

# Cost-effectiveness of Methadone Maintenance Treatment Centers in Prevention of Human Immunodeficiency Virus Infection

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## Original Article

### Abstract

**Background:** Acquired immune deficiency syndrome (AIDS) is one of the greatest social health problems in many communities in the twenty-first century. Methadone maintenance treatment (MMT) could decrease HIV infection among injection drug users (IDU). The main aim of this paper was to determine the cost-effectiveness of the governmental MMT program to prevent human immunodeficiency virus (HIV) infection among IDU.

**Methods:** This analytical study was performed through a before-after assessment during a one-year period. Using census sampling, 251 IDU referred to the public MMT program of Kerman, Iran, were selected. The expenditures of MMT centers were calculated in the view of government (public sector). The cost-effectiveness was calculated using TreeAge software.

**Findings:** MMT centers averted 86 new cases of HIV infection. The total cost of centers was US\$471 per client in the year. The share of IDU from current expenditures was 35% and from capital expenditures was 32%. Also, methadone per capita for each person who injected drug was US\$514. Per capita expenditure of HIV drug treatment was estimated US\$8535 per year. Incremental cost effectiveness ratio (ICER) was US\$2856 per year, which means governmental MMT program is cost-effective according to the World Health Organization (WHO) criteria.

**Conclusion:** MMT centers are cost-effective in preventing HIV infection and the access to this program should be facilitated for IDU.

**Keywords:** Cost-benefit analysis; Methadone; Maintenance; Therapeutics; HIV

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## Introduction

Acquired immune deficiency syndrome (AIDS) is an important disease which has become known as “the infection of the century”. Although human immunodeficiency virus (HIV) is on the downward trend in a number of countries, the general trend globally is upward.<sup>1</sup>

In 2013, about 1.5 million people died from HIV globally. It is estimated that about 35 million people were living with HIV at the end of 2013, also about 2.1 million people became newly infected by HIV in 2013.<sup>2</sup>

Despite international reports that show decrease in its prevalence in the world, HIV epidemic is growing in Iran. It is estimated that 96 to 100 thousands of people are infected with HIV in Iran, of which only 26090 cases have been identified.<sup>3</sup> HIV affects all body systems and increases the body susceptibility to the opportunistic infections, weight loss and eventually death.<sup>4,5</sup> Drug users are the main group subject to HIV infection.<sup>6</sup> More than 5% of persons with high-risk behaviors are infected with HIV.<sup>7</sup> HIV infection through unprotected sexual contact builds up not more than 10% of the total infections in Iran, so the HIV epidemic in Iran is basically among injection drug users (IDU), and as many as 70% of all HIV infections are attributed to unsafe injection drug use.<sup>8</sup>

On the basis of estimates, 4.3% of the world population or 7.4% of the population aged 15 years and above in the world are IDU. It is estimated that about 7.1%-8.2% of the population older than 15 years of age in Iran are IDU.<sup>9</sup> HIV transmission rate through IDU is 5%-10% in the world, 36% in the US and 60% in Iran.<sup>10</sup> One of the main prevention methods among people who inject opioids is methadone maintenance treatment (MMT).<sup>11</sup>

MMT could decrease high-risk behaviors among IDU. Also, MMT is considered as one of the main obstacles for HIV infection among IDU.<sup>12</sup> However health policy makers are concerned about effectiveness, accessibility and benefits of investment in MMT services.<sup>13</sup> Considering budget limitations, it is necessary to have complete information about investment in the MMT services compared to other healthcare services on the basis of cost-effectiveness measures.<sup>14</sup> The main aim of this study was to determine cost-effectiveness of

governmental MMT program to prevent HIV infection among IDU.

## Methods

In this study, history of injection data were gathered by self-reported method among 251 drug users in five MMT centers affiliated to the Kerman University of Medical Sciences, Kerman, Iran. High-risk behaviors were compared before and after the referral to MMT centers. We gathered data on the costs imposed to the government, i.e. the assets and current costs paid by government. We also used an instruction organized by the Joint United Nations Program on HIV/AIDS (UNAIDS) to determine the costs of HIV prevention. The main costs included everyday expenditure of construction, equipment, and vehicles and the current costs included staff wages, trips, consumables, transportation expenses, car rental, and current costs of personnel and buildings.<sup>15</sup>

To obtain the number of averted cases of HIV, we calculated the probability of infecting others and becoming infected in IDU.<sup>16</sup>

Formula 1 was used to calculate the probability of becoming infected among studying cases:

$$(1) P_{B \rightarrow A} = 1 - \{PB [(1 - ROT) n/2] + (1 - PB)\} m$$

In this formula, person A is the study participant and person B is the partner of the study participants who shared syringe with them.  $P_{B \rightarrow A}$  is the probability of person A becoming infected from other injection partners of person B. PB is the probability of HIV prevalence among IDU. ROT is the probability of HIV transmission through shared syringe,  $mt$  is the average of shared injections in each nest and  $mt$  is the number of injection partners of each IDU.

$nt$  was obtain from the following equation:

$$nt = n \times m \times (1/CR/2)$$

$n$ : the number of shared injections in one week  
 $m$ : the number of persons with whom the addict shared the syringe in each injection

CR: the rate of change in the injection partners of each IDU and outcome of  $d/\mu$

$d$ : the number of new persons entered and exited from each injection session in a special time

$m$ : the average of obtained  $m$  from the study

$mt$  was obtained from the following equation:

$$mt = 52 \times m/2 \times CR$$

CR: the rate of change in the injection partners of IDU and the outcome of  $d/\mu$

m: the number of shared addicts in each injection

52: the number of weeks in each year

In order to calculate the probability of infecting injection partners by the study participant, the following equation used:

$$P A \rightarrow B = 1 - \{PA [(1 - ROT) n/2] + (1 - PA)\} m$$

By multiplying the infecting probability in the number of injection partners of each IDU in each year, and then in the negative probability of them in terms of HIV infection, we obtained the number of infected persons from each IDU. After summing them, the total number of infected persons by the studied addict was obtained.

Since behavioral variables relating to high-risk injecting behaviors could change due to MMT services, new cases of HIV infection were calculated by subtracting the HIV infection estimation due to shared injection from the prevented cases of MMT centers before and after enrolling in the MMT programs.

In order to determine the cost of intervention, we used data on the costs of MMT programs. Also, in order to determine the cost of nonintervention, we used the cost of treatment and surveillance for each case during his/her longevity. In order to determine the costs of HIV prevention for MMT programs, we used the guidance prepared by UNAIDS. The centers' costs included current costs and capital costs. The personnel costs were calculated using wages and fees. Other current costs included methadone, consumed water, etc. calculated per year. Capital costs included buildings, equipment, furniture etc. The capital costs were calculated on the basis of lifetime benefit.

We used incremental cost effectiveness ratio (ICER) to assess a treatment or intervention. ICER is obtained by dividing incremental cost (or additional cost) of an intervention to incremental effectiveness (or additional effectiveness) of that

intervention (Formula 2).

$$(2) ICER = \frac{\text{Incremental cost}}{\text{Additional effectiveness}}$$

After running the model, to determine which variables have the highest impact on the cost-effectiveness results, we used tornado gram analysis.

## Results

The average age of IDU participated in the study was  $38.57 \pm 9.50$  years. Most of the study participants were men (96%) and single (35%). The most used opioid drug in higher age groups was traditional substance and chemical substances in lower age groups. For example, the most used opioid in the 46-50 years age group was opium (84%), but in the 21-25 years age group, the most used substance was opium sap (which is a chemical material). The average age at first use and first injection was 18 and 28 years old, respectively. Overall, 53 people (21%) with high-risk behaviors were infected with HIV, among them 43 people (81%) were men with the average age of 40 years old and the rest were women with average age of 41 years old. The most age group infected with HIV were 31-35 years (30%). Among 251 studied cases, 83 people (33%) had positive hepatitis C. By referring to the mentioned centers, current and capital costs were calculated on the basis of following tables. In the capital cost group, the share of IDU from all of costs was 32%. But overall, the share of buildings was 72% of total costs (Table 1).

Among current costs, IDU costs were 37%. The cost of expert groups was the highest (52%) and buildings maintenance cost was the lowest (0.03). The share of methadone among current costs was 7% (Table 2).

Per capita cost of MMT programs was US\$711. Before referring IDU to MMT programs, they had injected 2.5 times a day. After referring to the centers and through MMT, they injected lower than 0.02 times a day.

**Table 1.** Annual capital costs in the methadone maintenance treatment (MMT) centers

Cost*	Center 1	Center 2	Center 3	Center 4	Center 5
Building	0	4444.44	5555.55	3703.70	0
Machinery	0	74.07	74.07	0	0
Equipment	0	370.37	423.28	370.37	423.28
Other	0	740.74	962.96	814.81	962.96
Total	0	5629.62	7015.86	4888.88	1386.24

\*All costs are in US\$

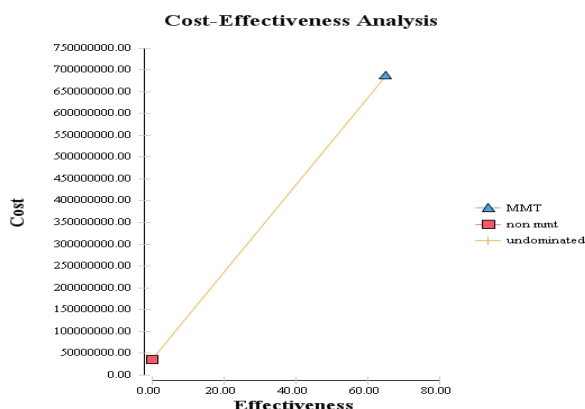
**Table 2.** Annual current costs in the centers

Cost*	Center 1	Center 2	Center 3	Center 4	Center 5
Employees wage	28888.88	53333.33	66666.66	11111.11	11111.12
Methadone therapy cost	0	4888.88	6666.66	12000.00	4888.88
Carfare	0	444.44	888.88	1333.33	888.89
Buildings maintenance cost	0	355.55	355.55	355.55	355.55
Expert group cost	0	31111.11	35555.55	66666.66	53333.33
Rent cost	0	0	0	0	4000
Total	28888.88	90133.33	110133.3	91466.66	74577.77

\*All costs are in US\$

The estimated number of HIV new infections were 139 among IDU before entering to MMT, while it reached to less than 68 cases after that. MMT program had averted 71 new HIV infections among IDU. Before referring to MMT program, 31 new cases of HIV were reported in a year and after referring to these centers, it reached to lower than 14 cases. So these centers averted 17 new infections through injection. Because of high cost of HIV treatment (US\$922 in a year), MMT programs are cost-effective.

Figure 1 indicates clearly that MMT programs have more costs and higher effectiveness than not referring to these centers. In fact, this figure indicates that an economical assessment study can specify in which contexts should the government invest in.



**Figure 1.** Cost-effectiveness of methadone maintenance treatment (MMT) centers

Table 3 indicates ICER as an important

**Table 3.** Incremental cost effectiveness ratio (ICER) model

Strategy	Effectiveness	Incremental effectiveness	Cost*	Incremental cost	ICER
Non-MMT	0	0	13298	0	0
MMT	65.0212	65.0212	254056	240758	3702

\*All costs are in US\$; MMT: Methadone maintenance treatment; ICER: Incremental cost effectiveness ratio

criterion in the economical assessment studies. ICER is the ratio of cost variation to effectiveness variation. In this type of studies, cost-effectiveness ratio should convert to quality adjusted life year (QALY), a widely used measure of health improvement that is used to guide health-care resource allocation decisions. ICER obtained US\$2856. The concept of this figure is that the government should spend US\$2856 for each HIV prevented. However, this figure is for a one-year period not the lifetime of a HIV patient. At first, on the basis of different studies, we specified each HIV averted is equivalent to how many QALY. The World Health Organization (WHO) has determined this figure equivalent to 0.7 QALY. Dividing US\$2856 to 0.7 QALY, the result was 4080. This recent figure specifies how much we should spend per QALY. It is necessary to point out that WHO has recommended that if different countries spend US\$50000 per QALY, the intervention strategy is still cost-effective. Another criterion for decision making is comparing ICER with 3 times GDP per capita.<sup>17</sup>

### Discussion

This study was performed on 251 IDU that received MMT in the Kerman governmental MMT centers. These centers have prevented 86 new HIV cases. Also, ICER was US\$2856, which indicates that the intervention has been cost-effective.

In a study by Keshtkaran et al. on MMT centers located in Shiraz, Iran, it was specified that these centers had prevented from 126 new HIV cases.<sup>18</sup>

Wammes et al. indicated that by expansion of MMT coverage from 5% to 40% in Indonesia, 2400 new HIV cases could be prevented.<sup>19</sup> In a research by Masaki et al. in China, it has been indicated that through a 5-years MMT program treatment for IDU, 3722 and 1960 HIV infections could be prevented in a 10-years period for high-risk and low-risk regions, respectively.<sup>20</sup> Because of the differences in the countries situation, the environment of studies, and also the type of model used to calculate the number of prevented cases, the number of prevented cases are different among countries.

Heidari et al. reported that 37.3% of 694 opioid dependents referring to the Shiraz MMT centers were IDU. Also, 23.3% of the opioid dependents had a joint injection one week before referring to the centers. This number decreased to 9.2% one week after referring to the centers.<sup>21</sup>

In the study by Keshtkaran et al., the cost of MMT centers was US\$204997 and the cost of surveillance and treatment of HIV prevented cases during lifetime period (nonintervention cost) was US\$13942756 USD. The ICER ratio was equivalent to US\$109035 per each HIV infection prevented. So, MMT centers had lower costs and higher effectiveness than nonintervention state.<sup>18</sup>

By paying attention to the cost-effectiveness of MMT centers and the nature of services presented in MMT centers, the protecting role of these programs and also the HIV preventing services, the government authorities should consider financial support for these centers. For MMT centers to be effective, addicts should participate continuously, there should be no drug therapy intervention by other health care providers, and all services related to MMT centers should be delivered in one place to avoid confusion.<sup>21</sup> One important advantage of MMT centers is the decrease in HIV transmission which is useful for

all society members. Development of MMT centers is still preferable in spite of dependence to methadone and its side effects on life quality.<sup>22</sup>

Since data collection was self-report, one of the study limitations is the participants' inability in remembering some of the requested information. So, later studies should use higher sample size with broader range in different regions. Although Farrel et al. stated that many policy makers in different countries are concerned about the effectiveness of MMT program, vague MMT design and its benefits and also increased drug use among society,<sup>23</sup> this study indicated that MMT centers decreased injections related to opioids and sharing equipment. In other words, MMT centers prevented transmission of HIV virus among IDU.

## Conclusion

Health policy makers can use the results of this study to develop strategic plans and administer necessary interventions for prevention and treatment of opioid dependents. By attention to high prevalence of shared injections among IDU which is the most important way of HIV transmission in Iran, it is necessary to implement broad interventions in this regard. To allocate needed costs from general budget, policy makers need information about the prevalence and mortality rate of HIV infection among IDU.

## Conflict of Interests

The Authors have no conflict of interest.

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## هزینه - اثربخشی مراکز درمان نگهدارنده با متادون در معتادان تزریقی به منظور

### پیشگیری از عفونت HIV

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#### مقاله پژوهشی

#### چکیده

**مقدمه:** افزایش تزریقات پرخطر، منجر به افزایش شیوع عفونت HIV (Human immunodeficiency virus) در میان مصرف کنندگان تزریقی مواد می‌شود. افزایش هزینه‌های مراقبت و محدود بودن منابع مالی، ضرورت ارزیابی اقتصادی جهت انتخاب بهترین مداخله‌ای را که منجر به کنترل HIV گردد، آشکار می‌سازد. مطالعه حاضر به تعیین هزینه- اثربخشی مراکز درمان نگهدارنده با متادون (Methadone maintenance treatment) یا MMT) به منظور پیشگیری از عفونت HIV در معتادان تزریقی پرداخت.

**روش‌ها:** این پژوهش به صورت مداخله‌ای بدون کنترل، در ۵ مرکز دولتی MMT شهر کرمان صورت گرفت. ۲۵۱ معتاد تزریقی تحت درمان این مراکز به مطالعه وارد شدند. تمام هزینه‌های تحمیل شده بر دولت محاسبه گردید. مدل ریاضی Everett به منظور تعیین موارد اجتناب شده از عفونت HIV مورد استفاده قرار گرفت. سنجش اثربخشی با استفاده از فرمول‌ها و الگوهای ریاضی انجام شد.

**یافته‌ها:** مراکز MMT موجب اجتناب ۸۶ مورد جدید HIV شدند. هزینه سرانه مراکز برای معتادان تزریقی ۱۷ میلیون و ۲۰۰ هزار ریال، هزینه متادون ۷۶۸ میلیون ریال و هزینه سرانه ثابت ۸۰۰ هزار ریال به دست آمد. سرانه هزینه درمان دارویی مبتلایان به HIV سالیانه حدود ۲۹۸ میلیون و ۷۲۸ هزار ریال برآورد شد. هزینه- اثربخشی افزایشی (ICER یا Incremental cost-effectiveness ratio) برای یک سال، ۹۹۹۷۴۳۹۰ ریال به دست آمد که حاکی از هزینه کمتر و اثربخشی بیشتر مداخله MMT نسبت به عدم مداخله بود.

**نتیجه‌گیری:** نتایج تحلیل حساسیت مدل نشان داد که با وجود تغییرات دامنه هزینه‌ها در خصوص هر مورد پیشگیری از HIV، همچنان مداخله MMT نسبت به عدم مداخله، هزینه- اثربخش می‌باشد. با توجه به اثربخشی و هزینه- اثربخشی بالای مراکز MMT، گسترش این مراکز جهت تحت پوشش قرار دادن افراد پرخطر به منظور پیشگیری از HIV ضروری به نظر می‌رسد.

**واژگان کلیدی:** تحلیل هزینه- اثربخشی، متادون، نگهداری، درمان، HIV

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