

The Economic Evaluation of PrEP Strategy among MSM

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Received: 01 Apr, 2019 | Accepted: 03 May, 2019 | Published: 10 May, 2019

Citation: Zhong Y, Zhong X, Peng B, Zhang Y (2019) The Economic Evaluation of PrEP Strategy among MSM. *J Epidemiol Public Health Rev* 4(1): dx.doi.org/10.16966/2471-8211.170

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Abstract

Objective: Pre-exposure prophylaxis (PrEP) for AIDS is a biomedical prevention strategy. This research aims to conduct an economic evaluation of PrEP strategy through an analysis of its cost-effectiveness and cost-utility.

Methods: Based on findings of previous studies and data from literature retrieval, this research adopts Markov model to compute the quality-adjusted life years (QALY) gained by MSM (men who have sex with men) as well as the cost and economic burden of disease with or without PrEP, and further analyzes PrEP's cost-effectiveness and cost-utility.

Results: (1) If promoting PrEP to 10 million MSM for one year, 340,000 new HIV infections (suboptimal medication adherence) or 507,000 new HIV infections (optimal medication adherence) can be prevented. (2) With suboptimal medication adherence, the total cost of PrEP for 340,000 people in 30 years is 52.74 billion RMB, while without PrEP, the economic burden of the disease reaches 95.49 billion RMB. The cost of using PrEP to prevent one HIV infection is 155,100 RMB, and it can save 15,700 RMB per QALY gained. (3) With optimal medication adherence, it costs 61.97 billion RMB to provide PrEP for 507,000 people in 30 years, while 142.39 billion RMB to bear the economic burden of disease without PrEP. The cost to prevent one infection is 122,200 RMB, and it saves 19,800 RMB per QALY gained.

Conclusions: The analysis of PrEP's cost-effectiveness and cost-utility indicates that this strategy is highly cost-effective and can be promoted among MSM in China.

Keywords: MSM; AIDS; PrEP; Economic evaluation; Markov model

Introduction

Nowadays, the global AIDS epidemic is in a grim state, which has begun to spread from high-risk groups to the general population. Besides, China's large population is a breeding ground for AIDS. Once it spreads to the general population, it will do great harm to the society and economy [1]. So far, many studies have been conducted on HIV/AIDS prevention and control in the world, among which pre-exposure prophylaxis (PrEP), a biomedical prevention strategy, has become a research hotspot. PrEP, refers to a way for HIV-negative individuals at high risk of infection to take antiretroviral drugs regularly before or during potential exposure in order to lower their chances of getting infected [2-3]. Many studies abroad have proved that PrEP is of effectiveness, safety, and economic value, and thus, the World Health Organization (WHO) has promoted the PrEP strategy as part of comprehensive measures for AIDS prevention and control in recent years.

In China, a ten-year study led by the research group of Chongqing Medical University has also proved that PrEP is both effective and safe. However, there is not enough economic evaluation targeted for PrEP strategy in China. This research aims to predict the cost-effectiveness and cost-utility of PrEP through Markov model and

provide a reference for further studies on PrEP and policy-making of China's Health Department.

Material and Methods

Source of Material

The data are derived from findings of previous studies (2012ZX10001007-007) as well as literature retrieval on the subject.

According to previous studies, the drug works for MSM (men who have sex with Men) only when it is taken both before and after sexual behavior and the overall drug-taking rate reaches at least 80%. The incidence density can be reduced by 3.4/100 person-year when MSM who use PrEP have suboptimal adherence (80%); by 5.07/100 person-year when they have optimal adherence (94%) [4]. Sources of other data are shown in table 1.

Research Methods

Establishing Markov Model: Take MSM that avoids to get infected with the use of PrEP as a whole, and utilize a Markov model to simulate their disease progression. In accordance with the natural course of HIV infection and the current situation in China, HIV-

Table 1: Calculation parameter list.

Parameter		Value	Reference
HIV incidence density prevented with suboptimal adherence		3.4/100 person-year	4
HIV incidence density prevented with optimal adherence		5.07/100 person-year	4
Initial Rate	HIV	1	
	AIDS	0	
	HIV with ART	0	
	AIDS with ART	0	
	Death	0	-
	Death Rate of HIV-infected persons	0.026	6
	Incidence Rate of AIDS for HIV-infected persons	0.057	7-8
	Treatment Rate of ART among HIV-infected persons	0.459	10-15
	Retention Rate of HIV-infected persons	0.458	-
	Death Rate of AIDS patients	0.37	6
	Treatment Rate of ART among AIDS patients	0.504	10-15
	Retention Rate of AIDS patients	0.126	-
	Death Rate of HIV with ART	0.01	6
	Incidence Rate of AIDS of HIV with ART	0.037	16-18
	Retention Rate of HIV with ART	0.953	-
	Death Rate of AIDS with ART	0.09	5
	Retention Rate of AIDS with ART	0.91	-
HUI of each state	HIV	0.8	
	HIV with ART	0.87	
	AIDS	0.68	
	AIDS with ART	0.82	19-20
Economic burden of disease	HIV	10098.5 RMB/year	
	HIV with ART	16,248 RMB/year	
	AIDS	33,817 RMB/year	
	AIDS with ART	36,795 RMB/year	21
	The number of MSM in China	10 million	22
	TDF	85 RMB/30 pills	-
	Frequency of sexual behavior	Once per week	4
	Discount Rate	3%	-

infected persons or AIDS patients are divided into five states: HIV, AIDS, HIV with antiretroviral therapy (ART), AIDS with ART and Death, with Death being the absorbing state. Transitions between these states are shown in figure 1. Treeage Pro 2011 is applied to establish the Markov model of AIDS. Take one year as a cycle and simulate it for 30 years.

Assumptions of the Markov Model: To simplify the model analysis, the following assumptions are made for the simulation:

1. Every year, a certain proportion of research subjects receive ART and all of them take doses regularly.

2. The model takes one year as a cycle, assuming that the economic burden of disease, as well as the transition probability, remains the same within one year.

3. Perform a semi-cycle correction on the initial and final states, assuming that transition among states or death occurs at the midpoint of each cycle, that is, the sixth month of each year [5].

Setting model parameters

(1) The initial probabilities of each state are: HIV (1), AIDS (0), HIV with ART (0), AIDS with ART (0), Death (0).

(2) The death rate of HIV-infected people, HIV patients with ART, AIDS patients: according to the study [6], the death rate of HIV-infected people = $0.005 \times 4/10 + 0.02 \times 3/10 + 0.06 \times 3/10 = 0.026$; the death rate of HIV patients with ART = $0.005 \times 4/10 + 0.01 \times 3/10 + 0.0154 \times 3/10 = 0.010$; the death rate of AIDS patients is 0.37.

(3) Incidence Rate of AIDS for HIV-infected persons: according to the study [7-8], when the incubation period of HIV is 11.5 years,

the instantaneous probability of progression from HIV to AIDS: $P1 = -[\ln(1-0.5)]/11.5 = 0.0603$, and the probability in a year: $P2 = 1 - \exp(-P1 \times t) = 0.059$ [9]. Therefore, the probability from HIV to AIDS = $(1 - 0.026) \times 0.059 = 0.057$.

(4) Treatment Rate of ART among HIV-infected people and AIDS patients: according to the study [10-15], assuming that the coverage rates of ART among HIV and AIDS patients are 50% and 80% respectively, the ART treatment rate of HIV-infected persons = $(1 - 0.026 - 0.057) \times 0.5 = 0.459$, and the ART treatment rate of AIDS patients = $(1 - 0.37) \times 0.8 = 0.504$.

(5) Retention Rate of HIV-infected persons = $1 - 0.026 - 0.057 - 0.459 = 0.458$. Retention rate of AIDS patients = $1 - 0.37 - 0.504 = 0.126$.

(6) Incidence Rate of AIDS for HIV with ART: according to the study [16-18], the median of infection progress of HIV with ART is 18 years, so the instantaneous probability $P1 = -[\ln(1-0.5)]/18 = 0.0385$, and the probability in one year $P2 = 1 - \exp(-P1 \times t) = 0.0378$. Therefore, the probability of HIV with ART developing into AIDS with ART = $(1 - 0.01) \times 0.0378 = 0.037$.

(7) Retention rate of HIV with ART = $1 - 0.01 - 0.037 = 0.953$.

(8) The death rate of AIDS with ART is 0.09 [5].

(9) Retention rate of AIDS with ART = $1 - 0.09 = 0.91$.

(10) The Health Utilities Index (HUI) of each state: according to the study [19-20], HUI of HIV-infected persons is 0.8; HUI of HIV with ART is 0.87; HUI of AIDS patients are 0.68; HUI of AIDS with ART is 0.82.

(11) Economic Burden of disease: by calculating the data provided by Zhang [21], the economic burden of HIV without ART, HIV with ART, AIDS without ART and AIDS with ART are 10098.5 RMB/year, 16,248 RMB/year, 33,817 RMB/year and 36,795 RMB/year respectively.

(12) PrEP Index: according to the survey conducted by the Ministry of Public Health of China in 2004, there are 5 to 10 million MSM in China [22]. We assume that the number of MSM is 10 million in this research. The drug of PrEP is Tenofovir disoproxil fumarate (TDF), 85 RMB per 30 pills. According to the study [4], penetrative sex among MSM happens once a week.

(13) The Discount: we assume that the discount rate is 3%.

Evaluation Index

The number of new HIV infections avoided = the number of MSM \times decreased HIV incidence density with optimal/suboptimal PrEP adherence \times 1 year. Cost-effectiveness ratio (CER) = cost of promoting PrEP / the number of new HIV infections avoided. Cost-utility ratio (CUR) = cost of promoting PrEP / quality-adjusted life years (QALY) gained by people with PrEP. Incremental cost-effectiveness ratio (ICER) / incremental cost-utility ratio (ICUR) = (the cost of launched programs - the cost of undeveloped programs) / (the effectiveness of launched programs - the effectiveness of undeveloped programs) = $\Delta C / \Delta E$ (ΔC represents incremental cost and ΔE represents incremental effectiveness).

Results

QALY results of Markov Model Simulation

Through the analog computation of the Markov model, the transition probability of each state and QALY in different stages are displayed in table 2. It is found that as the cycle goes on, the distribution of newly infected people in each state changes, and the death rate increases gradually.

Take the population who avoid getting HIV infected with PrEP in a year as a whole, and continue PrEP for 30 years. If this population take regular doses before exposition to AIDS from the start of prevention to the end of implementing PrEP and are not infected with HIV in the life cycle of research, each of them will gain 19.89 QALY.

If this population becomes new HIV-infected persons, each patient can gain 11.86 QALY through 30-year follow-up, management, antiviral treatment, and other measures.

The Cost and economic burden of disease calculated by Markov Model

If promoting PrEP to 10 million MSM for one year, with suboptimal medication adherence (80%), 340,000 new HIV infections can be prevented, and with optimal medication adherence (94%), 507,000 can be avoided.

When new HIV-infected persons are involved in the antiviral treatment management for 30 years, the average cost of one HIV-infected person is 280,840 RMB.

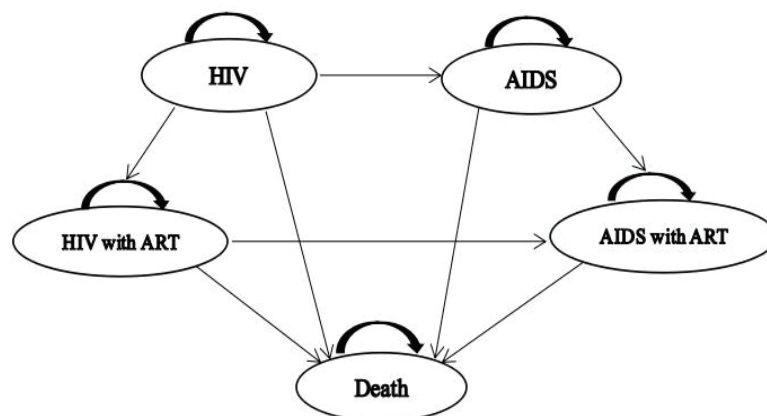


Figure 1: Markov Model of AIDS

Table 2: Transition probability of each state and QALY in different states.

Stage (year)	Transition Probability of Each State					QALY (person-year)		
	HIV	HIV with ART	AIDS	AIDS With ART	Death	QALY under infection	Cumulative QALY under infection	Cumulative QALY in a healthy state
0	1.0000	0.0000	0.0000	0.0000	0.0000	0.4000	0.4000	0.5000
1	0.4580	0.4590	0.0570	0.0000	0.0260	0.7811	1.1811	1.4709
2	0.2098	0.6476	0.0333	0.0457	0.0636	0.7460	1.9270	2.4135
3	0.0961	0.7135	0.0162	0.0823	0.0919	0.7102	2.6373	3.3286
4	0.0440	0.7241	0.0075	0.1095	0.1150	0.6752	3.3125	4.2171
5	0.0202	0.7102	0.0035	0.1302	0.1360	0.6410	3.9535	5.0797
6	0.0092	0.6861	0.0016	0.1465	0.1566	0.6076	4.5611	5.9172
7	0.0042	0.6581	0.0007	0.1595	0.1775	0.5750	5.1361	6.7303
8	0.0019	0.6291	0.0003	0.1699	0.1988	0.5434	5.6795	7.5197
9	0.0009	0.6004	0.0002	0.1780	0.2205	0.5128	6.1923	8.2861
10	0.0004	0.5726	0.0001	0.1843	0.2426	0.4834	6.6757	9.0302
11	0.0002	0.5459	0.0000	0.1889	0.265	0.4551	7.1309	9.7526
12	0.0001	0.5203	0.0000	0.1921	0.2875	0.4280	7.5589	10.454
13	0.0000	0.4959	0.0000	0.1941	0.3100	0.4022	7.9611	11.135
14	0.0000	0.4726	0.0000	0.1950	0.3324	0.3775	8.3386	11.7961
15	0.0000	0.4504	0.0000	0.1949	0.3547	0.3541	8.6927	12.4379
16	0.0000	0.4292	0.0000	0.1940	0.3767	0.3319	9.0246	13.0611
17	0.0000	0.4091	0.0000	0.1925	0.3985	0.3108	9.3354	13.6661
18	0.0000	0.3898	0.0000	0.1903	0.4199	0.2909	9.6262	14.2535
19	0.0000	0.3715	0.0000	0.1876	0.4409	0.2720	9.8983	14.8238
20	0.0000	0.3541	0.0000	0.1844	0.4615	0.2543	10.1526	15.3775
21	0.0000	0.3374	0.0000	0.1809	0.4817	0.2376	10.3901	15.9150
22	0.0000	0.3216	0.0000	0.1771	0.5013	0.2218	10.6119	16.4369
23	0.0000	0.3064	0.0000	0.1731	0.5205	0.2070	10.8189	16.9436
24	0.0000	0.2920	0.0000	0.1689	0.5391	0.1931	11.0120	17.4355
25	0.0000	0.2783	0.0000	0.1645	0.5572	0.1801	11.1921	17.9131
26	0.0000	0.2652	0.0000	0.1600	0.5748	0.1678	11.3599	18.3768
27	0.0000	0.2528	0.0000	0.1554	0.5919	0.1564	11.5163	18.8270
28	0.0000	0.2409	0.0000	0.1507	0.6084	0.1456	11.6619	19.2641
29	0.0000	0.2296	0.0000	0.1461	0.6243	0.1356	11.7975	19.6885
30	0.0000	0.2188	0.0000	0.1414	0.6398	0.0631	11.8606	19.8944

If promoting PrEP to this population for 30 years, with suboptimal adherence, the total cost of 340,000 people is 52.74 billion RMB; while with optimal adherence, the total cost of 507,000 people is 61.97 billion RMB. Details are provided in table 3.

The economic evaluation of PrEP strategy

With suboptimal adherence, the total cost of implementing PrEP for 30 years is 52.74 billion RMB, while the economic burden of disease caused by not implementing PrEP is 95.49 billion RMB. By promoting PrEP, a total of 2.73 million QALY can be saved, and the cost to prevent one HIV infection is 155,100 RMB, which can save 125,700 RMB. The cost to save a QALY is 7799 RMB through PrEP intervention, which can save 15,700 RMB per QALY gained.

With optimal adherence, the total cost of implementing PrEP for 30 years is 61.97 billion RMB. Without PrEP, the loss caused by the economic burden of the disease reaches 142.39 billion RMB. By promoting PrEP, 4.07 million QALY in total can be gained, and the cost to prevent one HIV infection is 122,200 RMB, which can save 158,600 RMB. The cost to save a QALY is 6,145 RMB through PrEP intervention, which can save 19,800 RMB per QALY gained. The results are shown in table 4.

Discussion

HIV/AIDS epidemic has caused multiple problems in the society, leaving orphans and the old unsupported, widening the gap between the rich and the poor, leading to social discrimination and social panic as well as damage to social image [1]. Direct impacts on families

Table 3: The economic burden of disease and cost of PrEP in each cycle of Markov model.

Stage (year)	Cost (RMB/ person)	Cumulative cost under infection (RMB/ person)	Total cumulative cost of PrEP with suboptimal adherence (billion)	Total cumulative cost of PrEP with optimal adherence (billion)
0	5049.25	5049.25	1.33	1.56
1	13602.44	18651.69	3.90	4.58
2	14562.11	33213.80	6.40	7.52
3	14769.25	47983.05	8.82	10.37
4	14651.67	62634.71	11.18	13.14
5	14362.71	76997.42	13.47	15.82
6	13973.02	90970.44	15.69	18.43
7	13520.24	104490.68	17.84	20.97
8	13026.79	117517.47	19.94	23.42
9	12507.48	130024.95	21.97	25.81
10	11972.95	141997.90	23.94	28.13
11	11431.22	153429.12	25.85	30.38
12	10888.61	164317.73	27.71	32.56
13	10350.12	174667.86	29.52	34.69
14	9819.75	184487.61	31.27	36.75
15	9300.65	193788.26	32.97	38.74
16	8795.30	202583.56	34.63	40.69
17	8305.60	210889.16	36.23	42.57
18	7832.95	218722.12	37.79	44.40
19	7378.37	226100.49	39.30	46.18
20	6942.51	233042.99	40.77	47.90
21	6525.74	239568.74	42.19	49.58
22	6128.23	245696.96	43.57	51.20
23	5749.90	251446.86	44.92	52.78
24	5390.56	256837.43	46.22	54.31
25	5049.87	261887.30	47.49	55.80
26	4727.39	266614.69	48.72	57.24
27	4422.61	271037.30	49.91	58.65
28	4134.95	275172.25	51.07	60.01
29	3863.78	279036.03	52.19	61.33
30	1804.23	280840.27	52.74	61.97

include changes in family structure and reduced income [1]. It also affects the economy by influencing social structure. According to Li Jingwen [23], the total loss of human capital caused by HIV/AIDS epidemic in China from 2006 to 2010 reaches 354.07 billion RMB, resulting in a total loss of 19.25 billion RMB in GDP.

Though plenty of AIDS-related economic evaluations in healthcare have been carried out at home and abroad, the existing evaluation standard is neither globally acknowledged nor reliable enough. However, studies by Kahn, Pinkerton, and others [24-25] have shown that if the cost of a prevention program to avoid one HIV infection is lower than the economic burden of treatment, the program is considered cost-effective. This research shows that the cost of PrEP to avoid one HIV infection is 125,700 RMB (with suboptimal adherence) or 158,600 RMB (with optimal adherence) lower than the cost of treatment. In terms of CUR evaluation, under the approach promoted

by WHO-CHOICE, an intervention, per QALY gained, costs less than three times the GDP per capita is considered cost-effective, whereas one that costs less than the GDP per capita is considered highly cost-effective [26]. In this research, it is found that promoting PrEP, per QALY gained, can save 15,700 RMB (with suboptimal adherence) or 19,800 RMB (with optimal adherence). To conclude, when the medication adherence of MSM is no less than 80%, PrEP is highly cost-effective and worth promoting among MSM.

It is found that the higher the adherence is, the better the effect of HIV prevention among MSM is. Besides, the cost of preventing HIV infection and saving QALY decreases, with more money saved. Therefore, to obtain better economic benefits, further studies need to discuss how to improve the medication adherence of MSM and the question that MSM with what characteristics should be targeted to promote PrEP.

Table 4: The economic evaluation of PrEP strategy among MSM.

Index	Suboptimal Adherence	Optimal Adherence
Number of new HIV infections prevented	340,000 person	507,000 person
The economic burden of disease in total	95.49 billion RMB	142.39 billion RMB
The total cost of PrEP	52.74 billion RMB	61.97 billion RMB
QALY gained by non HIV-infected or non-AIDS patients	19.89 year-person	
QALY gained by HIV-infected or AIDS patients	11.86 year-person	
QALY gained by PrEP	2,73 million	4,07 million
The incremental cost of PrEP	-42.75 billion RMB	-80.42 billion RMB
CER of PrEP	155,100 RMB/person	122,200 RMB/person
ICER of PrEP	-125,700 RMB/person	-158,600 RMB/person
CUR of PrEP	7799 RMB/QALY	6145 RMB/QALY
ICUR of PrEP	-15,700 RMB/QALY	-19,800 RMB/QALY

Acknowledgments

This study was supported by the National Key Project for Infectious Diseases of the Ministry of Science and Technology of China (grant number 2012ZX10001007-007). The authors thank all the participants and investigators for their help. All of the analysis, interpretations, and conclusions are solely from the authors.

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