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Estimating HIV incidence in Türkiye: results from two mathematical models

Emine Yaylali^{1*} and Zikriye Melisa Erdogan¹

Abstract

Background The number of HIV patients has been decreasing globally due to world-wide efforts to end this epidemic; however, HIV incidence has been significantly increasing in Türkiye in the last five years. This study aimed to develop mathematical models to analyze and forecast HIV incidence and prevalence in Türkiye up to 2030.

Methods First, we utilized a Bernoulli model and estimated the annual HIV incidence for risk groups such as heterosexuals (HET), men who have sex with men (MSM), persons who inject drugs (PWID) and female sex workers (FSW). We then developed a dynamic compartmental model of HIV transmission and progression to estimate the incidence of HIV from 2024 to 2030 and further determine the continuum of care levels, such as the proportion of people living with diagnosed HIV and the proportion of people receiving antiretroviral treatment. We also conducted sensitivity analyses for both models on key parameters to explore the robustness of our results.

Results The Bernoulli model indicates that the majority of HIV incidence is driven by two primary risk groups: men who have sex with men (MSM) (41%) and high-risk heterosexuals (HET) (38%). While the risk of HIV transmission is high for people who inject drugs (PWID) (0.07%) and female sex workers (FSW) (0.85%), their contribution to total incidence is lower due to their smaller population sizes. Results from the dynamic compartmental model predict that both the incidence of HIV and the number of HIV-related deaths will continue to rise over the next decade. HIV incidence is projected to reach 27,036 cases in 2025 and increase 2.9-times to 105,202 cases by 2030. According to our models, a significant portion of the HIV-positive population remains undiagnosed (49%), and individuals at high risk of HIV transmission (41% of estimated HIV incidence) are the primary drivers of the epidemic.

Conclusions The number of HIV cases could significantly increase with existing prevention efforts, and HIV could become a major public health threat in the near future in Türkiye.

Keywords HIV, Mathematical modeling, Infectious disease modeling, Compartmental models, Bernoulli process models

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Introduction

According to the World Health Organization (WHO) global estimates, 39.9 million people were living with HIV, while 1.3 million people became newly infected and 630,000 people died from HIV-related illnesses in 2023 [1]. There have been successful efforts in fighting this disease, and considerable progress has been made since it was first identified in the 1980s. However, HIV continues to be an important public health issue worldwide.

While HIV is one of the most significant causes of mortality and morbidity, its economic impact on governments and countries should also be considered. At least 17.6 million new HIV infections and 10.8 million AIDS-related deaths globally could have occurred between 2016 and 2030 if no prevention strategies were employed; on the other hand, 'ending the HIV epidemic by 2030 targets' could yield a 15-fold return on investments [2, 3].

When the number of infections and related treatment costs are considered, the monitoring, prevention and treatment of HIV, both locally and globally, gain much more importance. Data from the Turkish Ministry of Health show that 45,835 HIV patients, of which 2,438 were AIDS cases, were reported since the 1980s as of November 2024. Figure 1 indicates that the number of diagnosed HIV cases has increased significantly in recent years except for 2020 and 2021, when COVID-19 pandemic disrupted healthcare services resulting in a decrease in the testing and diagnoses [4]. Over the last ten years, diagnosed patients account for more than 80% of all reported cases to date, with a 4.5-fold increase in the number of diagnoses [5]. Owing to the extraordinary circumstances caused by the COVID-19 outbreak, which resulted in significant barriers for HIV diagnosis and testing, the 2020 and 2021 results were excluded. Türkiye is a low-HIV-prevalence country; however, the number

of diagnosed cases continues to rise steadily, contrary to the global trend of declining or stable incidence. Furthermore, Türkiye's Health System Performance Assessment by the WHO revealed that to provide an evaluation of HIV incidence, further scrutiny is necessary [6].

While mathematical models for infectious diseases have been developed for decades, interest in such studies has increased in recent years because of global outbreaks and pandemics such as Zika and COVID-19 [7, 8]. HIV modeling studies have been conducted to estimate HIV risk [9, 10], project the future of HIV epidemics at local or global scales [11, 12], determine the most cost-effective interventions [13, 14], assess whether it is possible to reach HIV prevention targets such as UNAIDS's 90-90-90 goals [15], and allocate resources optimally [16–19]. Researchers have benefited from various mathematical models, such as Bernoulli models, compartmental models, Markov models and simulation models, as well as optimization and resource allocation models [20–24].

Previous studies on HIV in Türkiye focused on the European Center for Diseases Control (ECDC) model; one study used a compartmental model with three compartments to estimate the reproduction number R_0 for HIV in Türkiye [25, 26]. Two other studies evaluated the continuum of care levels, which is an important indicator for understanding gaps in prevention efforts [27, 28]. However, none of these studies fully address the disease's complex behavior or, at the same time, include risk groups and behavioral factors of high-risk populations. It is important to represent groups such as female sex workers (FSW), persons who inject drugs (PWID) and men who have sex with men (MSM) in mathematical models since they are at greater risk of acquiring and transmitting HIV [29]. The majority of new HIV diagnoses often belong to high-risk populations in many countries. In the

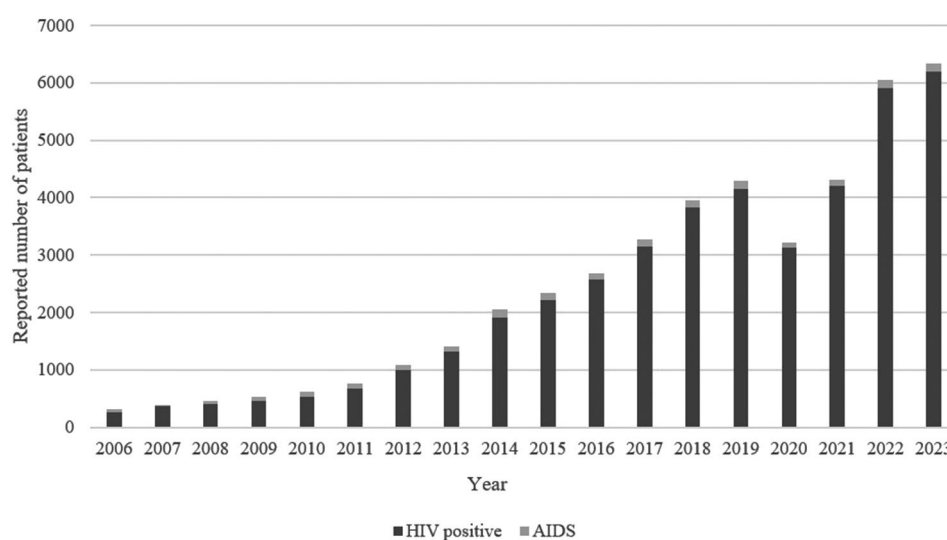


Fig. 1 The number of HIV/AIDS cases in Türkiye each year

last decade, reported cases in Türkiye have shown a similar trend, with an increasing percentage of HIV-positive individuals being young (20–34 years of age) and MSM [30, 31].

Our motivation is to identify multifaceted factors of HIV transmission in Türkiye and to understand the rapidly increasing HIV epidemic with the help of mathematical modeling. This study aims to develop mathematical models that project HIV incidence by incorporating risk groups and behavioral risk factors. These models provide a comprehensive picture of disease dynamics on the basis of the risk population, disease status, and continuum of care. We developed two types of mathematical models (the Bernoulli process model and the compartmental model) to forecast the future of HIV incidence in Türkiye and compared the results of the models. On the basis of the methodology, data needs and results, we analyzed the advantages and disadvantages of each model type and provided key insights and recommendations on which type of model to choose on the basis of the needs of the problem observed. The benefits of our study are twofold: (i) to present the future trajectory of the HIV epidemic in Türkiye and to provide key areas for HIV prevention in Türkiye and (ii) to showcase different types of modeling techniques, their data requirements and results for better model selection and conceptualization in future studies.

The remainder of this paper is organized as follows: In Sect. “**Materials and methods**”, mathematical models are explained in detail, and the results are presented in Sect. “**Results**”. Key insights, limitations, and future recommendations are discussed in the last section.

Materials and methods

Mathematical models of HIV often aim to forecast population-level outcomes with the help of individual-level inputs, and one of the critical population-level outcomes in these models is HIV incidence [26]. Similarly, in this study, two types of models, the Bernoulli model and the compartmental model, were constructed to predict HIV incidence in Türkiye. While it is possible to adapt other modeling methodologies, these modeling techniques are the most appropriate considering that there is limited surveillance of HIV in Türkiye; as a result, there are not sufficient data to populate data-heavy and/or individual-based models.

Bernoulli process model

The main assumption of the Bernoulli model is that there is a probability of HIV transmission for each risky act, such as unprotected sex or needle sharing [32]. This probability, known as the per-act probability of HIV transmission from an infected source, was assumed to be the same for each partner within each risk group in our model. In other words, HIV acquisition risk depends on

the type of risky behavior; protected/unprotected sexual intercourse; sharing needles; type of risk population; and HIV prevalence. In addition, we included the preventive benefits of condom use and HIV treatment in the model. We assumed that condom use decreases HIV transmission risk by 80%, and being on HIV treatment for the infected partner reduces HIV transmission by 96% [33, 34].

We divided our population into five risk groups: high-risk heterosexuals (HET high), low-risk heterosexuals (HET low), men who have sex with men (MSM), people who inject drugs (PWID) and female sex workers (FSW). Unfortunately, there are few data related to behavioral risk factors for HIV (e.g., sexual behavior, drug use) in Türkiye, and there are no national data. Therefore, we assumed that the married adult population aged 18–64 years was at low risk, and single persons in the same age group were defined as high-risk heterosexuals. This was done to identify high-risk heterosexuals in the model. While this assumption is a major simplification of sexual behavior, the number of sexual partners for high-risk heterosexuals was close to the same for low-risk heterosexuals, resulting in similar overall behavior in both risk groups.

The Bernoulli process model for HIV infection is represented with the equations below.

$$P_1 = 1 - \left\{ 1 - \pi_1 * NT * \left[1 - (1 - \alpha_n)^n (1 - \alpha_k)^k \right] \right\}^m \quad (1)$$

$$P'_1 = 1 - \left\{ 1 - \pi_1 * T * \left[1 - (1 - \alpha'_n)^n (1 - \alpha'_k)^k \right] \right\}^m \quad (2)$$

$$P_2 = \pi_2 * NT * \left(1 - (1 - \alpha_t)^t \right) \quad (3)$$

$$P'_2 = \pi_2 * T * \left(1 - (1 - \alpha'_t)^t \right) \quad (4)$$

P_1 and P_2 represent HIV transmission risks for HIV-positive people who are not receiving treatment, and NT indicates the proportion of people who are not receiving treatment, whereas P'_1 and P'_2 represent HIV transmission risks for HIV-positive people who are receiving treatment, and T represents the proportion of people receiving treatment. Owing to the lack of national-level estimates of HIV-positive people receiving treatment in Türkiye, we assumed that 68% of HIV-positive individuals are receiving treatment, which is the same as the world average [35, 36]. P_1 and P'_1 risks were identified by considering unprotected sexual intercourse risk behavior, whereas P_2 and P'_2 risks were calculated via needle-sharing risk behavior. The total HIV risk was determined by adding P_1 and P'_1 values for the HET, MSM and FSW risk groups while adding P_2 and P'_2 values for the PWID risk group. Then, we estimated HIV incidence for each

Table 1 Key parameters for the Bernoulli model

Symbol	Parameter	Value	Source
π_1	Prevalence of HIV		
	Heterosexuals	0.000184	[56, 57]
	Men Who Sex with Men	0.03	[58]
	Female Sex Workers	0.01	[59]
n	Number of unprotected sexual intercourse	89	[60–62]
k	Number of protected sexual intercourse	20.9	[60–62]
α_n	Per-act probability of transmission (Under no protection)	0.0161	[63]
α_k	Per-act probability of transmission (Under protection)	0.00322	[35]
m	Number of partners		
	HET (High)	2.29	*[64]
	HET (Low)	1	*
	MSM	3.67	*
	FSW	3	*
π_2	Prevalence of HIV for PWIDs	0.0066	[65]
α_t	Per-act probability of transmission for needle-sharing	0.0063	[66]
t	Annual number of times needle sharing	60	[67–69]

* Calculated on the basis of source

risk group by multiplying each population size by their risk. All calculations were performed via MS Excel. The parameters used in this process are given in Table 1, and model validation due to a lack of data was conducted on the basis of expert opinions.

To present a better understanding of the model estimations, a one-way sensitivity analysis was conducted. This analysis was applied by changing only one parameter value and collecting new results. We used both 20% more and 20% less of the base value of each parameter and

evaluated the ranges of estimated HIV incidence. This analysis enabled us to determine which parameters have the most/the least effect on the estimates.

Dynamic compartmental model (SI model)

In the early 1900s, dynamical systems approaches were applied to infectious diseases. The main principle of this approach is to assume that individuals in the population are either susceptible to infection, currently infectious, or recovered (previously infected and consequently immune) [37]. Dynamic compartmental models classify the population into several classes and name them compartments. Then, mathematical equations are created to represent individuals moving between the compartments [37]. There are several compartmental models, such as SI, SIR, SIS, SEIR, SEIRS, MSEIR, and MSEIRS.

Our compartmental model for HIV consists of eight compartments, as shown in Fig. 2. In the model diagram, S represents the susceptible population, and E represents deaths due to AIDS-related causes. In addition, deaths due to natural causes, δ , and the birth rate, ρ , were defined. Parameter β is the force of infection, which is a 3×3 matrix that takes into account three different risk groups (MSM, PWID and HET) and their continuum of care levels. The HIV continuum of care is illustrated horizontally in three stages (undiagnosed, diagnosed and on ART) and grouped vertically by their CD4 levels ($CD4 \geq 200 \mu L$ and $CD4 < 200 \mu L$). Patients with $CD4 \geq 200$ were regarded as HIV positive, whereas those with $CD4 < 200$ were assumed to be AIDS patients. All compartments are defined as follows: $CD4 \geq 200$ and undiagnosed (UA), $CD4 < 200$ and undiagnosed (US), $CD4 \geq 200$ and diagnosed (DA), $CD4 < 200$ and diagnosed (DS), $CD4 \geq 200$ and under treatment (on ART) (TA), $CD4 < 200$ and on ART (TS). Parameters p , q and

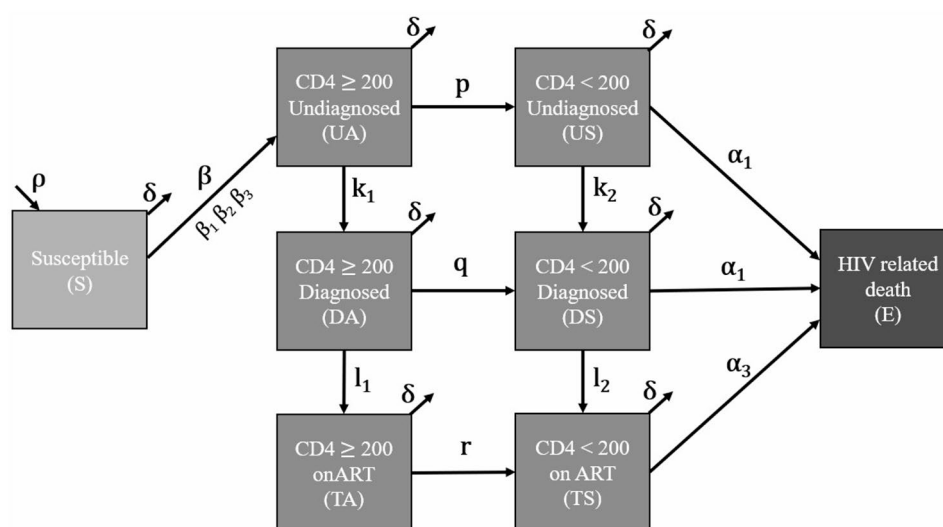
**Fig. 2** Dynamic compartmental model diagram

Table 2 Input parameters for the compartmental model

Symbol	Parameter	Value	Source
ρ	Birth rate	0,01818	[57]
δ	Natural death rate	0,00589	[57]
p	Infection progression rate for undiagnosed people	0,03	[42]
q	Infection progression rate for diagnosed and not under treatment patients	0,03	[70]
r	Infection progression rate for diagnosed and under treatment patients	0,0189	[70]
Calibrated input parameters			
β_1	Force of infection for undiagnosed patients	0.33–0.98	Calibrated
β_2	Force of infection for diagnosed patients	0.16–0.46	Calibrated
β_3	Force of infection for patients on treatment	0.01–0.02	Calibrated
α_1	HIV-related mortality rate for undiagnosed and diagnosed patients (2005–2013)	0.0523	Calibrated
α_3	HIV-related mortality rate for patients under treatment (2005–2013)	0.0098	Calibrated
α_1'	HIV-related mortality rate for undiagnosed and diagnosed patients (2014–2030)	0.0318	Calibrated
α_3'	HIV-related mortality rate for patients under treatment (2014–2030)	0.0028	Calibrated
k_1	Diagnosis rate	0.506	Calibrated
k_2	Diagnosis rate	0.509	Calibrated
l_1	Treatment rate	0.818	Calibrated
l_2	Treatment rate	0.878	Calibrated
Initial population parameters			
Population Size	MSM	40,000	Expert opinion
Population Size	PWID	59,895	[65]
Population Size	HET	46,938,000	[71]
Prevalence	MSM	0.03	[58]
Prevalence	PWID	0.0066	[65]
Number of PLHIV	MSM	1,200	*[58]
Number of PLHIV	PWID	395	*[65]
Number of PLHIV	HET	697	*[56]
Number of PLHIV	Total number of PLHIV	2,292	[56]
Continuum of care (%)	HIV positive	15%	*[56]
Continuum of care (%)	AIDS	85%	*[56]

* Calculated based on the source and details of calculation can be found in the Supplemental Appendix

r represent the progression of HIV. k and l represent the diagnosis rate and treatment rate, respectively, and α represents the death rate due to AIDS-related causes.

After that, a model was established via the differential equations below. All possible movements between compartments were transformed into mathematical equations. Since model outcomes for three different risk groups are needed, index i ($i = 1, 2, 3$) represents risk groups (MSM, PWID and HET), whereas the total population is denoted by N .

$$\frac{dS_i}{dt} = \rho N - \frac{S_i [\beta_1 U A_i + \beta_2 D A_i + \beta_3 T A_i]}{N} - \delta S_i \quad (5)$$

$$\frac{dU A_i}{dt} = \frac{S_i [\beta_1 U A_i + \beta_2 D A_i + \beta_3 T A_i]}{N} - k_1 U A_i - p U A_i - \delta U A_i \quad (6)$$

$$\frac{dD A_i}{dt} = k_1 U A_i - l_1 D A_i - q D A_i - \delta D A_i \quad (7)$$

$$\frac{dT A_i}{dt} = l_1 D A_i - r T A_i - \delta T A_i \quad (8)$$

$$\frac{dU S_i}{dt} = p U A_i - k_2 U S_i - \alpha_1 U S_i - \delta U S_i \quad (9)$$

$$\frac{dD S_i}{dt} = q D A_i + k_2 U S_i - l_2 D S_i - \alpha_1 D S_i - \delta D S_i \quad (10)$$

$$\frac{dT S_i}{dt} = r T A_i + l_2 D S_i - \alpha_3 T S_i - \delta T S_i \quad (11)$$

$$\frac{dE_i}{dt} = \alpha_1 (U S_i + D S_i) + \alpha_3 T S_i \quad (12)$$

$$N = \sum_i S_i + \sum_i U A_i + \sum_i D A_i + \sum_i T A_i + \sum_i U S_i + \sum_i D S_i + \sum_i T S_i \quad (13)$$

The compartmental model was coded in MATLAB [38], and differential equations were solved via the Runge–Kutta method. Before running the algorithm, the initial population, which was an allocation of MSM, PWID and HET individuals into eight compartments, was created using the parameters shown in Table 2.

The modeling approach was designed as a process with four different periods: a warm-up period (2005–2012), a calibration period (2014–2016), a model validation period (2017–2023) and an estimation period (2024–2030). The warm-up period was defined to help our model reach a stable state.

Model calibration

Some aspects of reality are unmeasured or unknown, and we are often confronted with models that require inputs for which no or only indirect data exist. In such cases, the calibration method can be used to select input values that lead to model outputs “as close as possible” to the available empirical data [39]. The calibration period was included because of a lack of data regarding important parameters. The steps of our calibration process are presented in Supplementary Fig. S1. Where possible, we defined minimum and maximum values for the calibrated input parameters based on published literature and generated values using a uniform distribution within these ranges. Supplemental Table S1 provides the ranges for the diagnosis and treatment rates. Other calibrated parameters were generated using a uniform distribution between 0 and 1, as all parameters represent probabilities.

In the first step of the calibration, the force of infection, diagnosis rate, and treatment rate were calibrated for 2014 and 2016. The model was run 100,000 times, and mean squared errors (MSEs) were obtained by taking the average of sum of squared differences between the actual number of diagnosed HIV patients and the estimated values for 2014, 2015 and 2016. Then, the MSE values were sorted, and the parameters with the least errors were chosen as the calibrated parameters. In the second step of the calibration, death rates due to AIDS-related causes were calibrated. The same calibration procedure was applied for the annual number of deaths due to AIDS-related causes, with 10,000 model runs for 2013, 2014 and 2015. The calibrated parameters and their values are shown in Table 2 and Supplemental Table S2. Afterwards, model results were collected for future estimations.

Model validation

Validation is a set of methods and techniques to assess a model's accuracy in generating relevant predictions. Following recommendations of ISPOR-SMDM guidelines on model transparency and validation, we evaluated face, internal and external validity of our models [40].

Four aspects of face validity—model structure, data sources, problem formulation, and results—are documented in detail. A subject matter expert, an infectious disease specialist with over 20 years of experience, has evaluated the model and its outcomes to ensure that the model's assumptions align with real-world conditions and that the results are appropriate.

For internal validity, both modelers verified the individual equations of two models and verified their implementation in code. With an extensive walk-through, the programmer explained the code to the other modeler and parameters that are calculated are validated by the other modeler independently. In addition, we ran extreme value analysis on some scenarios and evaluated our anticipated predictions with the model results.

For external validity, the dynamic compartmental model was validated against the number of diagnosed cases reported by the Ministry of Health between 2017 and 2023 [5]. This represents a partially dependent validation, as data from earlier years were used during model calibration. However, this dataset remains the most comprehensive record of reported cases, encompassing diagnoses from all regions of Türkiye as well as state and private hospitals. The Bernoulli model estimates HIV incidence by risk groups. Unfortunately, reliable data on the actual size or HIV incidence within these groups—such as MSM, FSW, and PWID—is unavailable in Türkiye due to the stigma, discrimination, and legal challenges faced by these populations. Consequently, the evaluation of the Bernoulli model results relied on the expert opinion of a subject matter specialist.

Results

Bernoulli process model

HIV incidence was estimated on the basis of HIV risk and population size for each risk group. Since we did not have information about the population size of MSM in Türkiye, we consulted experts in this area. Accordingly, we defined low, medium and high categories for the MSM population in Türkiye. Furthermore, we used two HIV prevalence rates for the MSM population obtained

Table 3 Estimated HIV incidence according to MSM category and HIV prevalence rates for MSM

HIV Prevalence	Category of MSM population size	MSM Population	HIV Incidence of MSM	Total HIV Incidence	Percentage of MSM (%)	Diagnosis rate (%)
0.03	Low	40,000	1,241	10,140	12.2	39.8
0.03	Medium	200,000	6,207	15,106	41.1	26.7
0.03	High	1,500,000	46,554	55,453	84	7.3
0.127	Low	40,000	5,110	14,009	36.5	28.8
0.127	Medium	200,000	25,552	34,450	74.2	11.7
0.127	High	1,500,000	191,641	200,539	95.6	2

from different studies, and the results are given in Table 3 [26, 41].

The experts evaluated the results; the medium-sized MSM population size and the 15,106 new HIV patients in 2019 were selected as the most reasonable outputs. In the first stage, we assumed that 68% of people living with HIV (PLHIV) were under treatment in this analysis. We then changed the treatment rate depending on the cohort studies (75.3%, 86%, 88% and 92%), and the results are presented in a table in the supplementary appendix (Supplementary Table S3) [27, 28, 42, 43]. For example, when the treatment rate was 86%, new HIV infections were calculated as 8,318, with 41% relating to MSM and a 48% diagnosis rate. The range for HIV incidence in 2019 was found to be approximately 4,000–166,000, according to these results.

The estimated HIV incidence rates for each risk group are summarized in Table 4. According to the results, the MSM risk group had the highest number of new HIV cases in 2019. High- and low-risk heterosexual individuals followed, with 5,735 and 3,093 new HIV cases, respectively. MSM was the riskiest group, with a probability of transmission of approximately 3%. The FSW group was riskier than the PWID group was, but the HIV incidence of PWID was greater than that of the FSW risk group because of population size. The total annual HIV incidence in 2019 was estimated at 15,106, according to the Bernoulli model.

For sensitivity analysis, 20% more of the selected parameter's value was regarded as 'the best', and 20% less of the same parameter's value was regarded as 'the worst' case. New HIV incidences are illustrated with tornado diagrams in Supplementary Fig. S2. Each parameter did not affect the HIV incidence in the same way. The sensitivity analysis revealed that HIV prevalence, per-act probability of HIV transmission without protection, the number of risky acts (unprotected sexual intercourse), and the average number of partners per year significantly affected the estimation of HIV incidence for MSM, HET and FSW. The HIV prevalence for PWIDs, per-act probability of HIV transmission in cases of needle sharing and the average annual number of times needle sharing were considered important parameters for the PWID group.

Table 4 Estimations of HIV incidence from the Bernoulli model for each risk population

Risk group	HIV Risk (%)	Population	HIV incidence (%)
HET (High)	0.02	28,123,158	5,735 (38)
HET (Low)	0.009	34,729,806	3,093 (20)
MSM	3	200,000	6,207 (41)
PWID	0.07	59,895	44 (0.3)
FSW	0.85	3,100	26 (0.2)
TOTAL	-	-	15,106

The per-act probability of HIV transmission with condom use and the number of risky acts by a partner during protected sexual intercourse are not important parameters because they have a much smaller effect on model results.

Dynamic compartmental model

The first step of calibration in the dynamic compartmental model enables us to reach the diagnosis and treatment rates. Thus, we defined the HIV treatment cascade for Türkiye as depicted in Fig. 3. According to the model, 51% of HIV patients knew that they have been infected with HIV, and 85% of diagnosed patients received treatment. Since the HIV treatment cascade was defined with a denominator that presented all people living with HIV (PLHIV), these rates were readjusted. It was found that among all PLHIV, 51% of patients knew their status, and 43.35% were under treatment.

To carry out the validation process of our model, a comparison was made between model results and official data from the Turkish Ministry of Health (Fig. 4). The annual number of diagnosed HIV positive and AIDS patients in 2017 were 3145 and 126, while our model estimated these values as 3048 and 436, respectively. In 2018, the annual numbers of diagnosed HIV positive and AIDS patients were 3823 and 130, according to national data. In the same year, model results were 3661 diagnosed HIV positive patients and 508 diagnosed AIDS patients. For the extreme value analyses, we reported the results in the Supplemental Table S4.

Model estimations for HIV positive and AIDS incidences are shown in Fig. 5. According to the results, the estimated number of HIV-positive patients was 6516, and the estimated number of AIDS patients was 678 in 2019. In 2023, these numbers were found to be 16,345 (1.5-fold increase) and 1481 (1.18-fold increase). According to the model results, 105,202 HIV-positive cases and 8056 AIDS cases could be reached by 2030 and consequently would increase approximately 15 times compared with estimations in 2019.

The annual number of AIDS-related deaths was estimated to be 18, 21 and 24 for 2016, 2017 and 2018, respectively. Model estimations for the annual number of deaths were compared with official data (Fig. 6). They were found to be very close to each other during both the 2013–2015 calibration period and the 2016–2023 validation period. As we assumed that no deaths existed at the beginning of the model, cumulative estimations were calculated by adding the annual number of deaths from 2013. The total number of deaths between 2013 and 2019 and between 2013 and 2023 were 151 and 330, respectively. The cumulative number of deaths was predicted to exceed 1400 at the end of 2030.

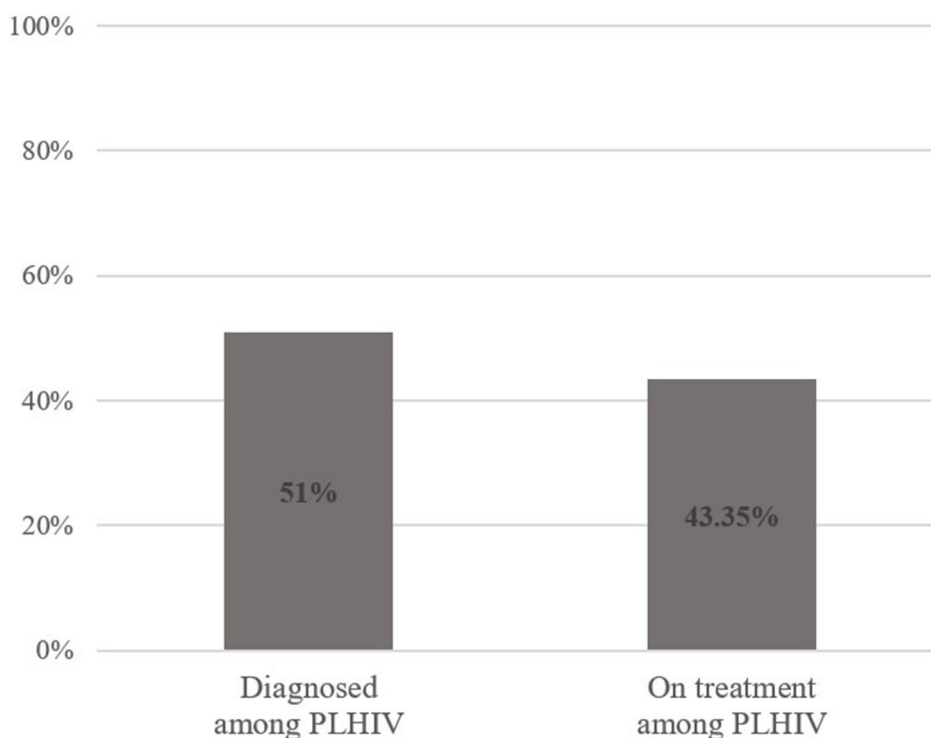


Fig. 3 HIV cascade in Türkiye based on the compartmental model

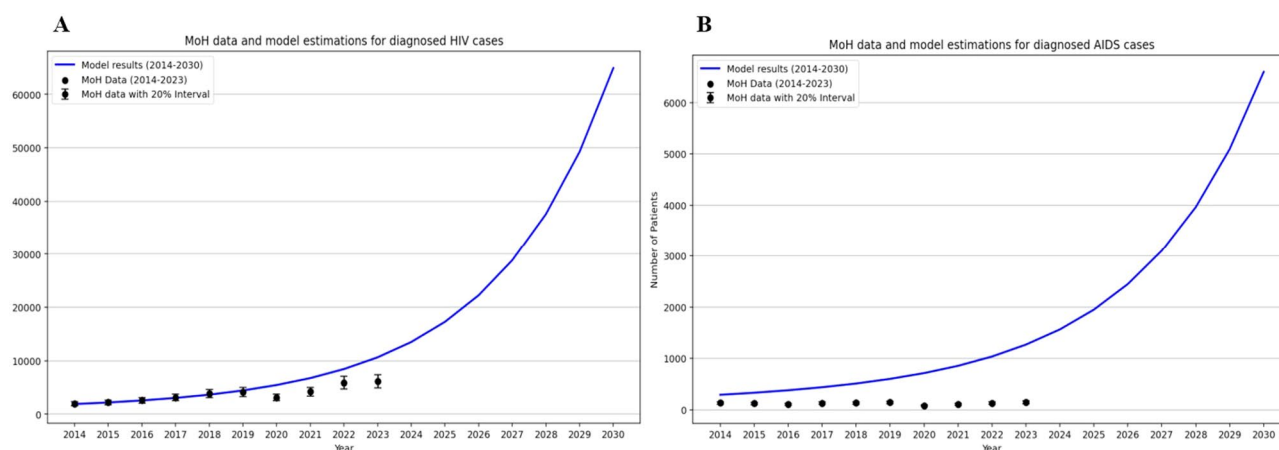


Fig. 4 The annual number of diagnosed HIV and AIDS patients from 2014–2030 based on model results and comparisons with official data

The estimated total number of HIV-positive patients (UA, DA and TA compartments) and the total number of AIDS patients (US, DS and TS compartments) according to their risk groups are shown in Supplementary Fig. S3. The majority of HIV patients can be identified as heterosexual, whereas the MSM risk group came after heterosexual. Moreover, the number of HIV patients in the HET group tended to increase during the estimation period. It is also important to note that all risk groups exhibit rising HIV incidence, consistent with real-life trends.

The sensitivity analysis for the compartmental model was performed by defining different cases

(Supplementary Fig. S4 and Fig. S5). In the base case, all the parameters take their initial values. In contrast, in the other cases, only one of the parameters, the diagnosis rate, treatment rate and force of infection, decreased by 20% or increased by 20%. Sensitivity analyses revealed that the force of infection has a stronger effect on model estimations. The effect of the diagnosis rate takes second place after the force of infection, whereas the treatment rate has the least effect. Hence, the calibrated parameters were ranked in descending order of importance as follows: force of infection, diagnosis rate and treatment rate.

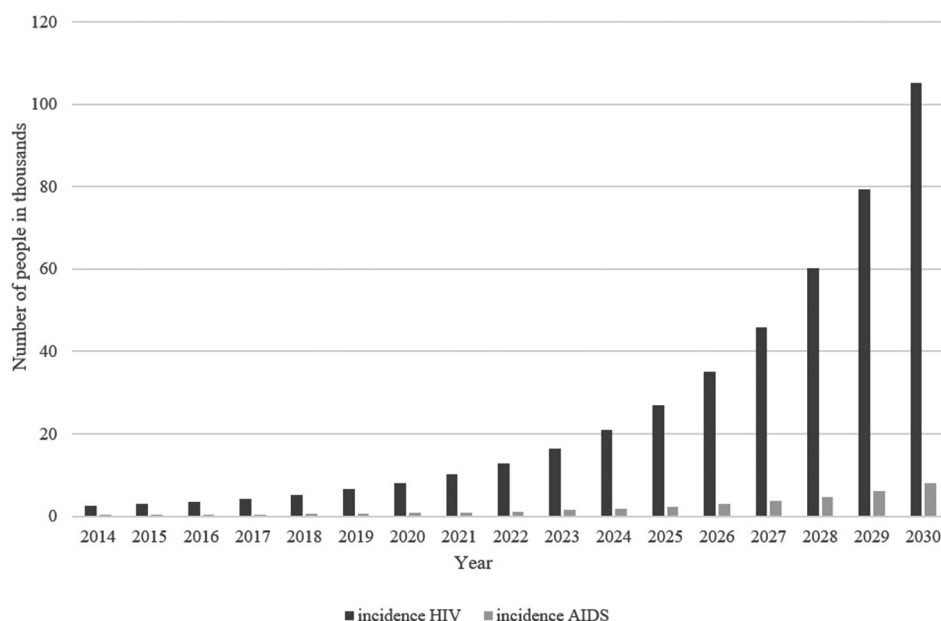


Fig. 5 Estimated HIV-positive and AIDS incidence rates from 2014–2030 on the basis of the model results

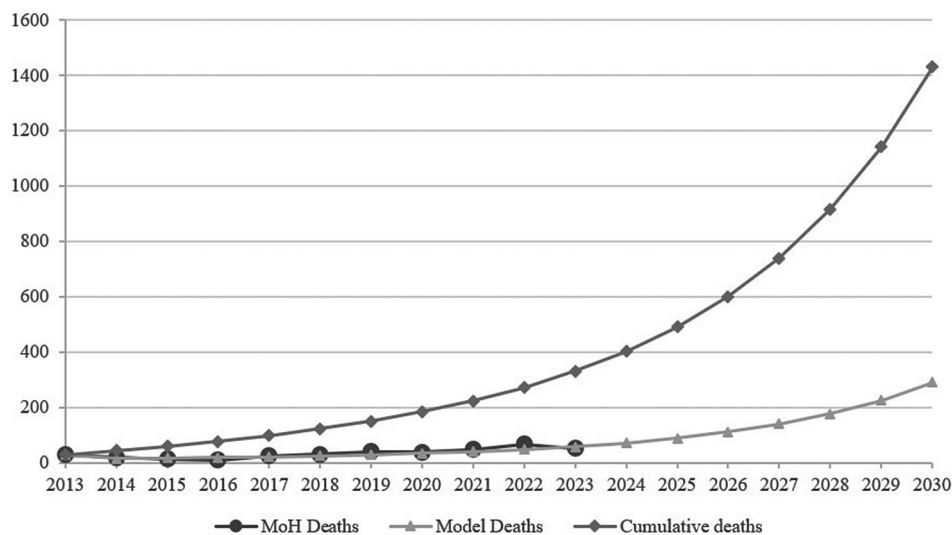


Fig. 6 Annual and cumulative number of deaths due to AIDS-related causes from 2013–2030 and comparison with official data

Discussion

HIV is one of the leading health problems worldwide. Fortunately, mathematical models allow us to follow the spread of the disease, determining outputs such as the number of new infections or deaths due to AIDS, as well as the number of PLHIV.

Although Türkiye is among the low-HIV prevalence countries, the annual number of diagnosed patients has drastically increased. Moreover, it is believed that reported numbers constitute only part of the disease, and the number of diagnosed cases is underestimated [44]. There is a poor registration system for establishing the exact number of cases [26]. Therefore, it is necessary to

investigate HIV progression in Türkiye. This study was conducted to project the future of HIV with the help of modeling techniques.

First, we benefit from the Bernoulli model with probabilities of transmission. MSM was found to be the riskiest group, while the majority of new infections were from the HET high-risk group. Hence, it was concluded that MSM and HET high-risk groups were the most important and can be regarded as targeted groups for potential interventions. The fact that focusing on the MSM population was found to be beneficial in fighting the disease is in line with various studies [45–47]. The sensitivity analysis of the Bernoulli model revealed that protection was an

effective way to prevent HIV transmission. The number of individuals engaging in protected sexual intercourse and the probability of HIV transmission with protected intercourse were found to be unimportant parameters in the model. The HIV incidence calculated with our model is approximately 3.5 times greater than the number of HIV cases diagnosed and reported in 2019. This gap shows that reducing the number of people with undiagnosed HIV could be key in preventing HIV in Türkiye.

Afterwards, a dynamic system approach was exploited by developing a compartmental model with a more complex structure than the Bernoulli model for long-term projection. Compared with the Bernoulli model, we integrated three additional characteristics as follows: (i) the CD4 level, which assumes the distinction between HIV-positive patients and AIDS patients; (ii) Diagnosis and treatment status, which indicates the HIV continuum of care; and (iii) HIV risk groups. Model estimations for the annual number of diagnosed HIV patients and the number of deaths due to AIDS were very close to reported numbers from the Ministry of Health, whereas the results for AIDS patients were greater than those reported previously. Among the risk groups, the highest number of HIV patients were heterosexual, as expected, due to the high population size of heterosexual individuals. The number of patients among MSM was second highest. According to the model, if the HIV situation in Türkiye continues at the same level, the annual HIV incidence will exceed 105,000, and the number of people living with HIV will reach about 500,000 in 2030. People who are unaware of their HIV status contribute to the spread of disease, as they maintain risky behavior. While the estimated diagnosis rate was 51% and the estimated treatment rate was 85%, some interventions should be put into practice to reach the 90-90-90 UNAIDS target.

Both models have shown that there is a growing number of both diagnosed and undiagnosed HIV patients in Türkiye, and if no effort is made to change the current trend, Türkiye will potentially face HIV as a major public health threat in the near future. Some other contributing factors are Türkiye's close proximity to higher-HIV prevalence countries (Eastern Europe and Central Asia) [48]; its growing tourism opportunities; increasing population, refugee and migration issues [49, 50]; developing economic and commercial sectors; and increasing number of people working and returning from abroad. In addition to these factors, an increasing number of drug users [51, 52] have also led Türkiye to become an HIV risk area. Thus, authorities should focus on risk groups and take immediate preventative action. The development of strategies for prevention, testing, and diagnosis will substantially reduce the number of infections. Thus, such a course of action should be pursued to implement

effective healthcare policies and provide the most beneficial healthcare solutions.

After having a good surveillance of HIV status, another important aspect is to close the gaps in the continuum of care. Since the diagnosis step presents a weakness, efforts could be focused on minimizing barriers and employing strategies to incentivize testing. As peer education has proven to be effective in behavioral change within high-risk populations [53], this strategy can be implemented to decrease infections in the population. Besides testing and treatment programs, information campaigns which led changing the attitude in the population about HIV and removing stigma and discrimination is another helpful strategy for high prevalence countries such as South Africa [54] and can be suggested for mitigating the disease spread. To establish an enhanced HIV surveillance system is important for presenting the real progress towards global targets and revealing the undiagnosed PLHIV. We do not have a national database including all reported case [30], and thus studies are conducted based on cohort-level data. National HIV surveillance system would help to make evidence-based public health decisions. To monitor and assess the national HIV response, lack of such system is considered as an unmet need [51]. As mentioned in this report [55], low prevalence countries should introduce a surveillance system that can detect HIV infections among risky populations earlier instead of late diagnosis.

The limitations of the study can be discussed in two different aspects: application limitations and methodological limitations. The lack of national data concerning important essential parameters, such as parameters related to sexual behavior and MSM population size, can be regarded as the main application limitation. Methodological limitations include the structure of the models. One of them is the Bernoulli model's dependence on parameters. It can be seen as a method that depends too much on its input parameters. Moreover, the Bernoulli model is a method with static features in its structure. Although we only provided annual HIV estimates for a single year, our methodology could be repeated each year by updating parameters on a rolling basis. On the other hand, the deterministic compartmental model is a dynamic method that generates estimations for many years, but its structure keeps the parameters stable during the estimation period. Additionally, one of the assumptions of the compartmental model is that individuals of the same compartments act homogeneously. That is, the behavior of individuals in each compartment is the same.

For future studies, the number of groups can be increased according to specific characteristics, such as the age and sex of the population, for the Bernoulli model. Moreover, this model can be extended for different stages

of HIV. Probabilistic sensitivity analyses can be applied to both models. For the compartmental model, the number of compartments can be increased by adding the acute infection and/or viral suppression phase to the continuum of care or including demographic characteristics such as age and sex. The viral suppression phase would contribute to enhancing the HIV cascade for Türkiye at the same time. The reason is that these types of models are beneficial for assessing Türkiye's performance with 90–90–90 targets. Bernoulli and compartmental models are used to perform cost-effectiveness analyses; thus, several prevention methods can be added to models to find the best prevention strategies.

Conclusion

Our study highlights the importance of a rising public health problem in Türkiye: increasing HIV incidence in the last decade. Our models suggest that there will be a considerable surge in the number of HIV infections in the future and that the burden of such changes in the health system and treatment costs could be devastating. Furthermore, our results show that prevention efforts should focus on persons who are at high risk of HIV infection, such as MSM, high-risk HET and FSW, to curb this upsetting trend.

Supplementary Information

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Supplementary Material 1

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Author contributions

E. Y. have made contributions to the conception of the work, performing the analysis, interpretation of the results, writing and revising the manuscript. Z. M. E designed the software, performed the analysis, interpreted the results and have drafted the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to the fact that there is no license to protect the code but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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