Evaluating the Impact of Test-and-Treat on the HIV Epidemic among MSM in China Using a Mathematical Model

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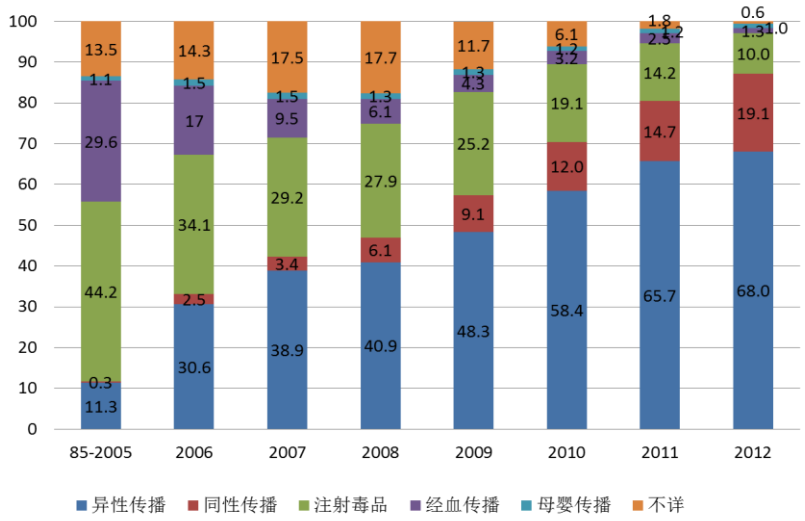
背景知识

艾滋病：

- 艾滋病（AIDS）是人类免疫缺陷病毒（HIV）攻击辅助性T淋巴细胞，造成机体免疫功能进行性下降，继而引发一系列机会性感染及相关肿瘤的慢性传染性疾病。

我国现状：

- 我国艾滋病疫情主要经历了三个阶段：传入期（1985 - 1988 年）、扩散期（1989 - 1993 年）和高速增长期（1994年 - 今）。传播途径由血液传播为主转变为性传播为主，男男同性恋传播增速明显；由在特定人群中流行过度到向一般人群扩散。



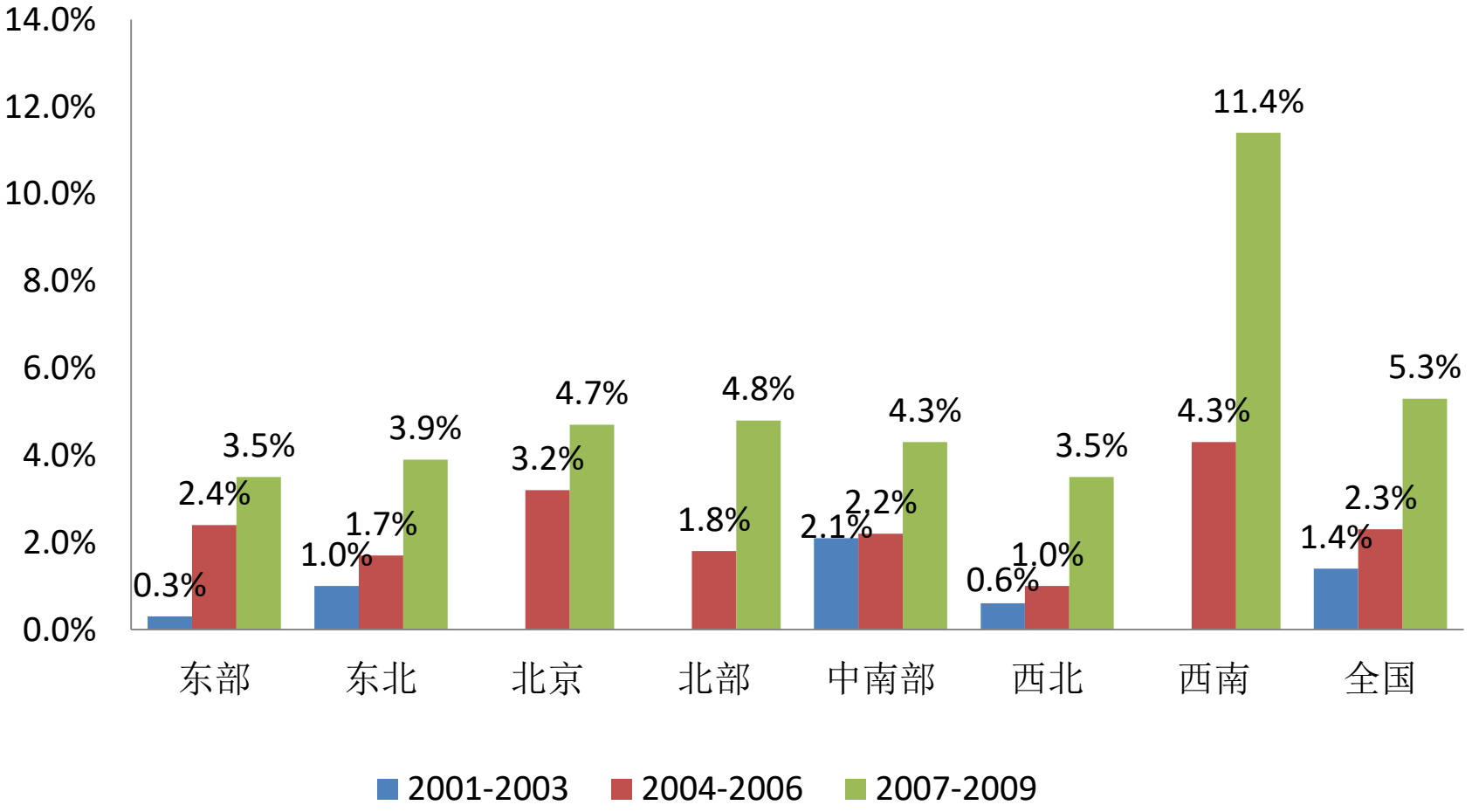
我国HIV/AIDS当年报告数					
	报告人数	异性（%）	男男（%）	吸毒（%）	当年死亡
2012年	82434	68	19	10	20003
2013年	90119	69	21	7	19716
2014年	103501	66	26	6	20650

背景知识

- The national HIV free antiretroviral therapy program (“Four-Free-One-Care Policy”) has been implemented since 2003. By the end of 2014, a cumulative number of more than 300,000 HIV/AIDS patients had received free antiretroviral therapy.

- The current treatment standard is CD4 cell count <350 cells/μl.

我国男男同性恋HIV/AIDS流行情况

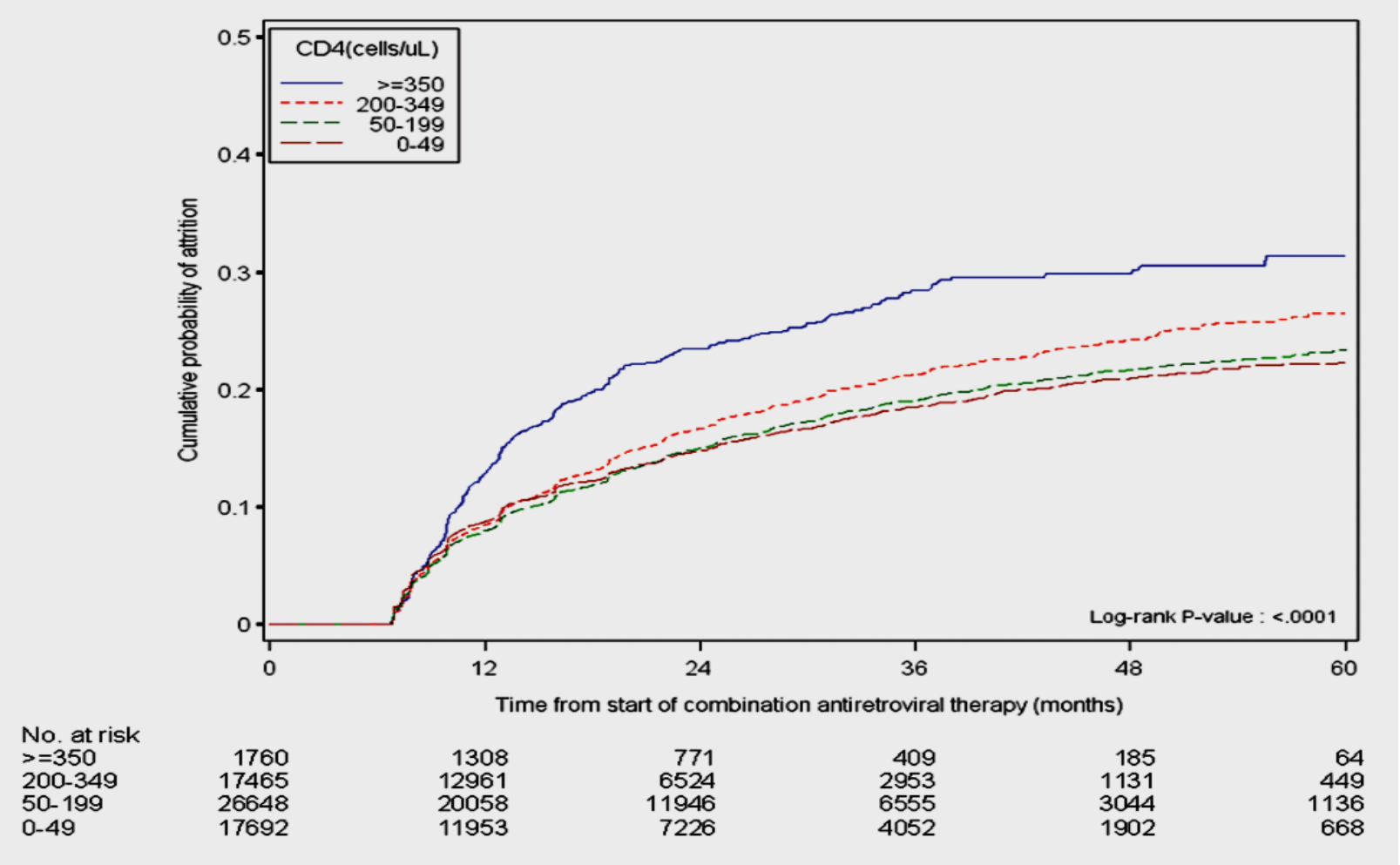


Chow EP, etc. Sex Transm Dis. 2011 Sep;38(9):845-57

男男同性恋人群12个月随访的前瞻性队列（北京，朝阳区）

年份		HIV(%)	梅毒(%)
2005	感染率	3.2(17/526)	11.2(59/526)
2006	感染率	4.8(26/541)	19.8(107/541)
	新发感染率	2.6	16.9
	保持率	86.2(437/507)	
2007	感染率	4.5(25/550)	29.3(161/550)
	新发感染率	3.37	9.32
	保持率	87.0(457/525)	
2009	感染率	6.3 (61/964)	17.7(171/964)
	新发感染率	8.09	5.92
	保持率	85.5(692/809)	

基线CD4水平与退出抗病毒治疗的概率

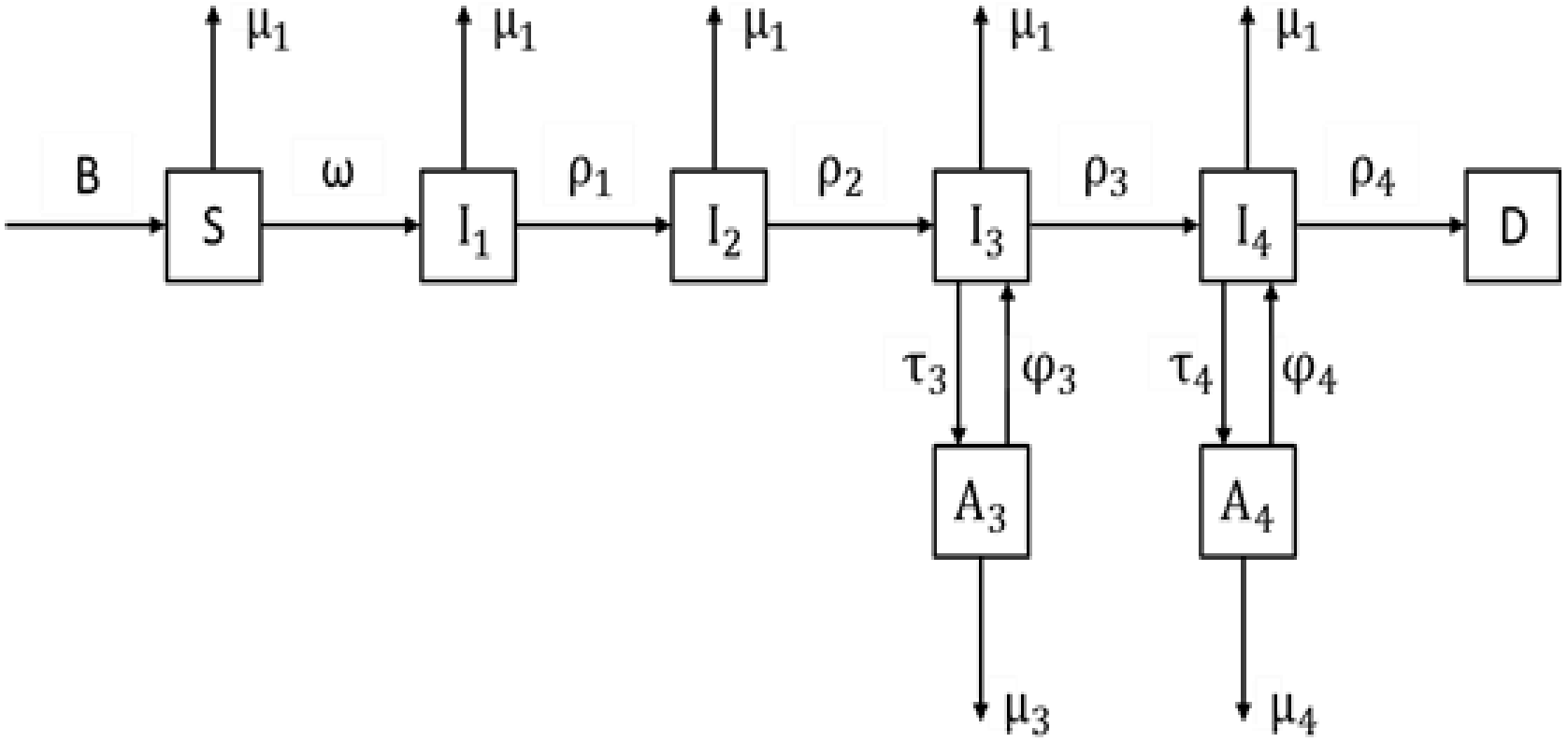


No. at risk						
>=350	1760	1308	771	409	185	64
200-349	17465	12961	6524	2953	1131	449
50-199	26648	20058	11946	6555	3044	1136
0-49	17692	11953	7226	4052	1902	668

对抗病毒治疗库2003-2010年的数据分析显示，治疗前基线CD4>=350的患者，退出治疗的概率更高。

Zhu *et al, PLOS One.* 2012, 7: e39414

The model



The model

$$
\begin{cases}
\dfrac{dS}{dt} = B - \omega - \mu_1 S \\
\dfrac{dI_1}{dt} = \omega - \rho_1 I_1 - \mu_1 I_1 \\
\dfrac{dI_2}{dt} = \rho_1 I_1 - \rho_2 I_2 - \mu_1 I_2 \\
\dfrac{dI_3}{dt} = \rho_2 I_2 + \varphi_3 A_3 - \rho_3 I_3 - \mu_1 I_3 - \tau_3 I_3 \\
\dfrac{dI_4}{dt} = \rho_3 I_3 + \varphi_4 A_4 - \rho_4 I_4 - \mu_1 I_4 - \tau_4 I_4 \\
\dfrac{dA_3}{dt} = \tau_3 I_3 - \varphi_3 A_3 - \mu_3 A_3 \\
\dfrac{dA_4}{dt} = \tau_4 I_4 - \varphi_4 A_4 - \mu_4 A_4
\end{cases}
$$

S: HIV susceptible part,

I_1: acute HIV infection part (first 3 months of infection),

I_2: early incubation period of HIV infection (early incubation) part (CD_4^+ T-cell count above 350 cells/μL),

I_3: late incubation period of HIV infection (late incubation) part (CD_4^+ T-cell count between 200 and 350 cells/μL),

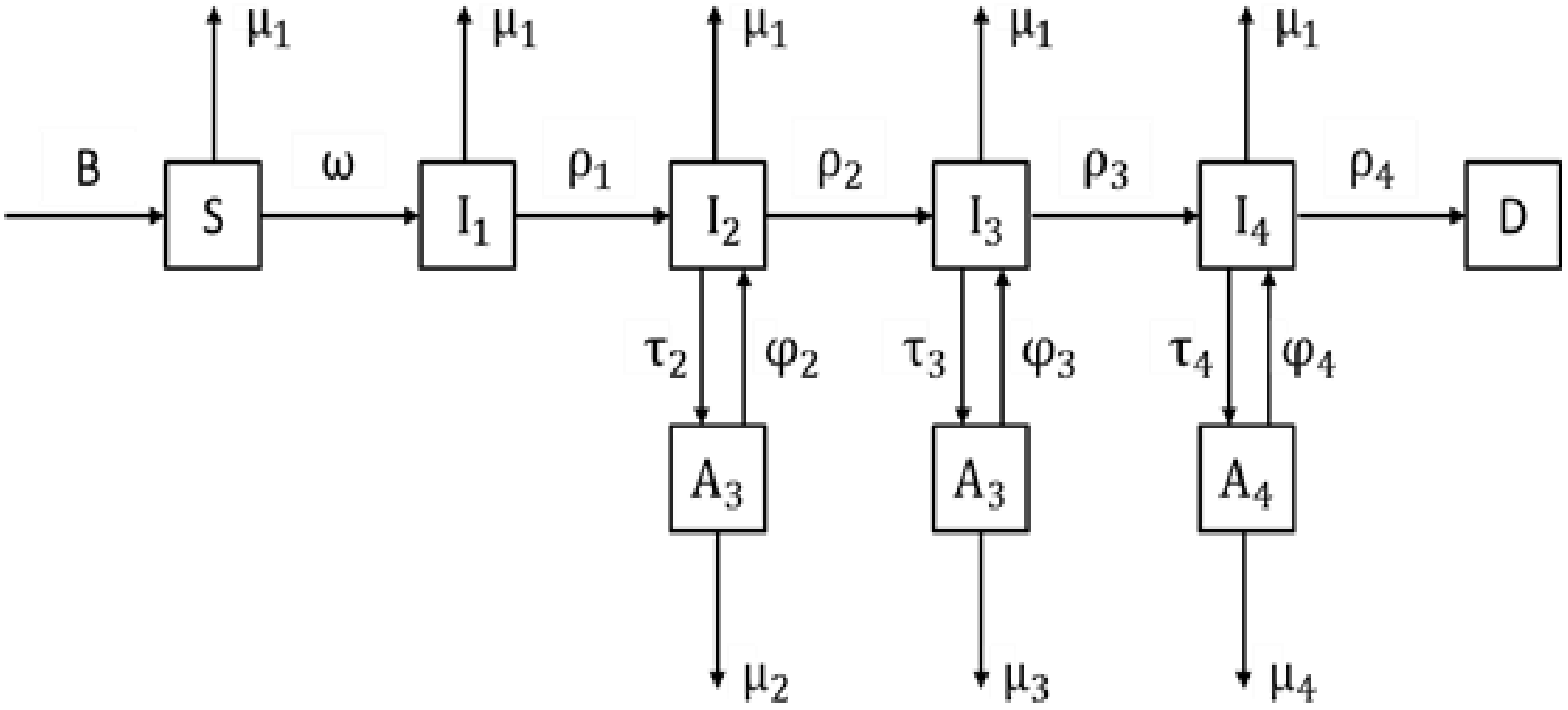
I_4: AIDS part (CD_4^+ T-cell count below 200 cells/μL),

D: People died from AIDS,

A_3: ART population from late incubation period of HIV infection,

A_4: ART population from AIDS part

The model


B
S
ω
I1
ρ1
I2
ρ2
I3
ρ3
I4
ρ4
D
μ1
μ1
μ1
μ1
μ1
τ2
φ2
τ3
φ3
τ4
φ4
A3
A3
A4
μ2
μ3
μ4

The model

$$
\begin{cases}
\dfrac{dS}{dt} = B - \omega - \mu_1 S \\
\dfrac{dI_1}{dt} = \omega - \rho_1 I_1 - \mu_1 I_1 \\
\dfrac{dI_2}{dt} = \rho_1 I_1 + \varphi_2 A_2 - \rho_2 I_2 - \mu_1 I_2 - -\tau_2 I_2 \\
\dfrac{dI_3}{dt} = \rho_2 I_2 + \varphi_3 A_3 - \rho_3 I_3 - \mu_1 I_3 - \tau_3 I_3 \\
\dfrac{dI_4}{dt} = \rho_3 I_3 + \varphi_4 A_4 - \rho_4 I_4 - \mu_1 I_4 - \tau_4 I_4 \\
\dfrac{dA_2}{dt} = \tau_2 I_2 - \varphi_2 A_2 - \mu_2 A_2 \\
\dfrac{dA_3}{dt} = \tau_3 I_3 - \varphi_3 A_3 - \mu_3 A_3 \\
\dfrac{dA_4}{dt} = \tau_4 I_4 - \varphi_4 A_4 - \mu_4 A_4
\end{cases}
$$

Data sources

- **Data sources**

  We chose the parameter values either through calculations using existing data or based on literature reviews (Table 1). The existing data included the HIV prevalence rate among MSM, CD4 count and ART uptake of HIV infected MSM which were obtained from the web-based Beijing HIV/AIDS information subsystem, part of the CRIMS. CRIMS routinely collects HIV data throughout the country including case reports, sentinel surveillance, behavioral interventions, CD4 count and ART.

Parameters

Table1. Values for input parameters for the model and references

Description of parameter	Value	References
Demographic characteristics of MSM population		
Proportion of MSM among sexually active men (≥15 years old)	1%-2%	[26]
Population size of MSM in 2010	108,000	[a]
Average life expectancy of HIV negative MSM	79 years	[27]
Sexually active life years of MSM	46 years	[26]
CD4 based natural history of HIV infection with or without ART		
Length of acute HIV infection	3 months	[22-23]
Length of early latent infection	4.33 years	[29]
Length of late latent infection	2.66 years	[29]
Length of AIDS period	2 years	[22,24]
Life expectancy of PLHIV initiating ART at early latent infection stage	79 years	[30-32]
Life expectancy of PLHIV initiating ART at late latent infection stage	33.7 years	[b]
Life expectancy of PLHIV initiating ART at AIDS stage	22.2 years	[b]
Treatment withdrawal or failure of HIV infected MSM		
Proportion of ART patients withdrawing or failing in treatment	3%-7%	[c]
Infectiousness of HIV infected MSM by disease stage		
Average number of people infected by a HIV positive MSM in a year	0.12-0.13	[d]
Acute infection	1.2-1.3	
Early latent infection	0.12-0.13	
Late latent infection	0.24-0.26	
AIDS	0.6-0.65	
Transmission risk of HIV infected MSM on ART		
Relative risk of Transmission of HIV infected MSM on ART versus those not on ART	0.04-0.1	[35]
HIV testing rate and ART coverage		
HIV testing rate under current practice	50%	[c]
HIV testing rate under test-and-treat strategy	50%-90%	
ART coverage under current practice	39%	[c]
ART coverage under test-and-treat strategy	39%-90%	

[a] Calculated from China population and employment statistics

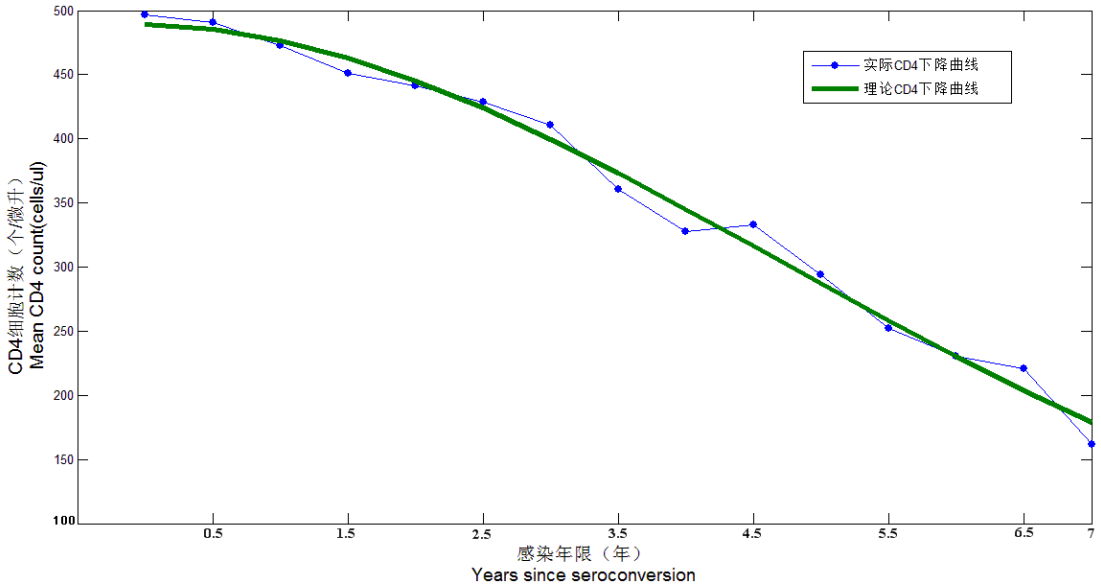
[b] Calculation method described in Supporting Information File S1

[c] Calculated from CRIMS

[d] Calculation method described in Supporting Information File S2

Parameters

Actual and theoretical curve of pre-ART CD4 decline of HIV-positive MSM



For HIV-positive MSM who had not received ART, the HIV incubation period was estimated to be 7 years. The length of the early period of HIV incubation was estimated to be 4.33 years, during which CD4 experienced an average decline of 35 cells/μl per year. The late period of HIV incubation was estimated to last 2.66 years, during which CD4 decreased at an average rate of 56 cells/μl per year.

S Luo, et al. Chin J AIDS&STD. 2013, 19(11): 780-784.

Parameters

- **Life expectancy of PLHIV (people living with HIV) initiating ART at different stage**

  Initiating ART at early latent infection stage: 79 years

  Initiating ART at late latent infection stage: 33.7 years

  Initiating ART at AIDS stage: 22.2 years

Analysis plan

- We predicted the annual number of new HIV infections, total number of new HIV infections and total number of PLHIV among MSM in Beijing for the time frame 2010 to 2022 under the following conditions: (1) current practice: a testing rate of 50% and ART coverage of 39%; (2) 70% test-and-treat coverage since 2013 (optimal condition 1): both testing rate and ART coverage reaching 70% in 2013; (3) 90% test-and-treat coverage since 2013 (optimal condition 2): both testing rate and ART coverage reaching 90% in 2013; and (4) scaling up test-and-treat coverage every year until it reaches 90% (optimal condition 3): testing rate increasing by 5% every year from 50% to 90% through 2013 to 2020 and thereafter remaining at 90% till 2022; ART coverage increasing from 39% to 55% in 2013, increasing by 5% every year from 55% to 90% through 2014 to 2020 and remaining at 90% till 2022.

Numerical results

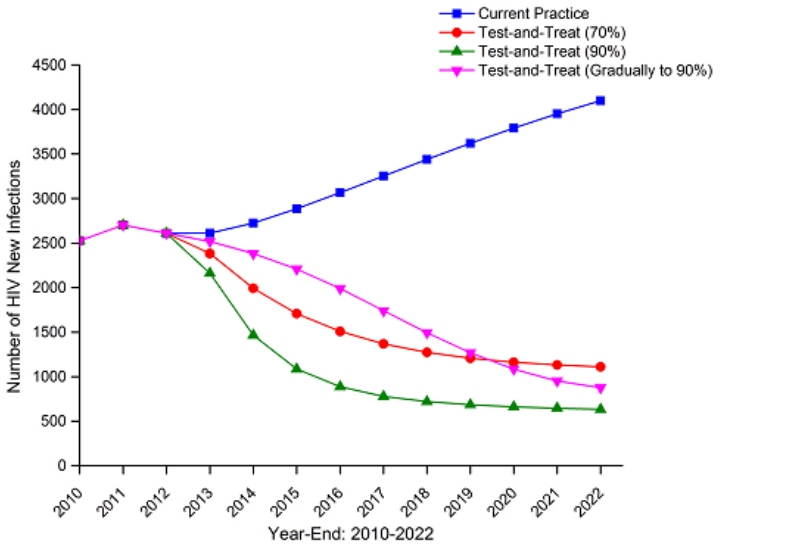


Fig 2. Number of HIV new infections among MSM, Beijing, 2010–2022.

doi:10.1371/journal.pone.0126893.g002

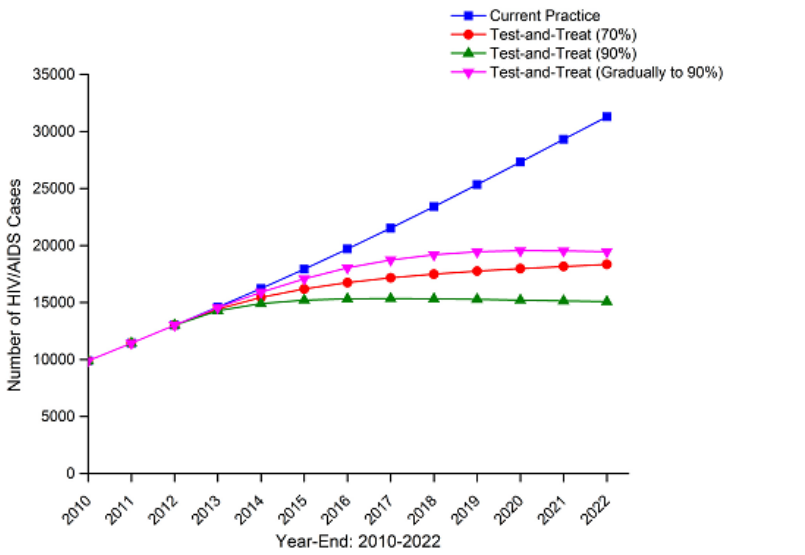


Fig 3. Number of MSM living with HIV/AIDS, Beijing, 2010–2022.

doi:10.1371/journal.pone.0126893.g003

Numerical results

Table2. Reduction of new HIV infections from HIV testing rate and ART coverage among MSM in Beijing

HIV testing rate & ART coverage	Value for parameter	Total number of new infections over 10 years (2013-2022)	% Decrease from current practice
Current practice			
	HIV testing rate=50% ART coverage=39%	33444	-
Test-and-Treat			
Optimal condition 1	HIV testing rate=70%，ART coverage=70%	14840	55.6%
Optimal condition 2	HIV testing rate=90%，ART coverage=90%	9718	70.9%
Optimal condition 3	Annual increase of testing rate by 5% from 50% to 90%, gradual increase of ART coverage from 39% to 90%	16511	50.6%

Note: We assume that the Test-and-Treat policy is started from the beginning of 2013.

Numerical results

Table3. Occurrence of 'turning point' on the curve of the HIV incidence at different levels of Test-and-Treat coverage

Occurrence of 'Inflection point'	HIV testing Rate	ART coverage	ART coverage by CD4 level	
			CD4>350/uL	CD4≤350/uL
	50%	55%	30%	80%
	55%	53%	25%	80%
At the end of 2020	60%	50%	20%	80%
	65%	48%	15%	80%
	70%	45%	10%	80%
	50%	58%	35%	80%
	55%	55%	30%	80%
At the end of 2015	60%	53%	25%	80%
	65%	50%	20%	80%
	70%	48%	15%	80%
	50%	60%	40%	80%
	55%	58%	35%	80%
At the end of 2013	60%	55%	30%	80%
	65%	53%	25%	80%
	70%	50%	20%	80%

Note: We assume that the Test-and-Treat policy is started from the beginning of 2013.

Numerical results

Table 4. Minimum Test-and-Treat coverage for achieving 25% reduction of HIV incidence among MSM in China

Impact on HIV incidence	HIV testing rate	ART coverage	ART coverage by CD4 level	
			CD4>350/uL	CD4≤350/uL
25% reduction of HIV incidence among MSM in 2015 compared with 2010	50%	75%	70%	80%
	55%	70%	60%	80%
	60%	65%	50%	80%
	65%	60%	40%	80%
	70%	55%	30%	80%

Note: We assume that the Test-and-Treat policy is started from the beginning of 2013.

Sensitivity analyses

Table5. Sensitivity analyses for MSM in Beijing

Scenarios	HIV testing rate=70%, ART coverage=70%		HIV testing rate=90%, ART coverage=90%		Annual increase of testing rate by 5% from 50% to 90%, annual increase of ART coverage by 10% from 10% to 90%	
	Total number of new infections over 10 years	% Change from current practice	Total number of new infections over 10 years	% Change from current practice	Total number of new infections over 10 years	% Change from current practice
Current practice [a]	33444					
Infectiousness of HIV+ MSM						
0.13-0.15	19973	40.3%	12831	61.6%	22193	33.6%
0.10-0.12	11008	67.1%	7368	78.0%	12229	63.4%
Relative risk of transmission of HIV+ MSM on ART versus those not on ART						
0.1-0.15	17494	47.7%	12273	63.3%	19207	42.6%
0.5-0.6	40995	22.6%	36044	7.8%	43326	29.5%
Percentage of ART withdrawal or failure						
7%-15%	18191	45.6%	12183	63.6%	19263	42.4%
15-20%	21500	35.7%	14700	56.0%	22062	34.0%

[a] The sensitivity analyses results are compared to estimates under current practice in which 50% of MSM receive HIV test, 39% of HIV positive MSM take ART, 12-13 per 100 people a year are infected with HIV from a HIV positive MSM, relative transmission risk of HIV positive MSM on ART is 0.04-0.1, and the proportion of ART withdrawal or failure is 3%-7%.

Sensitivity analyses

- Sensitivity analyses indicated that infectiousness of HIV positive MSM (both on ART and not on ART) (β) was the most sensitive parameter. If the infectiousness of HIV positive MSM (β) increased from 0.12-0.13 to 0.13-0.15, the reduction of HIV new infections over 10 years would decrease from 55.6% to 40.3% under a test-and-treat coverage of 70%. When the infectiousness decreased to 0.10-0.12, the total number of HIV new infection over 10 years would be reduced by 67.1%, much higher than 55.6% (Table 2, 5).
- Relative risk of transmission of HIV positive MSM on ART (ε) and proportion of treatment withdrawal or failure (φ) were moderately sensitive. If the relative risk of transmission (ε) increased from the current level of 0.04-0.1 to 0.1-0.15, then the reduction in HIV new infections over 10 years was decreased from 70.9% to 63.3% under 90% coverage of test-and-treat. When the relative transmission risk increased to a level as high as 0.5-0.6, there was almost no impact on reduction of HIV new infection even with 90% coverage of test-and-treat (Table 2, 5).

Sensitivity analyses

- If the proportion of treatment withdrawal or failure (φ) increased from 3-7% to 7-15%, the reduction of total number of HIV new infection over 10 years would decrease from 50.6% to 42.4% under a gradual increase to 90% coverage of test-and-treat strategy. When the proportion increased further to 15-20%, the reduction of HIV new infection over 10 years would decrease to 34.0% (Table 2, 5).

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Thank you for your attention!