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Modeling the Impact and Cost-Effectiveness of Pre-Exposure Prophylaxis for HIV Dynamics in Men Who Have Sex with Men in Portugal: A Comparative Study

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To my parents, you offered me infinity support.

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Abstract

Backgrounds: Portugal faces a challenging upward trend of HIV infections among men who have sex with men (MSM). The nation reported a notable 9% annual increase in newly diagnosed HIV cases among MSM from 2005 to 2019, underscoring a stark contrast with the declining rates associated with drug use and heterosexual intercourse, which decreased by 18% and 2% respectively. As traditional prevention and treatment strategies struggle to curb this trend, the role of pre-exposure prophylaxis (PrEP) has emerged as a crucial aspect of a comprehensive response to the epidemic. However, the practicality and effectiveness of PrEP distribution among the MSM population in Portugal remain largely unexplored.

Objectives: (1) Develop an agent-based model to capture of HIV dynamics among MSM in Portugal. (2) Implement a PrEP module in the model, from eligibility identification to uptake. (3) Conduct counterfactual inference to evaluate the efficacy and cost-effectiveness of PrEP under different adherence distribution and PrEP eliglibility policiy strategies.

Methods: Using a network-based HIV transmission model, we simulated lifetime costs, quality-adjusted life years (QALYs), and infections averted for different strategies using a health sector perspective. Strategies included a status quo (no interventions), 3 different PrEP adherence level interventions (low, middle, high), and 4 different PrEP eligibility criteria strategies (WHO, US, PNHS and EACS). Cost-effectiveness was evaluated incrementally using a $44,000/QALY gained threshold.

Results: The research highlights the significant influence of PrEP adherence levels on HIV prevalence over a 20-year period. Moderate to high adherence levels are vital, reducing HIV prevalence by approximately 31%. High adherence scenarios display a cost of €18,468 per QALY gained, indicating promising cost-effectiveness. On the other hand, low adherence scenarios yield results equivalent to, or worse than, scenarios without PrEP implementation, contributing to a marginal increase in HIV prevalence. Comparing different policy strategies, the US, EACS, and WHO strategies demonstrated greater reductions in HIV prevalence than the PNHS strategy, averting 50%, 40%, and 35% of HIV cases over 20 years, respectively. The cost-effectiveness of these strategies was found to largely depend on the intervention's duration, with those lasting beyond ten years exhibiting a cost-effectiveness ratio of less than €44,000/QALY gained.

Conclusion: Our research underscores the importance of PrEP adherence in controlling HIV among MSM in Portugal, revealing the cost-effectiveness of high adherence scenarios. Different policy strategies such as US, EACS, and WHO demonstrate varying effectiveness and cost-effectiveness. Future research should include overlooked high-risk groups for comprehensive HIV control measures.

RESUME

Contexte : Le Portugal fait face à une tendance ascendante préoccupante des infections par le VIH chez les hommes ayant des relations sexuelles avec des hommes (HSH). Le pays a signalé une augmentation annuelle notable de 9% des nouveaux cas de VIH diagnostiqués chez les HSH de 2005 à 2019, soulignant un contraste frappant avec les taux en baisse associés à l'usage de drogues et aux rapports hétérosexuels, qui ont diminué respectivement de 18% et 2%. Alors que les stratégies traditionnelles de prévention et de traitement peinent à endiguer cette tendance, le rôle de la prophylaxie pré-exposition (PrEP) est apparu comme un aspect crucial d'une réponse globale à l'épidémie. Cependant, la praticabilité et l'efficacité de la distribution de la PrEP parmi la population HSH au Portugal restent largement inexplorées.

Objectif : (1) Développer un modèle basé sur des agents pour capturer la dynamique du VIH parmi les HSH au Portugal. (2) Implémenter un module PrEP dans le modèle, de l'identification de l'éligibilité à l'adoption. (3) Mener une inférence contrefactuelle pour évaluer l'efficacité et le rapport coût-efficacité de la PrEP dans différentes stratégies de distribution de l'adhésion et de politique d'éligibilité à la PrEP.

Méthodes : En utilisant un modèle de transmission du VIH basé sur le réseau, nous avons simulé les coûts à vie, les années de vie ajustées en fonction de la qualité (QALY), et les infections évitées pour différentes stratégies à partir d'une perspective du secteur de la santé. Les stratégies comprenaient un statu quo (sans interventions), 3 interventions différentes de niveau d'adhésion à la PrEP (faible, moyen, élevé), et 4 différentes stratégies de critères d'éligibilité à la PrEP (OMS, US, PNHS et EACS). L'efficacité coût a été évaluée de manière incrémentielle en utilisant un seuil de $44 000/QALY gagné.

Résultats : La recherche met en évidence l'influence significative des niveaux d'adhésion à la PrEP sur la prévalence du VIH sur une période de 20 ans. Des niveaux d'adhésion de modérés à élevés sont essentiels, réduisant la prévalence du VIH d'environ 31%. Les scénarios à adhésion élevée affichent un coût de 18 468 € par QALY gagné, indiquant une efficacité coût prometteuse. En revanche, les scénarios à faible adhésion donnent des résultats équivalents ou pires que les scénarios sans mise en œuvre de la PrEP, contribuant à une augmentation marginale de la prévalence du VIH. En comparant différentes stratégies politiques, les stratégies américaines, EACS, et OMS ont montré des réductions plus importantes de la prévalence du VIH que la stratégie PNHS, évitant respectivement 50%, 40%, et 35% des cas de VIH sur 20 ans. L'efficacité coût de ces stratégies s'est avérée dépendre largement de la durée de l'intervention, celles durant plus de dix ans présentant un ratio d'efficacité coût de moins de 44 000 €/QALY gagné.

Conclusion : Notre recherche souligne l'importance de l'adhésion à la PrEP dans le contrôle du VIH parmi les HSH au Portugal, révélant le rapport coût-efficacité des scénarios à haute adhésion. Différentes stratégies politiques comme celles des États-Unis, de l'EACS, et de l'OMS démontrent une efficacité et un rapport coût-efficacité variables. Les recherches futures devraient inclure des groupes à haut risque négligés pour des mesures de contrôle du VIH globales.

Contents

List of Abbreviations

- PrEP: pre-exposure prophylaxis
- HIV: human immunodeficiency virus
- AIDS: acquired immunodeficiency syndrome
- MSM: men who have sex with men
- QALYs: quality-adjusted life-years
- ART: antiretroviral therapy
- STI: sexually transmitted infection
- HCV: hepatitis C virus
- ABM:agent based model
- EACS: European AIDS Clinical Society
- WHO: World Health Organization
- CDC: Centers for Disease Control and Prevention
- ICER: incremental cost-effectiveness ratio
- DALYs: disability-adjusted life-years
- ARV: antiretroviral
- TDF/FTC: tenofovir disoproxil fumarate/emtricitabine
- MSM-TG: men who have sex with men and transgender people
- PNHS: Portugal health system information
- ERGM: Exponential random graph models
- TERGM: Temporal Exponential Random Graph Models

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Chapter 1

Introduction

1.1 Epidemiology of HIV

Since 1981, the HIV/AIDS pandemic continues to pose a substantial global public health challenge [1]. According to the World Health Organization's 2021 report, the disease has claimed approximately 40.1 million lives, and nearly 38.4 million people are currently living with HIV globally. Among these, around 75% are undergoing antiretroviral therapy[2]. The global rate of new HIV infections reached its zenith in 1997 with 3.3 million cases annually, but it has been on a decline since then, registering approximately 1.5 million new cases in 2020. Notably, Sub-Saharan Africa bears the heaviest burden of HIV, with an estimated 61% of all new infections in 2018 occurring in this region[3].

Tracing the roots of HIV, the virus seems to have its origins in nonhuman primates in Central Africa. It is postulated to have transmitted to humans multiple times during the late 19th or early 20th century[4]. The HIV-1 group M strain, which is primarily responsible for the global epidemic, likely emerged in Kinshasa, the capital of the Democratic Republic of the Congo, around 1920[1]. The disease was first identified as AIDS in 1981, and the HIV virus was confirmed as the causative agent in 1983[5].

According to a report by UNAIDS, the global dynamics of HIV-1 have been transforming since 2013[6]. There have been promising reductions in new infections in many sub-Saharan African countries with high burdens of the disease. Moreover, there's been a decrease in AIDS morbidity and mortality rates, and significant progress in the accessibility of treatment and advancements in prevention science. These developments have fueled renewed hope that managing the HIV pandemic may be a feasible objective [7]. However, evidence on HIV prevalence and incidence from low, middle, and high income countries indicates that the HIV epidemics among gay, bisexual, and other men who have sex with men (MSM) are diverging remarkably and showing signs of expansion [8]. In numerous high-income countries like the United States, France, Sweden, Australia, and the Netherlands[8], HIV epidemics among MSM have grown during the Highly Active Antiretroviral Therapy (HAART) era. This is even when there is broad access to HIV prevention, treatment, and care services [9]. In contrast, MSM are often marginalized, criminalized, and difficult to access in many low and middle-income countries, exacerbating the risk of HIV transmission and acquisition.

Individual level risks for HIV infection, including low condom use, role of sexual acts, rates

of substance use, numbers of sex partners and others are informative but insufficient to explain HIV epidemics among networks of men, and to explain the marked disparities in subepidemics of MSM, wherein individual level risks may be modest, but cumulative acquisition probabilities high[10]. Findings from network level investigations and from the molecular epidemiology of HIV may be more informative of the differing dynamics of infection in these populations. The biological factors are essential to understanding these dynamics. Baggaley et al.[11] report that receptive anal intercourse has an extremely high transmission efficiency for HIV. The estimated per-act probability of transmission is around 1.4% (with a 95% Confidence Interval (CI) of 0.2–2.5%), while the per partnership likelihood stands at an alarming 40.4% (95% CI 6.0–74.9). This makes it approximately 18 times more likely than vaginal intercourse for HIV transmission. These figures result from a comprehensive meta-analysis, factoring in data from both heterosexual and male homosexual couples. This risk is primarily due to the high efficiency of HIV transmission through the rectal mucosa [8]. Recent insights from molecular epidemiology have helped elucidate the importance of these transmission dynamics at network levels[53]. MSM were significantly more likely than other persons to be in transmission clusters of other recent infections in Switerland and Spain [13][14]. And the fact, young MSM may be the least likely to be aware of their HIV status and on HAART, may also explain the limited impact of treatment as prevention (TasP) on these epidemics[15].These factors appear to explain the rapid and efficient spread of HIV through networks of MSM.

1.2 Modeling method of HIV dynamics for MSM

Mathematical models function as significant instruments in gauging the potential efficacy of interventions aimed at preventing infections. They play a pivotal role in guiding policy formation, particularly in circumstances where actual testing is logistically and ethically challenging[16]. Compartmental models, one such class of mathematical models, are frequently employed to study infectious diseases and delineate strategies for disease control [17]. In these models, each individual in a population is exclusively represented in one compartment (for instance, uninfected men aged between 20–30 years having more than ten sexual partners per annum who do not use PrEP), with the aggregate of all compartments representing the total population. These models are dynamic, the infection rate among susceptible individuals fluctuates corresponding to the infectious proportion of the population at any given time [18]. The numerical solutions of these models can be either deterministic or stochastic, disregarding or incorporating chance events respectively. Compartmental models have been widely adopted to comprehend the potential repercussions of preventive interventions in HIV and other infectious diseases, thereby assisting in priority setting [19].

However, it is crucial to understand that models of HIV/AIDS interventions are abstractions of reality, thus inheriting certain limitations. One of the significant challenges these models face is the accurate representation of sexual behaviour. Research has shown that the simulated effect of an intervention can be extremely sensitive to the assumed heterogeneity in sexual behaviour and the presupposed patterns of sexual mixing.

Compartmental models presume a random mixing of individuals within a group, rendering

them inadequate for portraying sexual and needle-sharing contact networks that are known to adhere to a scale-free properties network structure[20]. Furthermore, it is infeasible for such models to portray the level of heterogeneity in testing qualities, tester profiles, and testing scenarios, nor do these models account for specific sex acts and subsequent seroadaptive behaviours based on test results.

Conversely, Agent-Based Models (ABMs) enable the representation of heterogeneous interactions among individuals (e.g., concerning sexual risk behaviour, age demography, and individual response to treatment)[21]. This adaptability is particularly useful when the question or process under study is affected by heterogeneity. As individual heterogeneity is intrinsically associated with the transmission, prevention, and treatment of HIV and other Sexually Transmitted Infections (STIs), ABMs are particularly well-suited to estimate the most beneficial intervention for specific individuals. Moreover, IBMs facilitate explicit modeling of the sexual relationships forming the sexual network over which STIs and HIV are transmitted.

Recently, a number of HIV research studies have investigated the impact of varying intervention methods in reducing HIV infection rates. For instance, Jenness and team developed an agent-based model (ABM) specifically for MSM in Atlanta, revealing that a tenfold enhancement in either screening or retention in HIV care alone would not meet local EHE objectives. However, a combined approach would result in a 90% decline in 12 years [24]. A separate study conducted by Nosyk and team applied economic modeling to assess a mix of evidence-based prevention and care interventions across six US cities, with the aim of discovering the most effective combination of interventions to curb HIV infections [25]. Such studies highlight the significance of using locally relevant simulation models to evaluate the effect of interventions and provide numerical guidance in the development and implementation of local EHE strategies. Also to facilitate their use and impelementation, ABM simulation packages for HIV. There are TITAN model[26], Epimodel [27], LHM model[28], BARS [29],PATH 2.0 project[30] with different key features and limitations (table 1.1)

Model	**Key Features**	**Limitations**
TITAN	High-fidelity ABM, focuses on drug use	Assumes homogeneous mixing
PATH 2.0	Incorporates individual-level properties, models national-level dynamics	Likely misses critical local dynamics
Epimodel 2.0	Focuses on local dynamics and MSM population	Uses limited parameter fitting
BARS	Uses detailed local interaction network data	Relies on parameter fitting
LHM	Uses longitudinal sexual network data, combines treatment and prevention interventions	-

Table 1.1: Summary of Agent-Based Models in HIV Research

1.3 HIV among MSM population in Portugal

In 2016, Portugal reported one of the highest HIV diagnosis rates in Europe, with an incidence of 10.0 diagnoses per 100,000 population [31]. However, the joint implementation of highly active Antiretroviral Therapy (ART) and harm-reduction programs has led to a substantial decrease in new diagnoses in the last half-decade [32][33]. Despite the overall decline, the national surveillance data reveal a 9% annual rise in newly diagnosed HIV cases among Men Who Have Sex with Men (MSM) from 2005 to 2012. Meanwhile, the cases attributed to hazardous injection behaviour and heterosexual intercourse fell by 18% and 2%, respectively, within the same timeframe[34]. In 2013, male-to-male sexual contact accounted for 42.9% of all reported HIV cases in men and 30.3% of all cases[34].

Phylogenetic analyses have recently indicated that the most active HIV-1 transmission cluster in Lisbon is significantly associated with the young MSM demographic[35]. This distinctive transmission pattern and intervention efficacy imply a behavioral heterogeneity between MSM and other high-risk populations. Consequently, understanding the behaviors of MSM, such as testing rates, partnership formation, and condom usage, becomes a crucial foundation for HIV control in Portugal. To this end, Portugal participated in the European MSM Internet Survey (EMIS) in 2010, a cross-sectional study which demonstrated that testing frequency, a critical method in HIV control which is not randomly distributed in the community but is closely linked with age, education, and other socio-economic factors[36].

To mitigate sample bias and enhance causality, GAT Portugal launched the Lisbon Cohort of MSM, a facility-based open prospective cohort in a community-based voluntary HIV counseling and testing service catered towards MSM[37]. This initiative forms a dynamic tool to monitor HIV incidence and its determinants in this population, and is essential if we aspire to succeed in our response to HIV among MSM[38].

1.4 Motivation: the PrEP implementation in Portugal among MSM

The increasing number of HIV cases among men who have sex with men (MSM) in Portugal indicates that both individuals and public health interventions are failing in terms of utilizing available prevention tools effectively. HIV preexposure prophylaxis (PrEP) is an antiretroviral therapy-based strategy for preventing HIV infection in high-risk adolescents and adults[39][40](European Medicines Agency 2019; US Food and Drug Administration 2018). It has proven efficacy in reducing HIV acquisition among MSM, whether taken daily or on-demand[41]. Tenofovir disoproxil fumarate and emtricitabine were approved by the US Food and Drug Administration for HIV PrEP in 2012, and they are currently recommended by various national and international guidelines. In Portugal, PrEP usage was authorized in 2017, and it has been provided free of charge in public hospitals since February 2018, without discrimination based on legal status in the country[42].

Regarding PrEP distribution and implementation in Portugal, according to Paula Meireles et. al. [43] the percentage of individuals on PrEP has increased gradually from 0.15% in 2014 to 5.36% in 2019 as it can be seen in the figure below.

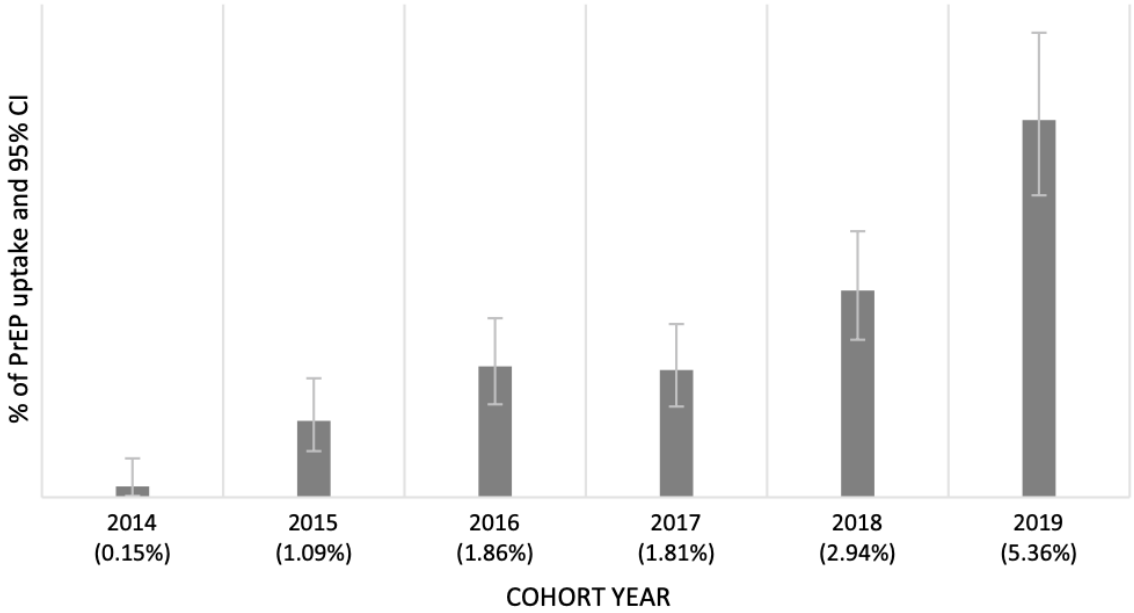

Figure 1.1: PrEP coverage evolution in Lisboa cohort

However, PrEP use in this cohort still remains really low when compared with the estimated global prevalence of self-reported PrEP use of 10.7% in 2017 by EMIS. Besides, in the Dublin Declaration of 2022 elaborated by the European Centre for Disease Prevention and Control (ECDC), showed that when compared with other European countries, the scale-up of PrEP still remains very low as it can be seen in figure 1.2.

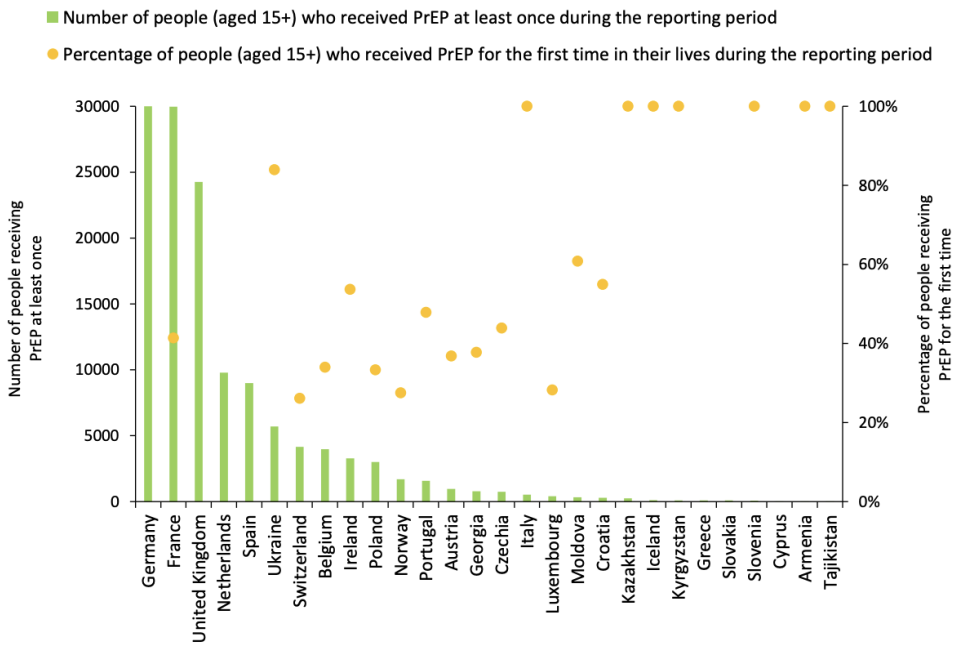

Figure 1.2: EU PrEP coverage from ECDC

The accurate definition of eligibility for PrEP plays a crucial role in assessing the effec-

tiveness of this prevention tool, as one significant measure will be the uptake among eligible individuals[44]. However, there are variations in the eligibility criteria across different guidelines. Generally, eligibility takes into account local HIV incidence rates and specific factors associated with HIV acquisition. Topics such as condom use, having HIV-positive partners, utilization of postexposure prophylaxis (PEP), diagnosis of sexually transmitted infections (STIs), or engagement in substance use during sexual activities are considered in these guidelines: the World Health Organization's Implementation Tool for Pre-exposure Prophylaxis of HIV Infection[51], the Centers for Disease Control and Prevention's US Public Health Service; Preexposure Prophylaxis for the Prevention of HIV Infection in the United States–2017 Update[50], the European AIDS Clinical Society's Guidelines Version 9[49], and the clinical guidelines from the PNHS (Ministry of Health Portugal 2018)[46]. By examining the seroprevalence among individuals categorized under different eligibility criteria in the Lisboa cohort study, it was observed that new HIV cases and incidence rates were highest among those defined as eligible for PrEP according to the PNHS guidelines[47].

Given that sexual behavior and related factors, such as condom use, number of partners, sexual practices, the existence of a steady partnership, the HIV status of sexual partners, and their suppressive status, can fluctuate over time, the definition of PrEP eligibility based on risk behaviors will also change correspondingly [48]. In addition, a previous theoretical study has already proved that current strategies of PrEP distribution may not be optimal in communities of men-having-sex-with-men in many countries. Targeting high risk MSM with PrEP may have a suboptimac on HIV control, and reinforce the stigma [45].

Hence, it is urgent to build a data-driven dynamical model which can represent complex HIV network system of the effectiveness of PrEP gudelines in populations of MSM, to find those strategies which are most effective in preventing infections in the community. Moreover, the cost of PrEP medications remains high in high-income regions, and the cost-effectiveness of integrating PrEP into universal healthcare systems within those guideline settings remains uncertain. In conclusion, while PrEP presents a promising potential in Portugal, its optimal implementation necessitates a thorough and rigorous evaluation of existing guidelines and their applicability to the local context.

1.5 Aim and Object

- To set up a computational agent-based model of HIV spread among MSM. This model will include partnter network formation&dissolution, use of prevention as a behavioral dynamical factor that evolves with perceived risk, availability of prevention, prevalence of HIV.
- To adapt this model communities of MSM in Lisbon, using HIV prevalence data, treatment data, behavioral data, from different sources and from different countries.
- Develope the PrEP implementation module in the model from PrEP eligibilty identification to PrEP uptake.

- To conduct counterfactual inference to evaluate the effectiveness of PrEP under different settings such as varying adherence proportions under Portugal's policy.
- Build the cost-effectivness model to estimate the effectiveness and cost-effectiveness of PrEP intervention under different policies.

Chapter 2

Methodology

2.1 Study design

This research employs a network-based, dynamic, stochastic model of HIV transmission dynamics to evaluate the cost-effectiveness of PrEP under different guidelines and adherence proportions in the figure 2.1. The study primarily targets the MSM population in Lisbon, who are enrolled in a cohort study[37].

The model is constructed and simulated using the open-source EpiModel (version 1.2.5)[27] software package on the R statistical computing platform. It has a weekyly time scale and a sythetic population of 1000men.

The model features a two-layer network encoding main partnerships and casual sexual contacts, both implemented using exponential random graph models (ERGMs). It simultaneously models HIV transmission and progression. The model accommodates individuals with heterogeneous characteristics, including race, circumcision status, sexual role, and propensity for unprotected anal intercourse (UAI) in sexual encounters.

Parameters for sexual behavior are drawn from the Lisbon cohort study[22] and the EMIS cross-sectional study[36], while the main parameters for partner network formation and dissolution are derived from the US Atlanta data[67]. Individuals of the male gender enter the population when they reach the age of 18 and are subsequently tracked until they reach the age of 39 or pass away, whichever occurs earlier.

The models initiate with a 12% prevalence, which mirrors the HIV equilibrium prevalence state in Lisbon's MSM at the start of the cohort[22], run through a burn-in period to eliminate transient effects of arbitrary infection seeding, and are then compared to observed HIV incidence and prevalence in these populations. Each scenario is modeled 20 times over a period of 20 years.

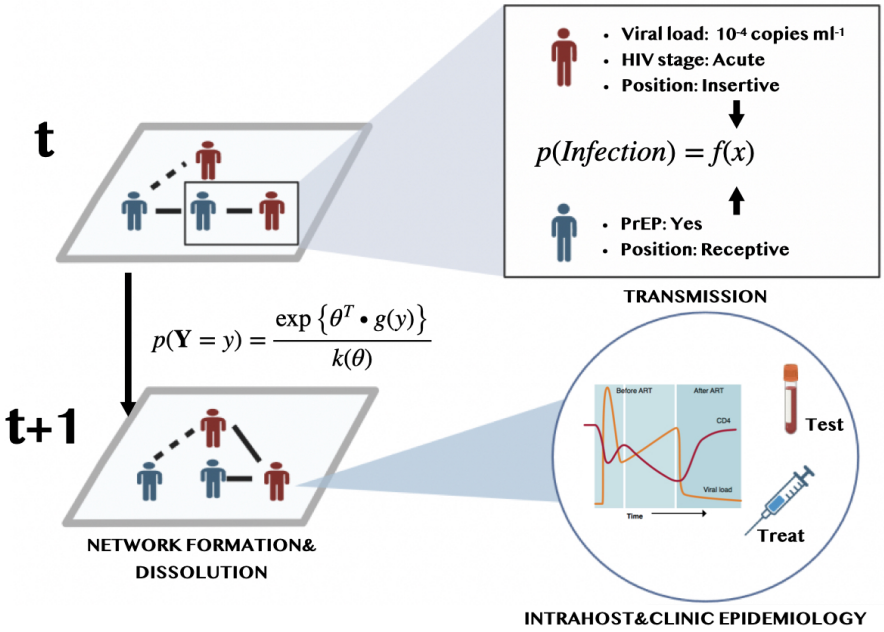

Figure 2.1: Model Description

2.2 Agent-Based Model

2.2.1 HIV Transmission and Progression

In this study, HIV transmission dynamics was modeled using exponential random graph models, which provide a flexible statistical approach for simulating dynamic partnerships based on behavioral data[68]. The network model consisted of three components: main partnerships, casual partnerships, and one-time partnerships.

The determinants of partnership formation varied depending on the type of partnership. These determinants included the number of Concurrent partners (degree), age homophily (preference for partners of similar age), and sexual role segregation (avoidance of pairing exclusively receptive or exclusively insertive individuals)[67].

For both main and casual partnerships, a constant rate of relationship dissolution was incorporated to reflect the average duration of each type of partnership[67]. The progression of clinical HIV followed the natural course of the disease and included antiretroviral therapy (ART) treatment profiles[65].

We can express our statistical models for relational dynamics through five equations. These equations represent the conditional log odds (logits) for the formation and persistence of relationships at time t. This includes both main and casual relationships, as well as the existence of one-time contacts.

$$
\begin{aligned}
&\text{logit}\left(P\left(Y_{ij,t}=1 \mid Y_{ij,t-1}=0, Y^C_{ij,t}\right)\right) = \theta_m^{+\prime}\partial\left(g_m^+(y)\right) && \text{Main partnership formation}\\
&\text{logit}\left(P\left(Y_{ij,t}=1 \mid Y_{ij,t-1}=0, Y^C_{ij,t}\right)\right) = \theta_c^{+\prime}\partial\left(g_c^+(y)\right) && \text{Casual partnership formation}\\
&\text{logit}\left(P\left(Y_{ij,t}=1 \mid Y_{ij,t-1}=1, Y^C_{ij,t}\right)\right) = \theta_m^{-\prime}\partial\left(g_m^-(y)\right) && \text{Main partnership persistence}\\
&\text{logit}\left(P\left(Y_{ij,t}=1 \mid Y_{ij,t-1}=1, Y^C_{ij,t}\right)\right) = \theta_c^{-\prime}\partial\left(g_c^-(y)\right) && \text{Casual partnership persistence}\\
&\text{logit}\left(P\left(Y_{ij,t}=1 \mid Y^C_{ij,t}\right)\right) = \theta_o'\partial\left(g_o(y)\right) && \text{One-time contact existence}
\end{aligned}
\tag{2.1}
$$

Where:

- $Y_{ij,t}$ = the partnership status of male i and j at time t (1 = in contact, 0 = not)
- $Y^c_{ij,t}$ = the network complement of i,j at time t, i.e. all partnerships in the network other than i,j
- $g(y)$ = vector of network statistics in each model
- θ = vector of parameters in the formation model

In the absence of ART, individuals progressed through disease stages with evolving HIV viral loads, which affected the rate of HIV transmission in serodiscordant partnerships. The per-act transmission probability was influenced by factors such as viral load[61], condom use[62], and the sexual position (receptive or insertive)[63]. These factors are mathematically encapsulated in the following model:

$$
ln(P) = \beta_0 + \beta_1 ln2.45^{Viralload-4.5} + \beta_2 lnx_{position} + \beta_3 lnx_{Acutestage} + \beta_4 lnx_{Condom} + \beta_5 lnx_{PrEP} \tag{2.2}
$$

After infection, individuals were assigned to clinical care trajectories that determined the rates of HIV diagnosis, ART initiation, and HIV viral suppression, aligning with empirical estimates of the prevalence of these states[66]. ART was associated with a reduction in viral load (and transmission risk)[64].

2.2.2 PrEP policy options compared and main assumptions relating to PrEP

This study simulated PrEP eligibility based on the behavioral conditions outlined in the Portugal recommendation, which included engaging in anal intercourse without a condom with steady or occasional partners and having at least one sexual partner with an unknown HIV status[22]. Based on previous studies conducted in high-income countries, it was assumed that there is a 20% probability of an individual initiating PrEP in any given week, since the eligibility (Table 2.3).

Distinct PrEP eligibilities were modeled based on the criteria established by the World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), and the European AIDS Clinical Society (EACS). The WHO criteria include engaging in any anal intercourse without a condom and having multiple sexual partners. The CDC recommends PrEP

consideration for all MSM, while the EACS specifically mentions engaging in anal intercourse without a condom in non-main partnerships (table 2.2).

Parameter	Value	Reference
QALY of uninfected(PrEP&No PrEP)	1	[56]
QALY of people living with HIV	0.7	[56]
Treatment cost of HIV infection, per week(Non-AIDS stage)	17000€	[57]
Treatment cost of HIV infection, per week(AIDS stage)	24000€	[57]
PrEP cost per week	638€	[60]

Table 2.1: Key parameter about cost effectiveness analysis per year

Region	Description	Reference
Portugal	UAI AND partner not tested in past 6 months.	[31]
WHO	UAI AND many sex partners.	[32]
EU	UAI in non-main partnerships.	[39]
US	All MSM	[40]

Table 2.2: PrEP policy in different regions

Once PrEP was initiated, individuals underwent diagnostic assessments at quarterly intervals, following the Portugal cohort protocol [32], which subsequently influenced HIV dynamics. Previous studies, such as the EMIS study, have indicated that a significant proportion of MSM (28%) have never been tested for HIV (table 2.3)[70].

While all guidelines mention the eligibility of individuals with positive STI diagnoses[32], and the Portugal guideline includes sex workers and individuals who have used injectable drugs, these specific attributes were not included in the simulation eligibility due to data limitations.

The effectiveness of PrEP is highly dependent on adherence. Based on a US cohort study, a correlation was assumed between adherence level and the reduction in the per-act probability of infection: 15% for low adherence (taking less or equal 2 doses per week) and 85% for high adherence (taking more than 2 doses per week) groups[55]. Initially, the adherence distribution in different adherence scenario was set as, low adherence scenario, 90% low adherence, 10% high adherence, middle adherence scenario, 50% low adherence and 50% high adherence. For high adherence scenario, 10% is low adherence, 90% is high adherence(table 2.4). Also in comparative study of different policy strategies, the ratio of adherence is 50% low adherence, 50% high adherence which is same as middle adherence scenario.

Parameter	Value	Reference
Efficacy of PrEP with high adherence	0.85	[55]
Efficacy of PrEP with low adherence	0.15	[55]
Test time interval when taking PrEP	3 months	[22]
Probability of starting PrEP when eligible	0.2	[40]

Table 2.3: Parameters associated with PrEP

Scenario	Proportion of people with low adherence	Proportion of people with high adherence
Low level adherence	90%	10%
Middle level adherence	50%	50%
High level adherence	10%	90%

Table 2.4: Different adherence level scenario

2.2.3 Model Calibration

In this study, we replicated the current HIV epidemic among MSM using recent model parameters, rather than modeling the time series of HIV transmission since the 1980s. Starting with a population of 1,000 MSM, HIV infection was initially seeded in 10% of the population. Burn-in simulations were then used to allow the natural dynamics of HIV transmission and other population features to evolve over time, aiming to establish a network of MSM independent of the initial conditions.

The approximate Bayesian computation with sequential Monte Carlo sampling (ABC-SMC) method was used to calibrate behavioral parameters by R package EasyABC (Version 1.6.1) . The calibrated parameter was an overall multiplier for the rate of acts within sexual partnerships over time, chosen based on the assumption of potential underreporting due to sensitivity biases.From there, each PrEP scenarios was simulated 25 times over 10 years.

For summary statistics against which to measure the performance of the model simulations, we choose two for this research project:

- The slope of the prevalence curve in the time series of the burn-in model for the last 10 years(520 weeks) is equal to 0,which implies the equiribulium state.
- The prevalence value at the end of the time series, 13% same as our cohort observational data[37].

2.3 Outcomes and economic analysis

2.3.1 Cost and Quality of Life

We take a healthcare perspective. For estimating the cost of PrEP, we focus on the annual cost of PrEP medication, specifically Gilead's Truvada, which is used by Portugal medical system[43]. The cost per year is €638 based on data from Ireland[60]. This estimation does not include costs associated with regular testing or monitoring, allowing us to concentrate on the direct costs of the PrEP intervention.

In evaluating the cost of HIV treatment, we considered both Antiretroviral Therapy (ART) costs and non-ART routine medical care costs. A retrospective study of the Portuguese National Health System indicated minimal variation in daily ART costs across different stages of HIV infection. Consequently, we assumed a uniform annual ART cost of 9000 euros for every patient under treatment[57].

Non-ART routine medical care costs, encompassing in-patient care and other medications, were differentiated based on the patient's disease stage. For patients not in the AIDS stage, we estimated an annual cost of 8000 euros. However, for patients in the AIDS stage, owing to the increased complexity and intensity of care required, the annual cost was estimated to be 15000 euros. These cost estimates provide a comprehensive view of the financial burden of HIV treatment, informing the cost-effectiveness analysis of PrEP implementation (table 2.3)[57].

Quality-Adjusted Life Years (QALYs) provide a measure of the quality and quantity of life lived, and are commonly used in health economics and cost-effectiveness analyses. In our study, the QALYs are estimated based on health state utilities derived from published studies on HIV-infected patients. We assign a utility value of 1 to individuals without HIV, representing a state of perfect health. For individuals with HIV, regardless of the stage of infection, including AIDS, we assign a utility value of 0.7. This reflects the decreased quality of life associated with living with HIV or AIDS[56].

2.3.2 Cost-effectiveness analysis

We computed the Incremental Cost-Effectiveness Ratios (ICERs) over a 10-year period. ICERs are a crucial metric in health economics, representing the additional cost of a specific health intervention per additional unit of health outcome achieved. In this case, the health intervention is the implementation of PrEP guidelines, and the health outcome is the reduction in HIV infections and increasement of total quality-adjusted life-years(QALY) among the MSM population in Portugal. We always assume to be cost-effective an ICER that is smaller than 2 times of average GDP each year of the country[58]. In the context of Portugal, health interventions are deemed cost-effective if their cost-effectiveness ratios fall below €44 000 per Quality-Adjusted Life Year (QALY) gained[59].

Chapter 3

Results

3.1 PrEP effectiveness of portugal guideline under different adhearence of PrEP

This section delineates the estimated dynamics of HIV prevalence spanning the period 2010 to 2040, encapsulating three decades. The decade 2010-2020 marks the burn-in process where we achieve a prevalence equilibrium state of 13%, approximating the actual scenario. Subsequently, we implement varying PrEP adherence levels as per the Portuguese National Health Service (PNHS) guideline from 2020 onwards. Under the middle and high PrEP adherence scenarios, we anticipate a decline in the overall HIV prevalence amongst Men who have Sex with Men (MSM) in Lisbon. Interestingly, the low adherence scenario seems to have a negligible impact on HIV prevalence (figure 3.1).

In a comparison with the scenario that assumes low adoption of PrEP and does not utilize the current strategy, no statistically significant impact on averted infections is evident. The fluctuations range from -20 to 16 cases (-10%, 6%), with a median of -1 case per 1000 people. This suggests that for every 1000 people, there is a median of -1 new HIV infection averted over the span of two decades. The strategy of moderate adherence exhibits a modest impact, averting between 7-34 (3%, 18%) cases, with a median of 15 cases of new HIV infections. Contrastingly, the high adherence strategy emerges as the most efficacious in comparison to the other scenarios, with a projected reduction spanning 42-72 (22%, 39%) and a median of 55 new HIV infections (table 3.1). The distribution of averted HIV infections post 20 years under distinct levels of PrEP adherence does not significantly alter the HIV dynamics under the influence of low and moderate adherence strategies (figure 3.3). This implies that these strategies could potentially contribute no effect to HIV control and prevention efforts when compared to a scenario devoid of any PrEP intervention.

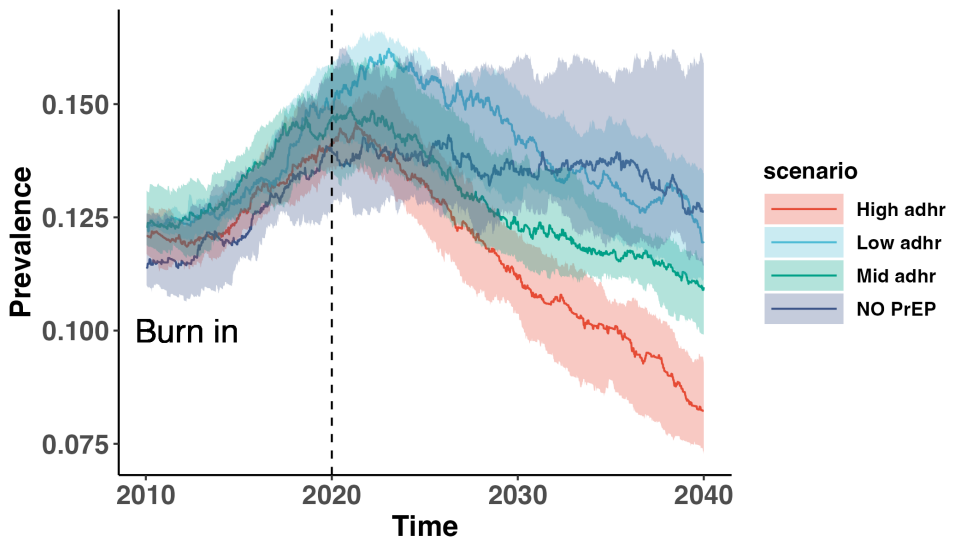

Figure 3.1: Effect of pre-exposure prophylaxis (PrEP) on the HIV prevalence among men who have sex with men (MSM), with about 1000 MSM on PrEP.

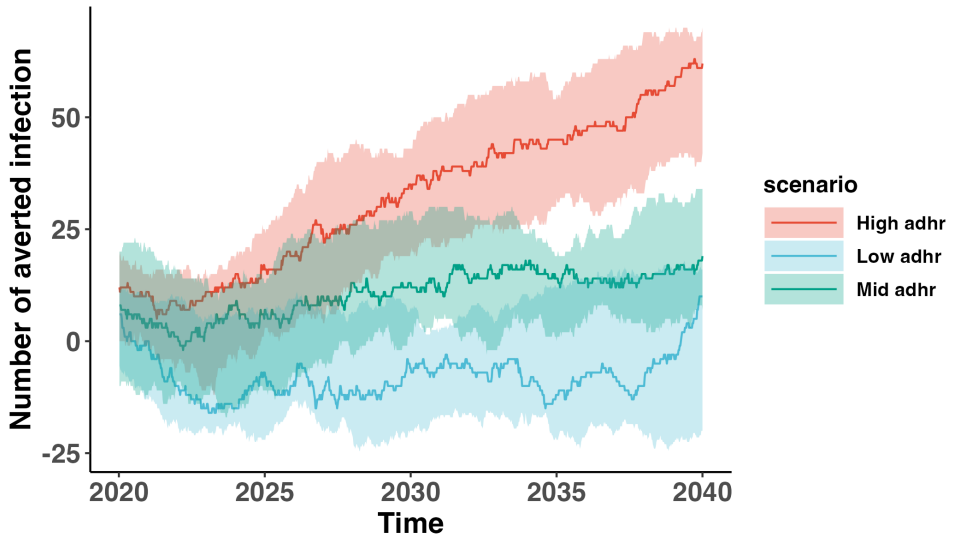

Figure 3.2: Number of HIV cases averted per 1000 poeple under different PrEP adherence

	High Adherence			Middle Adherence			Low Adherence		
Year	25%	Med.	75%	25%	Med.	75%	25%	Med.	75%
2	-5	8	16	-9	1	16	-18.0	-10	10.0
4	-4	15	19	-15	8	14	-19.0	-15	6.5
6	3	19	33	-7	8	23	-13.5	-9	9.5
8	11	26	44	-3	13	26	-21.0	-11	6.5
10	20	35	43	2	13	29	-20.0	-6	7.5
12	24	38	55	2	13	28	-16.0	-5	7.0
14	26	43	58	3	17	24	-18.5	-10	10.5
16	31	47	60	5	14	23	-21.0	-8	13.5
18	33	55	69	4	15	30	-20.5	-10	15.0
20	42	62	70	7	19	34	-20.0	10	16.0

Table 3.1: Number of infections averted by different PrEP adherence over 20 years

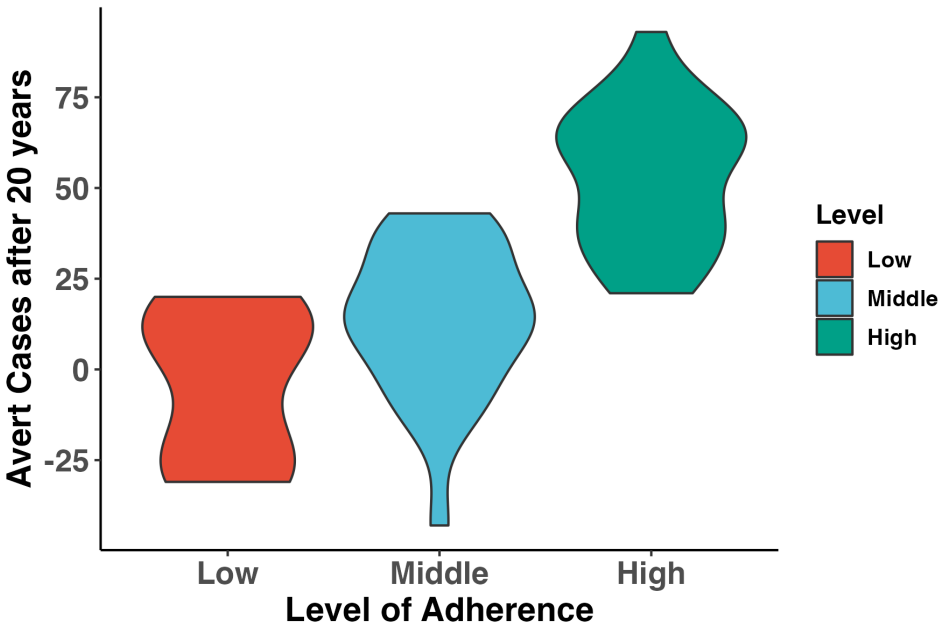

Figure 3.3: Density distribution of averted HIV cases per 1000 people after 20 years intervention under different PrEP adherence level.

3.2 Cost-effectiveness analysis of Portugal guideline under different adherence of PrEP

In the economic dimension, we estimate the total cost associated with HIV, which includes MSM HIV/AIDS healthcare cost, Highly Active Antiretroviral Therapy (HAART) cost, and PrEP cost. For the baseline scenario without PrEP, the total cost ub our simulated epidemic totals to 282,639,050 Euros over two decades from 2020 to 2040. Under the high adherence PrEP scenario, the total cost amounts to 291,341,780 Euros over the same period. In terms of total cumulative Quality Adjusted Life Years (QALY) in this population, the no PrEP baseline scenario results in 33,173 adjusted years, whereas the high adherence PrEP scenario yields 33,644 adjusted years. Consequently, our projection indicates a cost of €18,468 per QALY gained with the 20-year high-adherence PrEP intervention (table 3.2). Given a willingness-to-pay threshold of €100,000/QALY gained [72], this intervention holds considerable potential for implementation.

Inspecting the temporal progression of QALY, we observe that the total QALY of the two scenarios (No PrEP High adherence) is nearly identical until 16 years of intervention. This infers that the effectiveness of the PrEP intervention is not markedly significant. Similarly, comparing the Incremental Cost-Effectiveness Ratio (ICER) over time, the result at 16 years (€16,182 per QALY) is lower than the 20-year result (€18,468 per QALY). Usually, it is presumed that longer intervention durations result in greater gains. However, this counter-intuitive outcome warrants further investigation through a robustness test of the scenario, taking into account real-world

uncertainties. The prerequisite for cost-effectiveness is effectiveness better than the baseline. The probability of the PrEP intervention scenario's QALY surpassing that of the no-PrEP baseline scenario remains around 50% for the first 10 years, implying neutral effectiveness of PrEP. Simultaneously, the cost of PrEP continually increases, resulting in a consistently negative cost-effectiveness for the high-adherence PrEP scenario during this period. Moreover, after 20 years, the probability of accepting the PrEP strategy is only 60% (figure 3.4).

	No PrEP		High adherence		
Year	Total Cost	Total QALY	Total Cost	Total QALY	ICER
4	109254410	12805.80	109216790	12741.11	581.5912
8	150240010	17634.32	151296830	17536.96	-10854.1655
12	193016970	22614.80	195616300	22604.05	-241798.1395
16	237133290	27707.92	241757390	27993.67	16182.3272
20	282639050	33173.11	291341780	33644.33	18468.6882

Table 3.2: Case cost-effectivenes analysis result

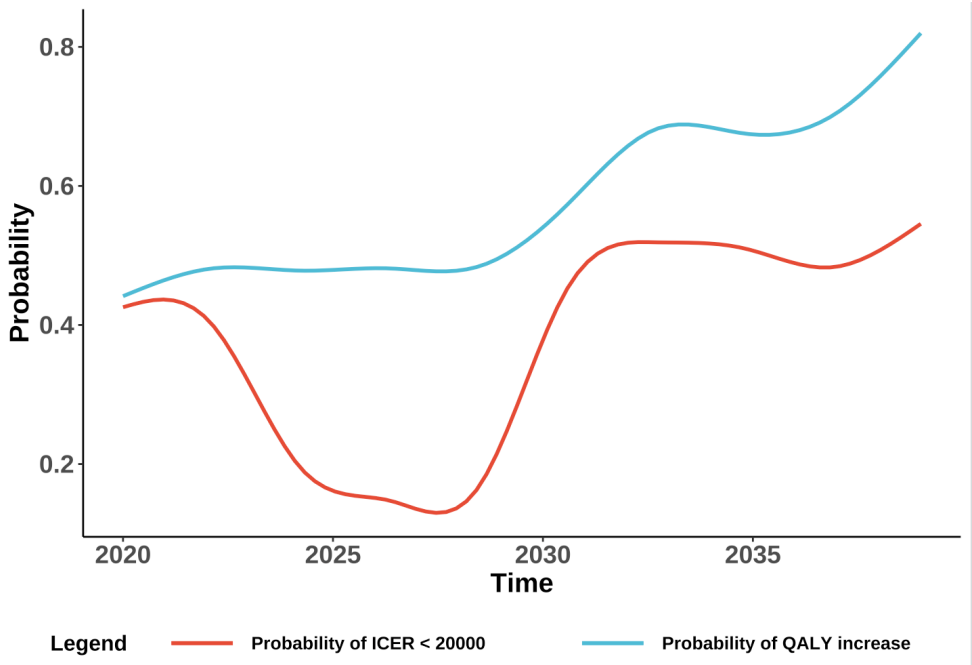

Figure 3.4: Probability of cost&effectiveness acceptability curve

3.3 Comparative Analysis of PrEP Effectiveness/PrEP policy options compared

A comprehensive comparison of the influence of pre-exposure prophylaxis (PrEP) on the prevalence of HIV amongst men who have sex with men (MSM) within diverse policy frameworks yields an unvarying positive effect across all considered scenarios. These policy strategies, encapsulating the no PrEP, EACS, PNHS, WHO, and US frameworks, each contribute to a notable

contraction in HIV prevalence, underscoring the efficacy of PrEP as an instrumental modality for HIV control amongst MSM across a range of policy environments (figure 3.5). However, the analysis simultaneously unveils discrepancies in the impact of these respective strategies. The strategies deployed in the US, EACS, and WHO contexts have superior effectiveness, marking a more substantial decrease in HIV prevalence relative to the no PrEP scenario.

Following a 20-year PrEP intervention period, the strategy proposed by WHO succeeds in averting 63 (55.5-80) every 1000 people instances of HIV infections, signifying a 34% reduction, the EACS strategy forestalls 100 (84-105) cases every 1000 people, tantamount to a 54% reduction, and the US scenario effectively obviates 92 (86.5-102) cases every 1000 people, accounting for a 49% decrease. Contrastingly, the effectuation of the PNHS PrEP policy yields a more multifaceted impact, averting a mere 18 (10-33) cases of HIV infections, equating to a 9% reduction (table 3.3).

In circumstances where PrEP implementation extends for a duration of 10 years, both the US and EACS strategies forestall 81 (72-87, 69-90) cases every 1000 people of HIV infections (44%), while the WHO strategy successfully mitigates 55 (39-65) instances (30%) every 1000 people(table 3.3). As such, the influence of these three scenarios denotes an ascending trajectory from 10 to 20 years(figure 3.6). Paradoxically, the PNHS strategy precludes 23 (8-33) cases every 1000 people of HIV infections (12%), a number that surpasses the results obtained from the 20-year implementation period. Moreover, the kinetic figure delineating cases of HIV infection averted infers that the impact of the PNHS strategy attains a state of equilibrium earlier(figure 3.6).

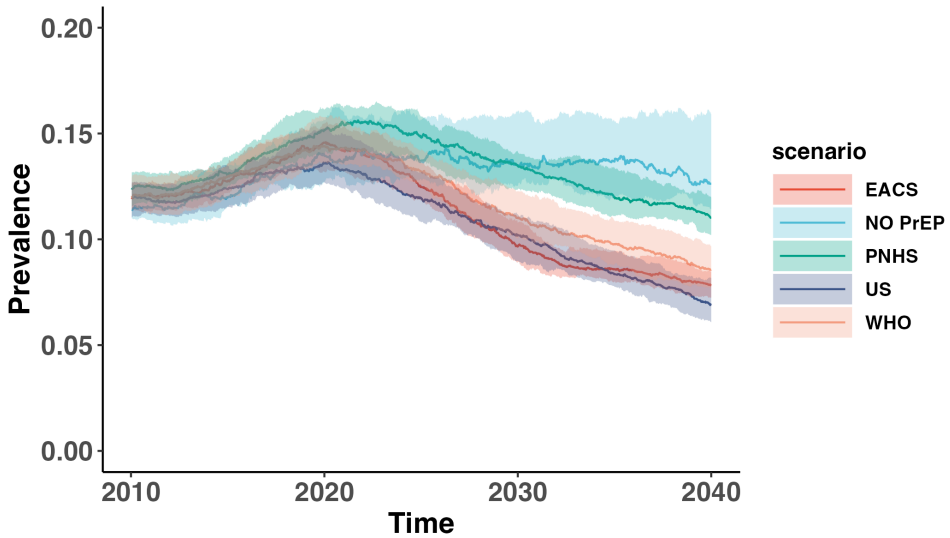

Figure 3.5: Prevalence of HIV among MSM under different country strategy by time

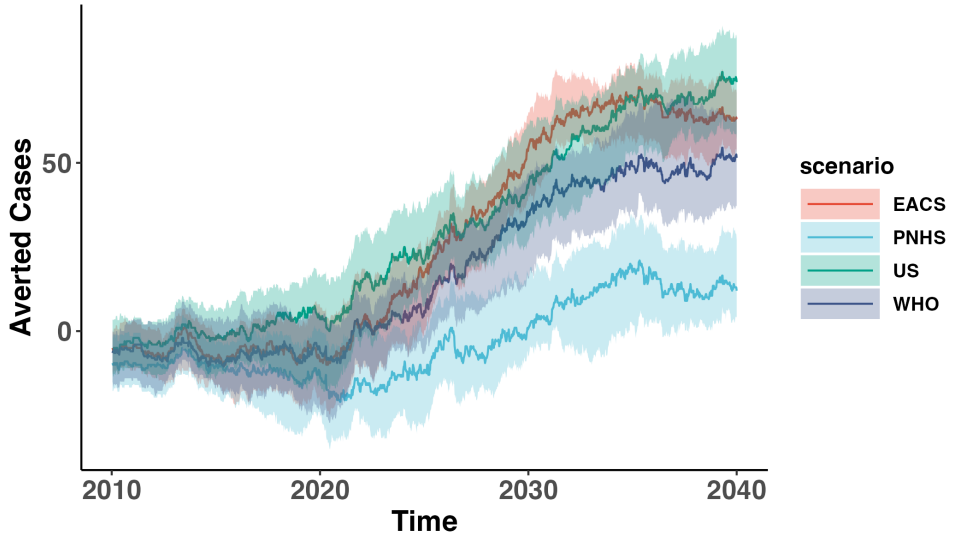

Figure 3.6: Number of HIV infection averted every 1000 people among MSM under different country strategy by time

	WHO			EACS			PNHS			US		
Year	25%	Med.	75%	25%	Med.	75%	25%	Med.	75%	25%	Med.	75%
2	27.0	33	37.0	41.5	47	57.0	-4.5	17	26.5	46.5	51	55.0
4	28.0	35	41.5	44.0	55	62.5	2.5	18	25.0	49.5	53	60.5
6	39.5	48	61.0	53.5	71	81.5	9.5	23	33.0	61.5	68	74.5
8	45.0	60	68.5	69.0	81	88.0	11.5	30	41.0	71.0	81	91.5
10	39.0	55	65.0	69.0	82	89.5	8.0	23	33.5	72.0	81	87.0
12	53.0	64	73.5	82.0	92	101.5	17.0	22	41.0	80.0	89	96.5
14	54.0	68	79.5	87.0	96	103.5	14.5	27	46.0	83.5	94	100.0
16	56.5	69	85.5	91.0	101	104.0	14.0	26	45.0	86.5	95	104.0
18	54.5	64	81.0	82.5	98	100.5	10.5	18	34.0	85.0	94	101.0
20	55.5	63	80.0	82.0	100	104.5	10.0	18	33.0	86.5	92	102.0

Table 3.3: Number of infections averted by different policy over 20 years

3.4 Cost effectiveness Analysis of PrEP under different guidelines

A scenario without any PrEP intervention was included as a reference point. The cost-effectiveness of these guidelines was evaluated over a span of ten and twenty years, using measures such as the accumulated costs of antiretroviral therapy (ART) and PrEP, Quality-Adjusted Life Years (QALYs), and the Incremental Cost-Effectiveness Ratio (ICER).

As shown in Table (table 3.4), the US guideline emerges as the most cost-effective strategy within a 10-year span, evidenced by the lowest positive ICER value of 29,744.745 in our simulated epidemics. This suggests that the additional cost for each QALY gained is less under the US policy compared to other guidelines with positive ICER values within the same timeframe. Also, the PNHS guideline exhibits a negative imapact on HIV control caused by stochastiy.

Table 3.5 elucidates the cost-effectiveness of these guidelines over a 20-year timeframe.

Here, the WHO guideline emerges as the most cost-effective, demonstrated by the lowest ICER value of 1,806.917. This indicates that over a more extended period, the WHO guideline proves to be more cost-effective compared to the other policies. Meanwhile, the ICER value for the PNHS guideline, which was negative at the 10-year mark, increases to 20,534.458 over 20 years. This signifies a decrease in cost-effectiveness over a more extended period.

Scenario	Accum. Art	Accum. Prep	Accum. Cost	Accum. QALY	ICER
NO PrEP	25449440	0	25449440	22539.97	Ref
WHO	25092240	2211160	27303400	22546.54	281888.655
EACS	24392800	3824550	28217350	22558.88	146375.796
PNHS	27123280	2361200	29484480	22497.58	-95209.220
US	23576960	5258290	28835250	22653.79	29744.745

Table 3.4: Case cost-effectiveness analysis under different policys after 10 years PrEP intervention

Scenario	Accum. Art	Accum. Prep	Accum. Cost	Accum. QALY	ICER
NO PrEP	40527360	0	40527360	35787.28	Ref
WHO	36493200	4695655	41188855	36153.38	1806.917
EACS	34300400	8202470	42502870	36100.95	6298.106
PNHS	41252400	5477235	46729635	36089.33	20534.458
US	33578560	11478190	45056750	36606.68	5527.730

Table 3.5: Case cost-effectiveness analysis under different policys after 20 years PrEP intervention

For the total cost of ART, other HIV related health care cost and PrEP during a 10-year implementation, the WHO strategy costs the least, about 27,303,400 EUR. Then the strategies of EACS and US total accumulated costs are around 28,000,000 EUR. The cost of the PNHS strategy is the highest, estimated as 29,484,480 EUR. When examining the proportion of cost source, it's obvious that the WHO strategy maintains a good balance between ART and PrEP cost. The EACS and US strategies invest heavily in PrEP, resulting in a lower ART or HIV-related health care cost due to better control. For the PNHS policy, although the PrEP cost is higher than the WHO strategies, because of subpar control performance, the cost of ART and HIV health care is still significant (table 3.4). For the 20-year PrEP implementation, the cost pattern, cost proportion, cost ranks are almost similar to the 10-year implementation cost (table 3.5).

Also, the evolution of HIV-related cost distribution shows that after 1 year of PrEP program start, the cost of PrEP per number of PrEP users each year is stable in the EACS, US, and WHO scenarios. However, under the PNHS strategy, the PrEP adoption process is much slower compared to other scenarios. Moreover, the cost of ART and other non-PrEP HIV-related medical care decreases each year gradually. And for this trend, the PNHS decrease is much slower compared to the other 3 strategies (figure 3.7).

At the current price of tenofovir and emtricitabine, PrEP is predicted to cost less than €44000 per QALY gained with a PrEP effectiveness of greater than 70%. After 20 years of PrEP implementation, all four strategies show less than €44000 per QALY gained, which means cost-effective. However, before 14 years, the PNHS ICER is higher than €44000 per QALY gained or null effectiveness. The WHO and US strategies perform better, which are cost-effective since 8 and 10 years of intervention, respectively. The EACS reaches the level of cost-effectiveness around in 2026(figure 3.8).

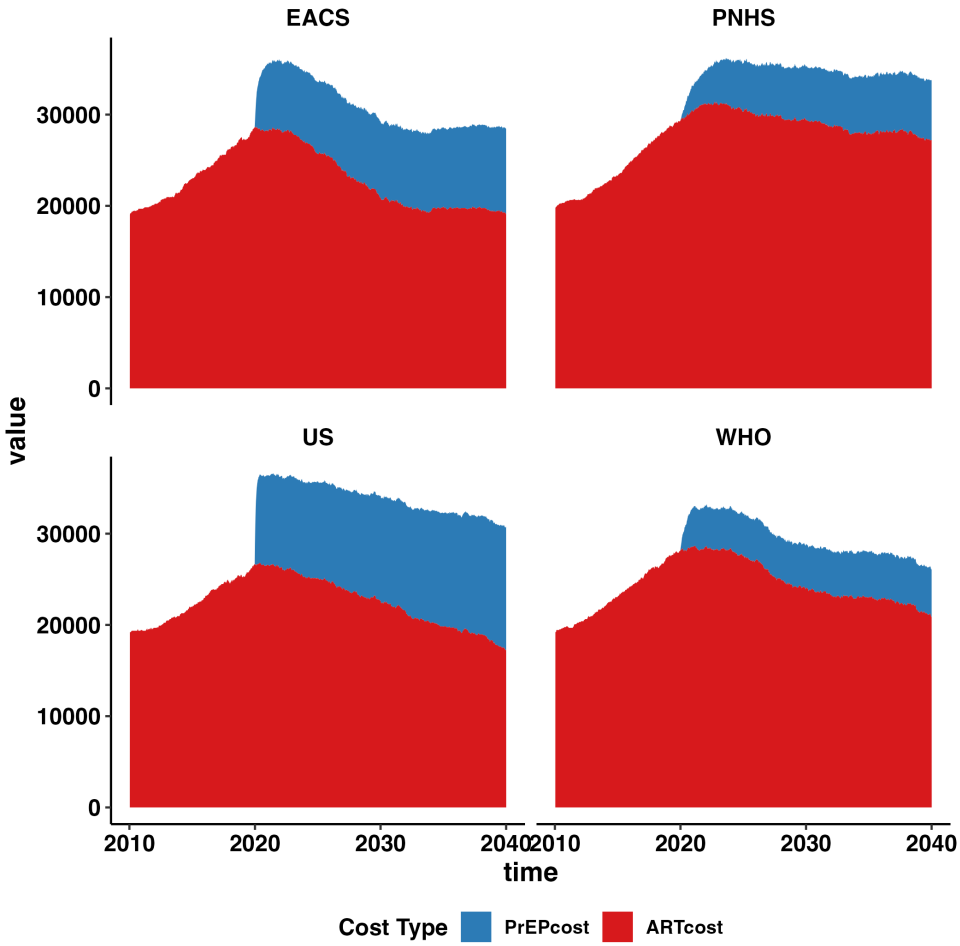

Figure 3.7: HIV care budget proportion by time

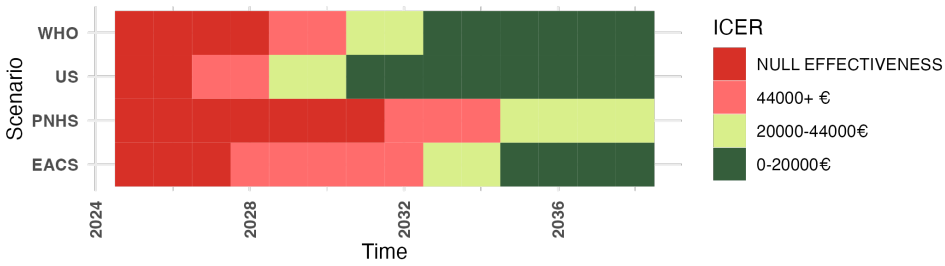

Figure 3.8: Cost-effectiveness of pre-exposure prophylaxis (PrEP) on the HIV epidemic among men who have sex with men(MSM),with about 1000 MSM on PrEP over 20years

Chapter 4

Discussion

This dissertation endeavored to delineate the complexities of HIV transmission within MSM communities through the utilization of agent-based modeling. The central objectives were to customize this model to the MSM community in Lisbon, assimilate PrEP within the model, assess the efficacy of diverse PrEP deployment settings, and conduct a thorough analysis of their cost-effectiveness. The implications of the study's outcomes extend to a deeper understanding of the effects of PrEP usage under various policy strategies and adherence levels on HIV prevalence among MSM. This understanding has consequential implications for strategies aimed at HIV control and prevention.

The data suggests that differing levels of adherence to PrEP, as prescribed under the Portugal National Health Service (PNHS) guidelines, could have a substantial impact on the prevalence of HIV among MSM in Lisbon over the next two decades. Moderate to high adherence levels appear pivotal to efficacious HIV control, while low adherence could prove ineffective or even detrimental. Interestingly, in a scenario of low adherence, the findings were comparable, if not worse, than a situation without any PrEP intervention at all. These results underscore the critical importance of adherence to PrEP to harness its potential benefits and spotlight the need for strategies that support adherence among MSM.

From a financial standpoint, a high-adherence PrEP scenario, despite incurring higher costs, exhibits a favorable cost-effectiveness ratio. In comparison with a baseline scenario without PrEP, the high-adherence intervention corresponds to a cost of €18,468 per QALY gained over a 20-year span. This is in line with findings from the Netherlands[72], UK[73], and Australia[74], but significantly less than in the US due to differing HIV prevalence, other disease settings, and the higher price of PrEP in the US[75]. With a willingness-to-pay threshold of €44,000/QALY gained, the high-adherence PrEP intervention appears to be a viable option for implementation. However, the likelihood of QALYs gained from this intervention surpassing those of the no-PrEP baseline scenario remains around 50% for the initial decade. This implies a neutral effectiveness of PrEP, suggesting that the cost-effectiveness of the intervention is highly contingent on the duration of the intervention, among other factors.

The study also compared various policy strategies for PrEP usage, namely, EACS, PNHS, WHO, and US strategies. Each contributed to a reduction in HIV prevalence, further highlighting the potential of PrEP as a strategic tool for HIV control across diverse policy contexts. However, the effectiveness of these strategies varied. The US, EACS, and WHO strategies demonstrated

a larger reduction in HIV prevalence compared to the PNHS strategy. The effect of the PNHS strategy appeared more subtle, averting a modest number of HIV infections over a 20-year intervention period.

A cost-effectiveness analysis of the various guidelines indicated that the US and WHO strategies emerged as the most cost-effective over 10- and 20-year periods, respectively. Interestingly, the PNHS guideline, although effective and less costly in a 10-year timeframe, demonstrated decreased cost-effectiveness over 20 years. This emphasizes the importance of considering the duration of intervention when assessing cost-effectiveness.

Finally, given the current price of tenofovir and emtricitabine, PrEP is predicted to be cost-effective with an effectiveness exceeding 70%. All four strategies showed less than €44,000 per QALY gained after 20 years, indicating cost-effectiveness. However, the PNHS guideline did not become cost-effective until after 14 years.

These findings collectively emphasize the crucial role of PrEP as an HIV control strategy among MSM. They underscore that adherence and policy guidelines play significant roles in its effectiveness and cost-effectiveness. The insights gained from this study could be instrumental for health policymakers in formulating informed strategies for PrEP implementation, thereby contributing to effective HIV control and prevention efforts.

Compared to other studies, our results demonstrate a minimal, uncertain effectiveness of PrEP, even with high coverage, when the proportion of adherence for PrEP is considered. This is counterintuitive, yet aligns with US estimations[75].

Our mathematical model and cost-effectiveness analyses bear several strengths. Firstly, this study is the pioneer in using an agent-based model to capture the heterogeneity of human behavior and simulate HIV dynamics in Portugal, providing a framework for future HIV studies in Portugal. Secondly, to our knowledge, this is among the first studies to predict the cost-effectiveness of PrEP use amongst MSM in a South European context, potentially providing beneficial information for decision-making regarding PrEP implementation. Finally, through the use of a transmission model, we account for the benefits of the snowball effect of PrEP as prevention.

Despite its strengths, our study also bears limitations. First, we applied Atlanta-specific MSM partnership network parameters, which may not accurately represent the network structure of Lisbon's MSM community. Secondly, due to data limitations, we assumed that individuals maintain consistent behavior, like the rate of condom use and number of sexual acts per week, during every partnership. This reduction in sexual behavior heterogeneity amongst the community may underestimate the effectiveness of targeted PrEP distribution. Thirdly, we did not factor in changes in sexual risk behavior due to PrEP usage, also known as risk compensation. This alteration could lead to decreased PrEP cost-effectiveness[80].

In every criterion, STI-positive individuals are considered a high-risk HIV population and are hence eligible for PrEP. However, due to the absence of reliable STI data and its associated under-testing issue, we did not incorporate STI dynamics into our model. Prior research has indicated a correlation between STI and HIV dynamics, underscoring the potential need for further consideration of this element[76].

Furthermore, the PNHS policy categorizes individuals who inject drugs and male sex work-

ers as high-risk populations[22]. Despite their potential significance in influencing the model, these populations were not included in our study[77]. EMIS data has demonstrated a sizable population with distinct sexual behaviors in these groups[78], suggesting the necessity for future exploration.

Additionally, while immigrants were not explicitly mentioned in the PNHS policy, prior phylogenetic research in Portugal has revealed that immigrant populations demonstrate different mixing patterns and are part of different clusters[35]. These distinctions could potentially have an impact on the dynamics of HIV spread and therefore warrant further investigation in future studies.

Regarding cost-effectiveness analysis, we have made considerable simplifications. We presumed that QALY would not be affected by age in our small age range population. But in the real world, the age range of people living with HIV is much larger, which would greatly influence the QALY. Also, we solely considered the cost of one kind of PrEP, Truvada, whose patent protection expired in February 2020. Hence, with the passage of time, the cost of generic PrEP used for treatment is likely to decline, possibly leading to an overestimation of cost[79]. Furthermore, we do not know the future relative price of ART. The lower the price of PrEP, the more significant this relative cost of ART becomes in our analyses. Regardless, even if the cost of ART decreases, the cost-effectiveness ratio remains far below the cost-effectiveness threshold.

Chapter 5

Conclusion

In conclusion, this study provides a comprehensive exploration of the dynamics of HIV spread among MSM communities in Lisbon, Portugal, through the use of an agent-based model. Our findings illuminate the crucial role of PrEP adherence and tailored policy strategies in the control and prevention of HIV. The model, though subject to certain limitations, underscores the cost-effectiveness of high-adherence PrEP scenarios, while also revealing the potential pitfalls of low-adherence scenarios.

It is evident that policy strategies such as those outlined by the US, EACS, WHO, and PNHS can contribute significantly to reducing HIV prevalence, each with varying levels of effectiveness and cost-effectiveness. However, it is vital to take into consideration the duration of the intervention, adherence levels, and other potentially influential factors like age, in any cost-effectiveness analysis.

Despite the promising potential of these strategies, the model did not incorporate certain high-risk populations, such as STI-positive individuals, people who inject drugs, and male sex workers, due to data limitations. Moreover, the unique patterns exhibited by immigrant populations were not considered in this study. Future research is warranted to include these overlooked populations and factors, in order to provide a more holistic and accurate view of HIV dynamics and control strategies.

In sum, our findings underline the importance of strategic PrEP use and adherence, as well as the need for customized policies tailored to specific community settings, for effective HIV control among MSM in Lisbon. The insights gleaned from this research could significantly contribute to health policy decision-making and the implementation of effective strategies for HIV prevention and control.

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