remain perpetually at risk due to the mobility of the shared population. The model firmly indicates that spatial heterogeneity in pre-exposure prophylaxis uptake creates epidemiological reservoirs in under-served areas, which subsequently act as continuous ignition sources for neighboring regions. Therefore, while targeting hubs is highly efficient, it must be balanced with minimum baseline coverage thresholds in peripheral areas to prevent the establishment of these localized reservoirs.

5. Conclusion

5.1 Summary of Key Findings

This research has presented a robust metapopulation framework to analyze the complex spatial dynamics of the human immunodeficiency virus under varying levels of pre-exposure prophylaxis uptake. By systematically disaggregating the population into interconnected urban, suburban, and rural patches, the model successfully captured the critical mechanisms of spatial transmission that are routinely overlooked by traditional homogeneous mixing models. The rigorous simulation scenarios demonstrated that the spatial allocation of preventive resources significantly dictates long-term epidemiological trajectories. Specifically, the findings confirm that a targeted approach, which disproportionately concentrates prophylactic interventions within high-density, highly connected urban hubs, is substantially more efficient at reducing overall regional incidence than a strategy of uniform resource distribution [26].

Furthermore, the analysis highlighted the profound impact of human mobility networks on localized public health outcomes. The continuous movement of individuals between patches creates interdependent risk environments, where the epidemiological security of a resource-rich urban center is inextricably linked to the healthcare access of its surrounding rural periphery. The simulations clearly showed that high inter-patch mobility can severely dilute the protective benefits of localized interventions, allowing under-resourced patches to function as persistent epidemiological reservoirs that continuously reseed the virus across the broader spatial network.

5.2 Policy Implications and Future Directions

The insights derived from this metapopulation analysis hold significant implications for the design and implementation of public health policy. Traditional paradigms of resource allocation, which frequently distribute funding based strictly on per capita population metrics, are highly suboptimal for controlling infectious diseases characterized by complex spatial network dynamics [27]. Policymakers must adopt a more nuanced, network-informed approach, leveraging comprehensive human mobility data to identify structural transmission hubs. By viewing municipalities not as isolated administrative units, but as integrated components of a broader regional system, public health authorities can coordinate cross-jurisdictional strategies that maximize the interruption of transmission chains.

While this modeling framework provides a significant advancement over non-spatial approaches, it is not without limitations. The current model utilizes deterministic transitions and static mobility matrices, which may not fully capture the extreme stochasticity of localized outbreak events or sudden behavioral shifts in response to public health campaigns. Future research should prioritize the integration of dynamic, time-varying mobility networks, potentially incorporating real-time geographic data streams. Additionally, expanding the metapopulation structure to include concurrent, intersecting networks of different transmission modes would provide an even more comprehensive understanding of the epidemic. Ultimately, embracing spatial complexity in mathematical modeling is an essential prerequisite for optimizing the deployment of biomedical

interventions and advancing toward the definitive global elimination of the human immunodeficiency virus.

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