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## The HIV treatment cascade in people living with HIV in Iran in 2014; mixed-method study to measure losses and reasons

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### Abstract

The study assessed the HIV treatment cascade of people living with HIV (PLWH) in Iran and the reasons for gaps in HIV services in 2014. We did the cascade analysis using the WHO HIV test-treat-retain cascade analysis tool (2014). To measure the gaps, we check the records for all PLWH reported to the national HIV surveillance till September 2014 to define how many were alive, linked to HIV care, assessed for CD4 count, started antiretroviral therapy (ART), and reported to be alive up to five years after ART. To assess the reasons for gaps in the cascade, we ran desk review, four focus group discussions (FGD) and fifty one in-depth interviews with key informants including PLWH. Spectrum model estimated 75,700 PLWH in Iran, of whom, only 22,647 people (%30) were diagnosed. Of those who were diagnosed with HIV, 16,266 people (%72) enrolled in HIV care. About 13% of all PLWH retained in HIV care and only 9% (6,745 people) had ever tested for CD4 count. Only 8% (6,018 people) of all PLWH received ART by September 2014. We

#### Ethical approval

Not required (We used the data of national HIV registry system for this study that prospectively didn't assign human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Therefore, ethical approval was not needed for this study).

#### Conflict of Interest

The authors have no conflict of interest.

found the biggest gap in the HIV treatment cascade to be HIV diagnosis as only 30% of PLWH have been diagnosed. Innovative strategies to improve HIV testing, particularly those work best for key populations, is critical to reach the 90–90–90 targets.

## Keywords

HIV treatment cascade; people living with HIV; Iran

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## Introduction

Worldwide, accessing to antiretroviral therapy (ART) for 15 million HIV-positive people who are not on treatment is one of the ten goals of the universal access program. Shortage in HIV care engagement includes late HIV diagnosis, linkage to and retention in HIV care, insufficient use of ART, and suboptimal adherence to therapy, pose significant barriers to achieving optimal treatment outcomes.<sup>1</sup> Coverage of ART in the Eastern Mediterranean region, where Iran is located, is less than 14%, the lowest in the world. The huge number of undiagnosed and so untreated people living with HIV (PLWH) makes the region the only region in the world where the rate of treatment coverage is very low.<sup>2</sup>

According to estimation made by Spectrum modeling in 2014, more than 75,000 (Uncertainty Interval [UI] 49,600 to 135,400) people living with HIV in Iran. The major driver of the HIV epidemic in Iran is unsafe drug injection, while over recent years the heterosexual transmission has been increasing.<sup>3</sup> Recent years HIV data shows a decrease in the male to female ratio with an increase in the rate of heterosexual transmission (8.3 to 2.4 M/F ratio).<sup>3</sup> To assess the HIV program systematically and comprehensively, we need to look at all steps of HIV treatment cascade from diagnosis to treatment and the effect of treatment. The “HIV treatment cascade“ is a tool to identify strengths and weaknesses of delivery of services to PLWH in process of care cascade by closely examining the proportion of PLWH and engaged in each of the five separate stages of the HIV care cascade (HIV diagnosis, linkage to HIV care, staying in HIV care, getting ART, and sustaining undetectable viral loads). By using this tool, policy makers and program managers are able to pinpoint where gaps may exist in the services. It also helps to prioritize and target at available resources and to monitor national progress in response to HIV.<sup>1</sup>

For the first time, our study was carried out to assess the treatment cascade of PLWH in Iran and the reasons for gaps in the HIV treatment cascade by desk review, expert opinion and key informants' interviews.

## Methods

We did the cascade analysis using the WHO HIV test– treat–retain cascade analysis tool (2014).<sup>4</sup> First, a technical working group was developed to lead and conduct the analysis. The technical working group also received technical supports from a steering committee that included key persons working in the field of HIV and key stakeholders. The cascade analysis included quantitative and qualitative methods to measure the gaps and to assess the reasons for such gaps in the HIV treatment cascade.

For the quantitative analysis, we used Spectrum model to estimate the number of PLWH. Using the national HIV registry system by September 2014, there were 28,663 persons diagnosed with HIV. By linking the patients' data to mortality data, we found and excluded 6016 cases of deaths. Then, we looked at HIV care data which included visits by physicians, CD4 count and medical exams for opportunistic infections by inquiries from health facilities providing services to PLWH. Any person with a data indicates that referred to a triangular clinic and tested for confirmatory test considered to be linked to HIV care and those who were visited the triangular clinic at least twice a year considered to be retained in care. All PLWH who had a record of ART prescription were considered as those initiated ART. Uncertainty intervals in the percentages for each steps of the HIV treatment cascade were estimated based on uncertainty in the number of PLWH. We measured the survival rate at 12, 24 and 60 months after ART in those who started the medication.

To assess the reasons for drop out from the HIV treatment cascade and the status of receiving care and treatment services and related variables for PLWH, we did a cross sectional study with questionnaire-based interviews with HIV experts and also among 273 PLWH enrolled in care across the country (174 on ART and 99 eligible for ART but not under treatment). The qualitative analysis included focus group discussions (FGD)<sup>5</sup> and in-depth interviews with 18 policy makers<sup>6</sup> and 51 health officers dedicated to local HIV program at triangular, Drop-in Centers (DIC) and Methadone Maintenance Treatment (MMT) centers.<sup>7</sup> We had two FGD with health care workers at triangular clinics and, and two FGD with those health workers in DIC and MMT centers, and two FGD with PLWH. Using a guide (with an opening section, and follow-up questions about barriers and facilitators for each of steps in the cascade), one FGD leader probe questions on different steps in the HIV treatment cascade and reasons for the gap and how barriers could be addressed. All FGD were audio recorded and the files transcribed to typed files. The FGD were analyzed by the content analysis; First, the text was reviewed carefully and relevant parts of the text were determined and coded, then the themes were summarized. We have chosen the themes based on the barriers reported for each step in the cascade and the potential solutions. Our themes and mythology were chosen based on the WHO guide on HIV test-treat-retain cascade analysis.<sup>4</sup> For coding, we used Microsoft Word Office software.

For the in-depth interviews with policy makers and key informants, we used a structured open format questionnaire. We interviewed 18 key informants with expertise in HIV epidemiology and programs, 51 health care providers from three different cities and 3 PLWH. All interviewed were transcribed and analyzed as we described above for FGD data analysis.

## Results

About 75,700 (UI 49,600 to 135,400) people estimated to live with HIV in 2014 in Iran (Figure 1-A). By September 2014, 22,647 people were diagnosed with HIV and alive which corresponding to only 30% (UI 17 to 46%) of all PLWH alive. Of those who were diagnosed with HIV, 16,266 people enrolled in HIV care. About 13% (UI 7 to 19%) (or 9,568 people) of all PLWH retained in HIV care while only 9% (UI 5 to 14%) (6,745 people) had ever

tested for CD4 count. Only 8% (UI 4 to 12%) (6,018 people) of all PLWH received ART by September 2014. Survival on treatment at 12, 24 and 60 months after ART was 84.8%, 72.9%, and 55.8% among those who started medication, respectively. Among those who were diagnosed with HIV, 72% were in care, 42% retained in care, and only 27% received ART (Figure 1-B).

From September 2013 to September 2014, 113,413 persons were tested for HIV by public health sector, of whom 112,011 people (98.7%) were given their test results, and of whom, 1,404 (1.2%) were tested positive. Over the same period, 84.7% (1,225 out of 1,445) of the patients who started ART were retained on ART in 12 months follow up.

Reasons for losses in HIV treatment cascade are presented in Table 1. As we did not see heterogeneity and major different point of views among different key informants, we did not report the qualitative results by type of key informants. For gaps in HIV diagnosis, several barriers such as existing stigma (particularly within family) for HIV and related risk behaviors, lack of knowledge among key populations on HIV testing and available services, inexperienced health workers in working with key populations, low perception of HIV risk among the key population at risk and lack of motivation and partnership in private health sector were reported frequently by the key informants. They also provided some recommendations including increasing knowledge and demand for HIV testing, simplifying the HIV diagnosis process, and involvement of private sector in HIV testing services.

Frequently mentioned barriers for enrollment in HIV care were poor seeking care in the majority of affected key populations, poor motivation for self-care in patients because of other priorities, marginalized population and those living in areas out of public health access, insufficient number of counselors well-trained for counseling, insufficient support for transportation and some specific services. Key informants also provided some recommendations to address the barriers such as recruitment of trained and motivated personnel, people with one rapid test result to be linked to HIV services, increase access to mental health services, use peer group and positive club capacities to establish trusted between communication of PLWH and service providers.

For ART initiation and retention in ART, reported barriers included adverse drug reactions or fear for drug interactions with Methadone and narcotic drugs, insufficient knowledge about benefits of ART, high pill number, psychological and mental problems. Participants also provided suggestions for improvement ART services such as the need to have the supply change management of anti-retroviral drugs to be improved, fixed dose combinations to be procured in order to have simpler regimens available, a program for monitoring adherence to ART to be defined and implemented carefully in the triangular clinics.

Results of PLWH survey conducted among 273 PLWH enrolled in care across the country (174 on ART and 99 eligible for ART but not under treatment and one unknown status) are presented in Table 2. Totally, 217 of PLWH were male (79.5%) and there was no significant difference between men and women (P-Value: 0.3). Majority of PLWH in both groups were 25–44 years old and there was a significant difference between two groups in regarding the age groups (p-value: 0.04). A total of 4% of the PLWH were illiterate, but there was a

significant difference between the two groups in high school or academic education (P-value: 0.02). Only 17% of PLWH had a permanent job, but there was a significant difference between the two groups in regarding the job status (P-value: 0.002). In terms of transmission risk there is a significant difference in injecting drug between the two groups (P-value: 0.008). Also between the two groups, there was a significant difference in the explanation in the post-test counseling about the ART effects, ART side effects and the dietary regimen (P-value: 0.05, 0.001 and 0.02 respectively). The study showed 35.7% of PLWH followed up by referral center and there was no difference between those on ART and not ART. Survey revealed that 59% of those receiving ART and 69.7% of those not on ART, have received some type of supportive services including financial, employment, nutritional, transportation supports as well as health insurance and membership of positive club. No significant difference has detected between two groups. In total, about one-third of the PLWH had a history of not receiving a service due to lack of financial ability and lack of that service in the city. The difference between the two groups was not significant in any of these records. The study showed 95.1% of PLWH were satisfied by services provided in triangular clinics, and there was no difference between those on ART and not ART.

## Discussion

We found that less than one in ten (10%) PLWH in Iran have ever initiated ART until 2014. The biggest gap in the HIV treatment cascade is HIV diagnosis as only 30% of PLWH have been diagnosed. The treatment strategy in 2014 which required a CD4 count < 500 cells/ $\mu$ l, caused a loss of about 16,000 people in the continuum of care after diagnosis. Per updated ART guideline in Iran,<sup>3</sup> CD4 is not anymore needed for ART initiation, and so, we expect that part of the reasons for gaps have already been addressed. We also identified several reasons for losses in the HIV treatment cascade as well as recommendations to improve them.

Our findings showed that to reach 90–90–90 UNAIDS targets, Iran needs to improve diagnosis and linkage to care programs, particularly for the key populations. The 1.2% positivity rate in 2013–14 was very low and targeted or index case testing is critical to find the numerous undiagnosed people. Although HIV rapid test has become available in 1017 health facilities, but usage of such services by the member of key populations (like people who inject drugs) is still low. Only one third of people who inject drugs tested for HIV in the last year,<sup>8</sup> and only two third of female sex workers in 2015 reported recent HIV testing.<sup>9</sup> The current HIV testing and counseling program in Iran requires people to visit facilities, which for member of the key population is a barrier. Scaling up community-based non-clinical testing programs,<sup>3</sup> offering HIV self-testing<sup>10</sup> and peer-driven HIV testing<sup>11</sup> which showed to improve HIV testing in other settings need to be considered to improve such a big gap in diagnosis.

Retention in HIV care also need to improve in Iran. Studies in the United States for mobile-based intervention among MSM<sup>12</sup> showed improvement in retention in HIV care. Peer navigation and supports intervention and supports for patient transportation<sup>13</sup>, family centered approaches<sup>14</sup> and the use of lay healthcare providers<sup>15</sup> all showed to be effective

strategies to improve retention. All these potential effective models need to be adapted and piloted for the Iran settings.

Since July 2017, Iran adapted and implemented the test and treat strategy for all HIV diagnosed patients. This strategy may improve part of gap that resulted from time lag between HIV care and treatment. In Iran, private sector has a major role to deliver the diagnostic and therapy services to people living in urban settings.<sup>16</sup> Educating and working with providers in the private sector is a key to improve HIV treatment and also retention of those who are on treatment, if the country has a plan for expansion of HIV services at district level. Other group of providers, mostly as the lay providers, that can help in navigating and supporting PLWH to retain on ART and have a positive life. In Iran, many harm reduction and prevention services are being delivered by NGOs.<sup>17</sup> They have successfully reached and provided such prevention services to members of the key populations mostly those injecting drugs. Involving NGOs in post ART program for follow-up and improving retention, and have the NGOs to provide support to those on ART as well as delivery of program to address mental health need to be explored and piloted.

The structural barriers including long distances between where people live and where services are, and transportation need to visit the clinics was also mentioned by some key informants. This could be addressed by some stipends for transportation<sup>18</sup>, conditional small cash programs and incentives for those who made their clinic visits on time<sup>19</sup>, which not only improves adherence, but also encourages marginalized population with low income to visit more often the services.<sup>19</sup>

Perceived or real stigma has also been reported as one of the barriers for HIV testing and treatment. Educating communities and patients for their rights<sup>20</sup>, normalizing HIV testing by campaigns<sup>21</sup> and by wisely involving partners and families as supporting groups<sup>14</sup> can reduce the stigma associated with HIV and increase the chance of using the existing services. HIV self-testing has many potentials<sup>10</sup>, but strategies to improve linkage to confirmatory and treatment services after self-testing need to be adapted or developed for Iran and other similar developing settings. Health providers also should be trained<sup>15</sup> and monitored to provide stigma-friendly services and environments welcoming people in particular those engaged in stigmatized behaviors like same-sex or sex-work sexual contacts or drug injection.

Based on the results of PLWH survey, about 36% of those on not ART live with their permanent or temporary spouses, which means they do not have the benefits of treatment themselves, and their spouses are also deprived of it. About 96% of PLWH have a minimum level of reading and writing literacy that can be used from writing textbooks for educating them, but 4% of others need special methods for educating illiterate people. The counseling was well discussed on the ways of transmission and the ART effects, but the amount of information provided in the post-test consultation was lower in ART side effects, particularly that those on not ART have been less likely to benefit from the treatment group in this case. This can affect on patient expectations of treatment and its subsequent adherence.

Our study had three limitations. First, the number of PLWH was estimated by modeling which subjects to model assumptions and uncertainties. Second, adherence to ART and viral load were not measured or reported systematically for people on ART and so, we were not able to assess them. Last, we used all registered HIV cases data until 2014 to analyze the overall cascade, which may not reflect the cascade of recent diagnosed patients, or the subgroups defined by demographic characteristics or high-risk behaviors.

Despite the limitations, clearly the biggest gap in HIV treatment cascade in Iran is the gap in case finding and diagnosis. Innovative strategies to improve HIV testing, particularly those which work best for the key populations, is critical to reach the 90–90–90 targets. Future continuum of care analysis should consider adding viral suppression and ART adherence indicators and also evaluate the cascade by demographic characteristics and high-risk behaviors. Using the potentials of private sector and NGOs to deliver HIV services and reducing the stigma in families, communities and health care settings are necessary to scale-up and improve the HIV cascade in Iran.

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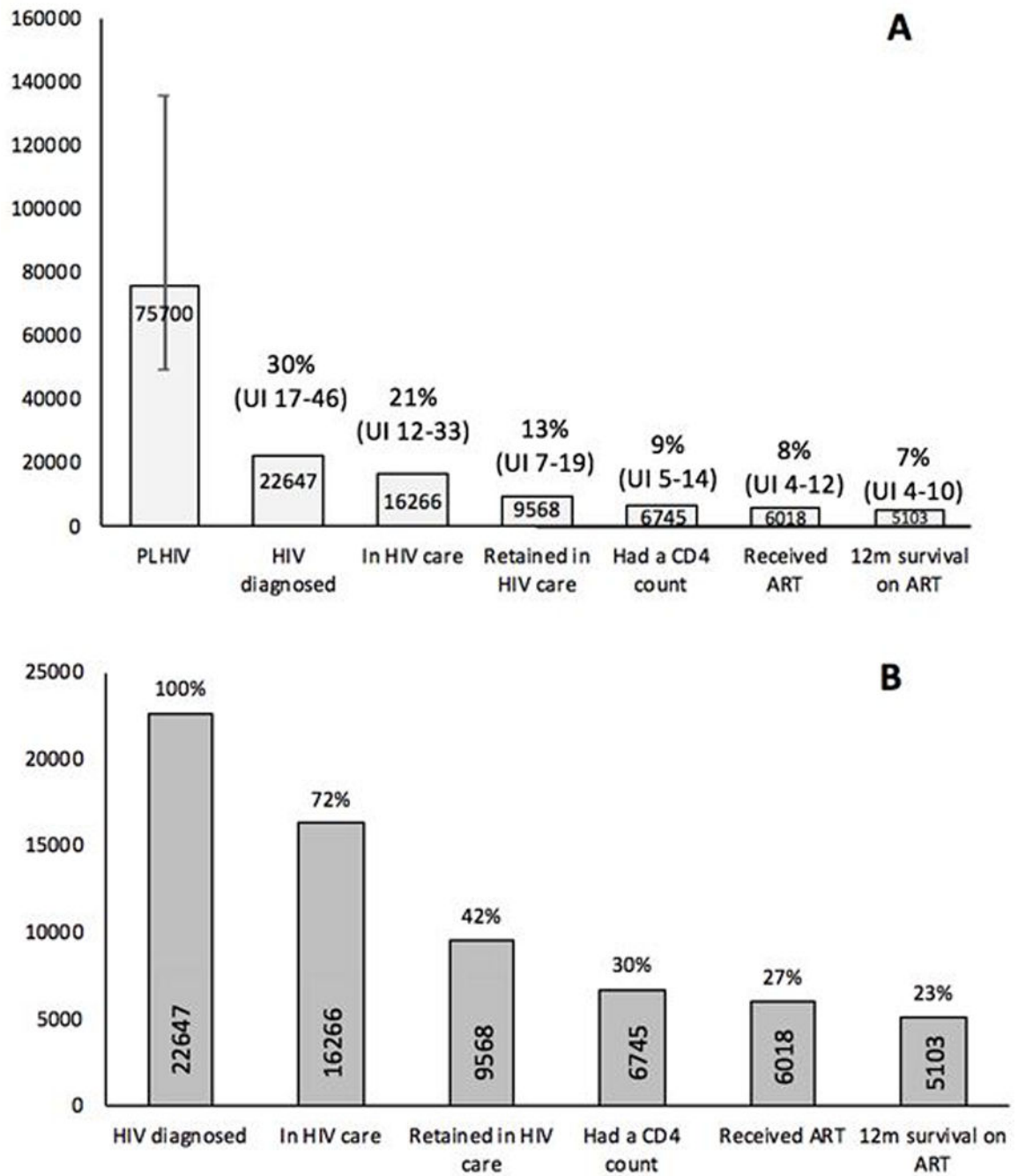
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**Figure 1.** Number and percentage of people living with HIV (PLWH) in selected stages of HIV treatment cascade, Iran 2014. A: Percent of estimated number of PLWH, uncertainty intervals (UI) in % were estimated based on UI in the number of PLWH. B: Percent of all HIV diagnosed patients

**Table 1.**

Reasons for losses in HIV treatment cascade and recommendation to reduce them, Iran 2014

Steps	Experts' opinion on reasons for losses	Experts' recommendations and possible resolutions
<b>Step 1: HIV diagnosis</b>	<ul style="list-style-type: none"> <li>• Stigma in the society level (especially in family)</li> <li>• Insufficient information in the community (especially key populations)</li> <li>• Insufficient experience of health care workers</li> <li>• Low risk perception and/or poor motivation on HIV testing among key populations</li> <li>• Insufficient involvement of private sector</li> </ul>	<ul style="list-style-type: none"> <li>• Increasing demand for testing</li> <li>• Simplifying HIV diagnosis process</li> <li>• Increasing private sector involvement</li> <li>• Scale up education and counseling for marriage candidates and promotion of voluntary counselling and testing services</li> <li>• Specific consideration for high-risk groups</li> </ul>
<b>Step 2: Enrolment in HIV care</b>	<ul style="list-style-type: none"> <li>• Poor self-care in the majority of affected key population</li> <li>• Problem in supply chain management</li> <li>• Poor motivation of patients because of other priorities;</li> <li>• Marginalized population and those living in areas out of public health access;</li> <li>• Stigma;</li> <li>• Insufficient capacity and number of counselors for counseling;</li> <li>• Insufficient support for transportation and some specific services.</li> </ul>	<ul style="list-style-type: none"> <li>• The trained and motivated personnel might increase enrollment greatly</li> <li>• People with one rapid test result should be linked to HIV services</li> <li>• Patient education programs should be enriched with developing materials</li> <li>• Increasing access to mental health services</li> <li>• Utilization of peer group and positive club capacity to establish a communication between PLHIV and service provider centers.</li> <li>• Using of infrastructures and available capacities such as capacity of private sector or family physician for delivering care and treatment in other districts</li> </ul>
<b>Step 3: Initiation of ART and retention in ART</b>	<ul style="list-style-type: none"> <li>• Experience of adverse drug reactions or fear of that interactions with Methadone and narcotic drugs as well,</li> <li>• Inappropriate knowledge and belief about positive effects of ART,</li> <li>• High pill number,</li> <li>• Psychological and mental problems,</li> <li>• Conflicts with family members,</li> <li>• Stigma and fear of disclosure</li> </ul>	<ul style="list-style-type: none"> <li>• The supply change management of antiretroviral drugs must be improved.</li> <li>• Considering the fixed dose combinations in order to have simpler regimens available.</li> <li>• Monitoring adherence program must clearly have defined and be performed in the triangular clinics.</li> <li>• Using of infrastructures and available capacities such as capacity of private sector or family physician for delivering care and treatment in other districts.</li> <li>• Mental health should be provided to these patients and their families.</li> </ul>

**Table 2.**

Results of PLWH survey conducted among 273 PLWH

	On ART	Stop ART	Total	P-Value
<b>Sex</b>				0.3
Male	135 (77.6 %)	82 (82.8 %)	217 (79.5 %)	
Female	39 (22.4 %)	17 (17.2 %)	56 (20.5 %)	
<b>Age</b>				0.04
15–24	0 (0 %)	2 (2.1 %)	2 (0.7 %)	
25–44	124 (72.5%)	81 (83.5%)	205 (76.5%)	
45<	47 (27.5%)	14 (14.4%)	61 (22.8%)	
<b>Marital Status</b>				0.08
Single	55 (32 %)	42 (42.9 %)	97 (36 %)	
Married	84 (48.8%)	35 (35.7%)	119 (44%)	
Divorced / Widow	33 (19.2%)	21 (21.4%)	54 (20%)	
<b>Education</b>				0.02
Illiterate	9 (5.2 %)	2 (2 %)	11 (4 %)	
Elementary	56 (32.3%)	47 (47.5%)	103 (37.9%)	
Guidance / High School	94 (54.3%)	48 (48.5%)	142 (52.2%)	
Academic	14 (8.2%)	2 (2%)	16 (5.9%)	
<b>Employment</b>				0.002
Full-time / Part-time Job	91 (53%)	32(33%)	123(45.7%)	
Jobless/ Illegal Businesses	48 (27.9%)	49 (50.7%)	97 (36%)	
Housewife	30 (17.4%)	14 (14.7%)	44 (16.4%)	
Retired/ Studying	3 (1.7%)	2 (1.6%)	5 (1.9%)	
<b>Transmission Risk</b>				0.95
Injecting Drug Use	111 (64.2%)	78 (79.6%)	189 (69.7%)	0.008
Heterosexual Relationship	68 (39.3%)	50 (51%)	118 (43.5%)	0.062
Homosexual Relationship	10 (5.8%)	6 (6.1%)	16 (5.9%)	0.9
Blood Transmission	3 (1.7%)	1 (1%)	4 (1.5%)	0.64
Mother to Child	1 (0.6%)	1 (1%)	2 (0.7%)	0.68
Spouse with Risk Factors	3 (1.7%)	2 (2%)	5 (1.8%)	0.86
HIV Infected Spouse	26 (15%)	9 (9.2%)	35 (12.9%)	0.16
Occupational or non-occupational Exposure	3 (1.7%)	1 (1%)	4 (1.5%)	0.64
Others	12 (6.9%)	7 (7.1%)	19 (7%)	0.95
<b>Post-test Counselor</b>				0.009
Physician	68 (39.8%)	50 (51.5%)	118 (44%)	
Counselor	89 (52%)	34 (35.15%)	123 (45.9%)	
Both	5 (2.9%)	8 (8.2%)	13 (4.9%)	
Others/ None	9 (5.3%)	5 (5.2%)	14 (5.2%)	
<b>Post-test Counseling Content</b>				
ART Effects	126 (75.9%)	62 (64.6%)	188 (71.8%)	0.05
ART Free	137 (82.5%)	75 (78.1%)	212 (80.9%)	0.38

	On ART	Stop ART	Total	P-Value
ART Side Effects	96 (57.8%)	35 (36.5%)	131 (50%)	0.001
Transmission Mode	161 (97%)	93 (96.9%)	254 (96.9%)	0.96
Window Period	91 (54.8%)	42 (43.8%)	133 (50.8%)	0.08
Condom Use Instruction	111 (66.9%)	65 (67.7%)	176 (67.2%)	0.88
Dietary Regimen	80 (48.2%)	32 (33.3%)	112 (42.7%)	0.02
<b>Active Follow-up From the Counseling Center to Link</b>				0.13
Yes	29 (31.5%)	17 (45.9%)	46 (35.7%)	
No	42 (45.7%)	10 (27%)	52 (40.3%)	
Self-referral	21 (22.8%)	10 (27%)	31 (24%)	
<b>Supports Received</b>				0
Monetary Aids	33 (32%)	18 (25.7%)	51 (29.5%)	0.37
Insurance	72 (69.2%)	55 (78.6%)	127 (73%)	0.17
Employment Service	3 (2.9%)	1 (1.4%)	4 (2.3%)	
Positive Club	47 (45.2%)	28 (40%)	75 (43.1%)	0.49
Food	20 (19.2%)	14 (20%)	34 (19.5%)	0.9
Transportation	6 (5.8%)	2 (2.9%)	8 (4.6%)	0.37
<b>Could not Afford to Pay for Other Needed Services</b>				
Yes	55 (31.6%)	26 (26.5%)	81 (29.8%)	0.38
<b>Did not Use the Other Needed Services as They Were not in My Home Town</b>				
Yes	48 (27.9%)	37 (37.4%)	85 (31.4%)	0.11
<b>Patients Satisfaction for Counseling Services</b>				
Yes	162 (94.2%)	88 (96.7%)	250 (95.1%)	0.37