RESEARCH ARTICLE

Modeling the impact of Different Intervention Strategies on HIV Transmission among MSM in China

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ABSTRACT

Objective: This study utilized a mathematical model to compare the dynamics of the Human Immunodeficiency Virus (HIV) epidemic in men who have sex with men (MSM) in China by different antiviral therapy strategies, and explored the impact of anti-retroviral therapy (ART), voluntary counseling and testing (VCT) and condom use on the transmission of HIV among MSM individually.

Design: The study is a research of theoretical epidemiology

Methods: A mathematical model was built to simulate the HIV and Acquired Immunodeficiency Syndrome (AIDS) epidemic among MSM in China starting in 2015. The different antiviral therapy strategies and the individual effects of these HIV/AIDS interventions among MSM were analyzed. A one-way sensitivity analysis was conducted to determine how the model results were impacted by each parameter individually.

Results: Compared to antiviral therapy strategies, cumulative HIV infections and AIDS cases will be reduced by 87.3% and 80.7%, respectively, in a universal test-and-treat strategy. Compared to current antiviral therapy strategies, cumulative HIV infections and cumulative AIDS cases will be reduced by 34%and 26.7%, respectively, in a universal test-and-treat strategy.

Based on an estimated minimum coverage, if ART against HIV infection is increased every one double, by 2025 cumulative HIV infections and AIDS cases have an average reduction of 24.2% and 23.2%, respectively. If the coverage of VCT is increased every one double, cumulative HIV infections and AIDS cases have an average reduction of 14.2% and 13.5%, respectively. If the instances of condom use are increased every one double, cumulative HIV infections and AIDS cases will have an average reduction of 69.5% and 66.3%, respectively.

Conclusions: Compared to current antiviral therapy strategies, a universal test-and-treat strategy can significantly reduce cumulative HIV infections and cumulative AIDS cases. Improving the coverage of current antiviral therapies, the coverage of VCT and the increase of condom use can effectively control the epidemic of AIDS among MSM in China. Among the three intervention strategies, increasing condom use coverage was found to be the most effective.

Keywords: MSM, HIV/AIDS, Intervention, Anti-retroviral therapy, Voluntary counseling and testing, Condom use

1. Introduction:

Annual numbers of new HIV diagnoses in China according to surveillance data were 104 thousands in 2014. HIV/AIDS continued to control in low level overall popular. In recent years, the characteristics of the AIDS epidemic in China has changed, the proportion of sexually transmitted rising rapidly and developed into a major route of HIV transmission, and Men who have sex with men (MSM) has become the core of the crowd (1). In China, the proportion of reported cases resulting from homosexual contact in year 2005 to 2011 was 0.4%, 2.5%, 3.4%, 5.9%, 8.6%, 10.8%, and 13.0%, respectively (2). The prevalence of HIV among MSM was increasing year by year, has reached an average of 5% in large and medium cities, and was greater than 10% in the main cities of the Southwest (2). Among all people living with HIV, the proportion of people infected by homosexual contact increased from 14.7% in 2009 to 17.4% in 2011 (3). Evidence from studies has shown that gay and bisexual men perceived numerous psychological and emotional benefits associated with barebacking(4), and barebacking was a risk factor for HIV transmission, moreover HIV infection rate via homosexual contact was much higher than heterosexual contact(5, 6). In mainland China MSM bore a high burden of HIV since the traditional cultural may cause them to want to be hidden[5], so approximately one half of MSM reported also had sex with a woman and one third had been married to a woman(7). Therefore, MSM may play a bridging role in the spread of HIV and other STDs from the high-risk population to the general population. In a word, MSM have become one of the high-risk groups for HIV infection and transmission.

Recent evidence suggested that anti-retroviral therapy (ART) reduces the probability of HIV transmission, particularly if initiated at early stages of the disease (8-10). Therefore, the Chinese Center for Disease Control and Prevention had assisted eight pilot cities to carry out ***universal test-and-treat strategy*** for MSM about AIDS since 2013. Regardless of the

CD4+T cell level, people who infected HIV just into treatment in this strategy. ***Current antiviral treatment strategies*** is that only when people who infected HIV and the CD4+T cell level less than or equal to 350 can be treated. Previous mathematical models showed that ART would substantially reduce the new infections and deaths (11-15), but one important concern was that increased ART use created more multidrug-resistant strains (12). There were studies demonstrating that antiviral therapy can extend the life expectancy of HIV/AIDS infected individuals, but extended life span increased the risk to infect others (11). Voluntary counseling and testing (VCT) was one of the important measures to control the transmission of HIV (16). Junjie Wang used a mathematical model to simulate the impact of VCT on the transmission of HIV (17), which found that increased VCT coverage rate can effectively reduce the transmission of HIV among MSM. Condom use has been considered to a effectively measure to control the transmission of HIV, some studies showed that the low frequency condom use was the risk factor for the transmission of HIV among MSM(18). Junjie Wang and Chunpeng Zang used different mathematical models to simulate the impact of condom use on the transmission of HIV, which found that increased condom use frequency can effectively reduce the transmission of HIV among MSM (13, 17).

Previous studies have focused on the impact of ART, VCT or condom use on the transmission of HIV among MSM in qualitative. The current study will assess the impact of different antiviral therapy strategies (no antiviral therapy strategy, current antiviral treatment strategy, universal test-and-treat strategy) on HIV infections and AIDS cases.

2. Methods:

Model Structure: We constructed a compartmental HIV transmission model, based on the characteristics of HIV prevalence. Our model structure followed the model used by Chunpeng Zang (13). Figure 1 displayed our compartmental HIV model, whereby individuals in our population progress over the different stages of the infection. Treatment eligibility was based on different antiviral therapy strategies. The model was integrated numerically and tracked the dynamics of the population in each compartment as it changed over time.

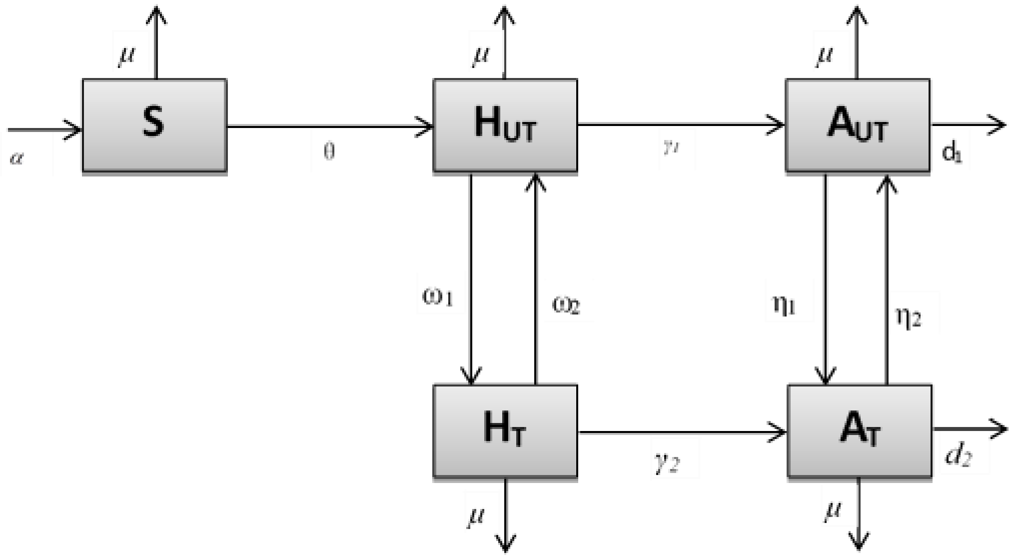

Figure 1. The flow diagram of model with antiviral therapy: individuals in our model were divided into 5 key HIV infection statuses: susceptible or HIV negative (S), HIV infected but not treated (H_{UT}), HIV infected and treated (H_T), progression to AIDS but not treated (A_{UT}), and progression to AIDS and treated (A_T).

α *annual recruitment number of susceptible people*
θ Force of infection
μ *The natural death rate*
γ_1 The conversion rate of H_{UT} to A_{UT} crowds
d_1 AIDS case fatality rate in A_{UT} crowds
d_2 AIDS case fatality rate in A_T crowds
ω_1 Conversion rate H_{UT} crowds to H_T
ω_2 Conversion rate from H_T crowdsto H_{UT}
η_1 Conversion rate from A_{UT} crowdsto A_T
η_2 Conversion rate from A_T crowds to A_{UT}
γ_2 Conversion rate H_T to A_T

System of differential equations of Compartment model

$$\begin{cases} \frac{dS}{dt} = \alpha - \theta S - \mu S \\ \frac{dH_{UT}}{dt} = \theta S + \omega_2 H_T - \omega_1 H_{UT} - \gamma_1 H_{UT} - \mu H_{UT} \\ \frac{dH_T}{dt} = \omega_1 H_{UT} - \omega_2 H_T - \gamma_2 H_T - \mu H_T \\ \frac{dA_{UT}}{dt} = \gamma_1 H_{UT} + \eta_2 A_T - \eta_1 A_{UT} - (\mu + d_1) A_{UT} \\ \frac{dA_T}{dt} = \gamma_2 H_T + \eta_1 A_{UT} - \eta_2 A_T - (\mu + d_2) A_T \end{cases}$$

3. Data and Parameter Estimation:

Sentinel surveillance results have shown that the HIV positive rates among MSM population in different regions have been consistently greater than 1% and are increasing year by year, since 2005. Therefore we choose year 2005 as a starting point.

Lu et al (19) estimated that the number of MSM who had anal sex behaviors were 3,600,000-7,100,000 in China 2005.

Assuming that the estimated number obeyed the uniform distribution(20), we carried out 1000 times by MonteCarlo Method, the mean was 5,353,400. So there were 5,353,400 MSM in China 2005. There were 540,000-760,000 HIV infections and AIDS cases, the mean was 650,000, and AIDS cases were 65,000-85,000, the mean was 75,000 in China 2005(21). There were 34,700-60,400 MSM of HIV infections and AIDS cases, the mean was 47,500 in China 2005(19). Therefore, MSM accounted for 7.3% of the total HIV infections and AIDS cases in 2005. We assumed that 7.3% of the total AIDS cases were MSM in 2005. So there were 5,475 MSM AIDS cases, and 42,025 were HIV infections in 2005. In 2005, about 69.4% MSM infected with HIV were conformed to the treatment guidelines(22), and the treatment coverage was 75%(23). Therefore, the rate of MSM infected with HIV who received treatment was 52.05%, and the rate of MSM was AIDS cases who received treatment was 75%. So in 2005 the population of susceptible (S) was 5305900, the population of HIV infected but not treated (H_{UT}) was 20151, the population of HIV infected and treated (H_T) was 21874, the population of progression to AIDS but not treated(A_{UT}) was 1369, and the population of progression to AIDS and treated (A_T) was 4106.

α: annual recruitment number of susceptible people

$$\alpha = m \cdot P \cdot (1-\mu)^{14} \cdot b \cdot a$$

m represented the proportion of MSM account for sexually mature males (>14 years), *m*=3.5%(24). *P* represented the total population of each year(25). *b* represented the birth rate of each year(25). *a* represented the proportion of boys account for newly-born population of each year(25). *P*, *b* and *a* were data from 1992 to 2011. μ represented the natural death rate, μ=0.0143(26).

θ: Force of infection means the transition coefficient of individuals from the susceptible to the infection states

$$\theta = \frac{\kappa_1\beta_1 H_{UT} + \kappa_2\beta_2 H_T + \kappa_3\beta_3 A_{UT} + \kappa_4\beta_4 A_T}{N}$$

κ represented the number of unprotected anal sex acts in per unit time. β represented the infection probability of single unprotected anal sex. $\kappa\beta$ was called the transmission coefficient, and different infected have different $\kappa\beta$. $\kappa_1\beta_1$ represented the transmission coefficient of (H_{UT}), $\kappa_1\beta_1$=0.284(27-30). $\kappa_2\beta_2$ represented the transmission coefficient of (H_T), $\kappa_2\beta_2$=0.0264[27, 28, 31]. $\kappa_3\beta_3$ represented the transmission coefficient of (A_{UT}), $\kappa_3\beta_3$=0.599[27, 28, 31]. $\kappa_4\beta_4$ represents the transmission coefficient of (A_T), $\kappa_4\beta_4$=0.284(13).

The definition, baseline value and source of the remaining parameters were shown in Table 1.VCT rate and condom use rate were the results of the comprehensive of many literature. In general test and treat strategy ω1=0.75 since 2013.

Table 1. Parameters and baseline values

Parameters	Definition	Value	Source
γ_1	Progression rate from H_{UT} to A_{UT}	0.1	[31, 34]
γ_2	Progression rate from H_T to A_T	0.05	[35]
ω_1	Antiviral therapy coverage rate for H_{UT}	0.35	[36]
ω_2	Exit rate of H_T	0.08	[14]
η_1	Antiviral therapy coverage rate for A_{UT}	0.75	[24]
η_2	Exit rate of A_T	0.08	[14]
d_1	Disease-related death rate for A_{UT}	0.3	[37, 38]
d_2	Disease-related death rate for A_T	0.05	[37, 38]
V	VCT coverage rate	0.15	[19, 39]
C	Condom use rate	0.5	[19, 40-42]

Abbreviation: A_T, progression to AIDS and treated. A_{UT}, progression to AIDS but not treated. H_T, HIV infected and treated. H_{UT}, HIV infected but not treated. VCT, voluntary counseling and testing.

4. Sensitivity Analysis: We conducted a one-way sensitivity analysis to determine how the model results were impacted by each parameter individually. In particular, we re-estimated the model by varying each parameter around the baseline values, while holding all other parameters fixed. This allowed us to understand which parameters most influence our results.

5. Results:

Reduction of HIV infections after universal test-and-treat strategy:
Figure 2 displayed results about the comparison of different treatment strategies for HIV/AIDS epidemic among MSM. In no antiviral therapy strategy cumulative HIV infections and cumulative AIDS cases will increase from approximately 40,000 and 5000 in 2005 to approximately 2,760,000 and 570,000 in 2025, respectively. In current antiviral therapy strategy the number will increase to approximately 530000 and 150,000 in 2025 respectively, and in universally test-and-treat strategy the number will increase to approximately 350,000 and 110,000 in 2025 respectively.

Universal test-and-treat strategy Compare with no antiviral therapy strategy, cumulative HIV infections and cumulative AIDS cases will reduce on 87.3% and 80.7%, respectively. Compare to current antiviral therapy strategy cumulative HIV infections and cumulative AIDS cases will reduce on 34% and 36.7% in universal test-and-treat strategy.

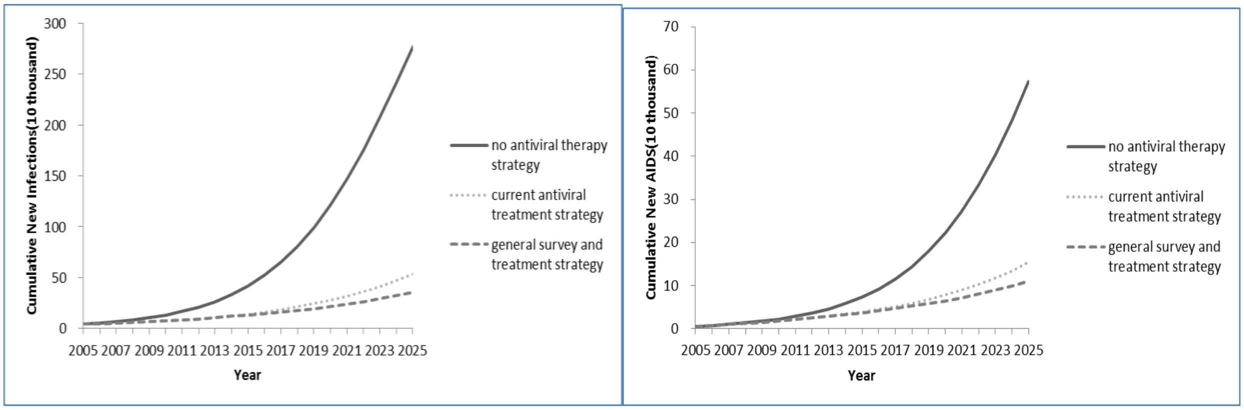

Figure 2. The comparison of different treatment strategies for HIV/AIDS epidemic among MSM

Effects of different interventions: Figure 3 displayed results about the effects of different interventions for HIV/AIDS epidemic among MSM.

Figure 3 (a_1) and figure 3 (a_2) showed that when ART coverage rate in HIV infected (ω_1) under baseline value cumulative new infections and cumulative new AIDS cases increased over a 20-year period from 42025 and 5475 in 2005 to approximately 530,000 and 150,000 in 2025, respectively. With the increased of ω_1 in the same year, cumulative new infections and cumulative new AIDS cases would reduce respectively. Based on estimated minimum coverage, if ω_1 increase every one double by 2025 cumulative HIV infections and cumulative AIDS cases with an average reduce on 24.2% and 23.2% respectively.

Figure 3(b_1) and figure 3(b_2) showed that no matter how much was the value of η_1, the number of cumulative new infections and cumulative new AIDS cases were similar. With the increase of η_1 in the same year, cumulative new infections would reduce, but cumulative new AIDS cases would increase.

Figure 3(c_1) and figure 3(c_2) showed that when *V* under baseline value cumulative new infections and cumulative new AIDS cases increased over a 20-year period from 42025 and 5475 in 2005 to approximately 1600000 and 330000 in 2025 respectively. With the increase of *V* in the same year, cumulative new infections and cumulative new AIDS cases would reduce. Based on estimated minimum coverage, if *V* increase every one double by 2025 cumulative HIV infections and cumulative AIDS cases with an average reduce on 14.3% and 13.5% respectively.

Figure 3(d_1) and figure 3(d_2) showed that when *C* under baseline value cumulative new infections and cumulative new AIDS cases increased over a 20-year period from 42025 and 5475 in 2005 to approximately 240000 and 60000 in 2025 respectively. With the increase of *C* in the same year, cumulative new infections and cumulative new AIDS cases would reduce. Based on estimated minimum coverage, if *C* increase every one double by 2025 cumulative HIV infections and cumulative AIDS cases with an average reduce on 69.5% and 66.3% respectively.

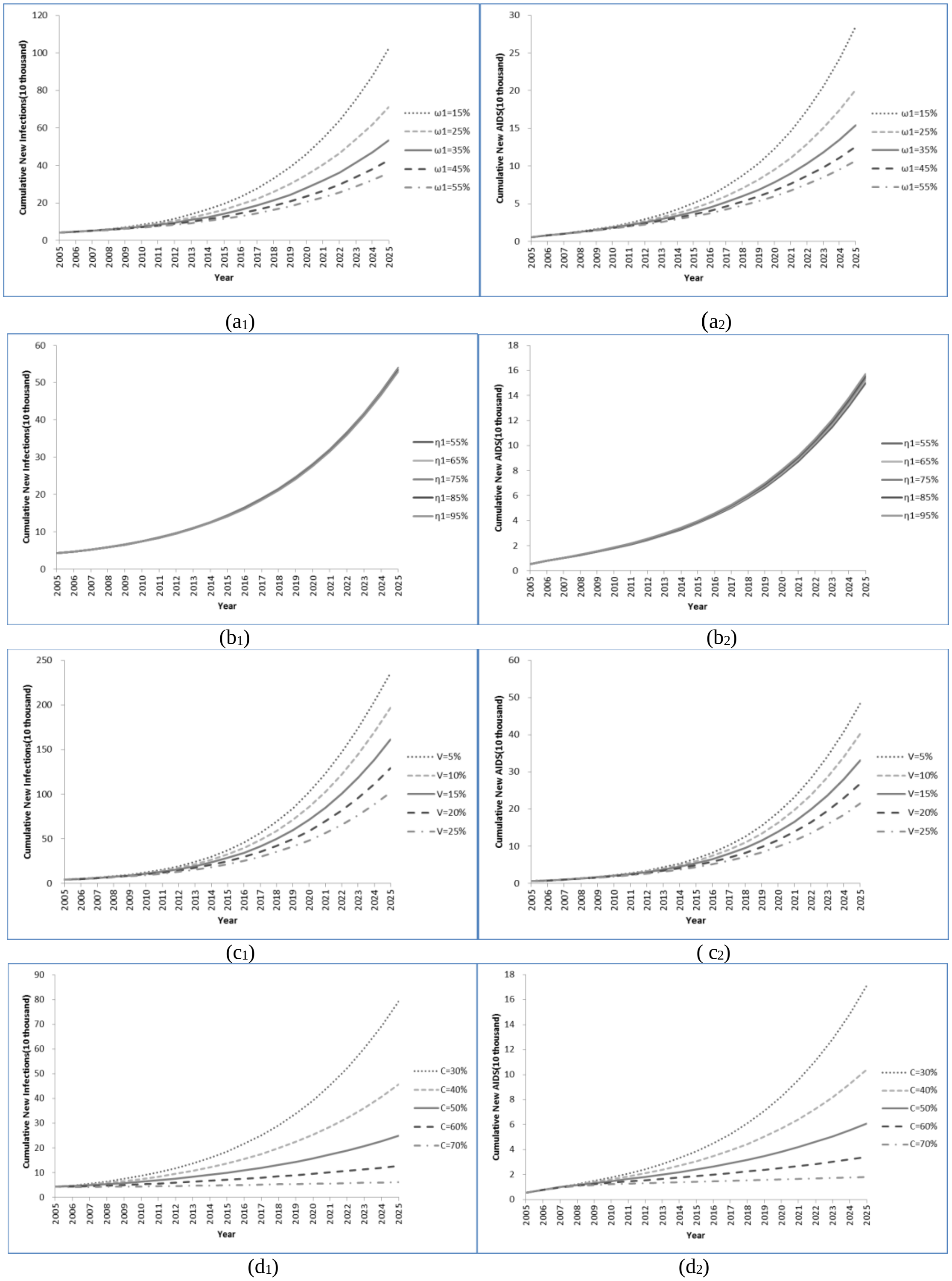

Figure 3. The effects of different interventions for HIV/AIDS epidemic among MSM
Abbreviation: ω_1, antiviral therapy coverage rate for HIV infected but not treated. η_1, antiviral therapy coverage rate for progression to AIDS but not treated. *V*, voluntary counseling and testing coverage rate. *C*, condom use rate.

Sensitivity Analysis: We conducted a one-way sensitivity analysis for different parameters. Table 2 indicated that ω_2, γ_2, d_1 and d_2 had a great impact on both cumulative new infections and cumulative new AIDS cases, but γ_1 only had a great impact on cumulative new AIDS cases. Although these parameters had a great impact on results, did not change the trend of results, and results were only sensitive to the parameters that represent interventions (ω_2, γ_2, d_1,d_2 and γ_1).

Table 2. The effects of different parameters for HIV/AIDS epidemic among MSM

Parameters	Baseline Value (%)	Ranges (%)	2025 Cumulative New infections (10,000)	2025 Cumulative new AIDS cases (10,000)
m	3.5	[1.5,5.5]	[51.5, 54.6]	[15.1, 15.6]
ω_2	8	[4,12]	[46.6, 59.9]	[13.6, 17.1]
η_2	8	[4,12]	[53.0, 53.8]	[15.7, 15.1]
γ_1	10	[5,15]	[52.7, 53.8]	[11.1, 19.6]
γ_2	5	[3,7]	[50.0, 56.4]	[12.0, 18.7]
d_1	30	[20,40]	[58.1, 49.6]	[17.6, 13.7]
d_2	5	[3,7]	[56.8, 50.4]	[17.3, 13.8]

6. Discussion: The modeling results indicated that universal test-and-treat strategy can effectively reduce HIV compared to other strategies. Compare to no antiviral therapy strategy, current antiviral therapy strategy, universal test-and-treat strategy can significantly reduce cumulative HIV infections and cumulative AIDS cases, and slightly increase the survival about HIV infections and AIDS patients. To 2025, the number of MSM living with HIV who had universal test-and-treat strategy is 12% (350000/2760000) of them who had no antiviral therapy strategy. Therefore, these strategies would have better effects. These findings were consistent with those of studies (13, 15, 17, 32).

Improve frequency of condom use was the best way to control HIV/AIDS epidemic among MSM. Increasing the coverage of ART among HIV infections ($\omega1$) could effectively reduce HIV infections and AIDS cases, but increasing the coverage of ART among AIDS cases ($\eta1$) could not reduce HIV infections and even increase AIDS cases. In fact, HIV infections were easy to be ignored, and would not receive antiviral treatment. Therefore, universal test-and-treat strategy is very important for controlling HIV epidemic among MSM. VCT and the use of condoms could effectively reduce HIV infections and AIDS cases. Among three interventions, increasing the frequency condoms usage was the best effect. Increasing one times of condom use frequency, the number of MSM living with HIV would reduce an average of 69.5% to 2025.Therefore, reducing the frequency of unprotected anal sex behaviors was the best way to reduce HIV infections and AIDS cases.

Though the one-way sensitivity analysis, we found that some parameters had a great impact on results, but these parameters were affected by the parameters that represent interventions, and the trend of results did not change, so our results were stable.

There were some limitations in this study. Firstly, our study only considered that MSM who was infected with HIV by MSM, and not considering by other groups. Only considering the transmission of HIV among MSM by anal sex behaviors, and not considering by others. Secondly, our model was not stratified by risk, ethnicity, or age. Future models should attempt to achieve more granularities. Then, we did not consider costs of ART, VCT and condom use. Future research should include a cost-effectiveness analysis to identify the optimal policy.

In summary, universal test-and-treat strategy is the best among three antiviral therapy strategies. Each of the three interventions would effectively control the HIV/AIDS epidemic among MSM, but it was hard to completely control the HIV/AIDS epidemic among MSM. Increasing the condom use was the best among these interventions.

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