HIV/AIDS IN TURKEY

Prof. Dr. Mehtap TATAR

Polar Health Economics and Policy Studies - 4

Ankara- 2019

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

3TC	: Lamivudine
ABC	: Abacavir
AIDS	: Acquired Immune Deficiency Syndrome
ART	: Antiretroviral Therapy
ATV	: Atazanavir
AZT	: Zidovudine
BIC	: Bictegravir
bid	: Twice daily
cART	: Combined ART
COBI	: Cobicistat
DRV	: Darunavir
DTG	: Dolutegravir
EASC	: European AIDS Clinical Society
EFV	: Efavirenz
ELV	: Elvitegravir
ETR	: Etravirine
EU	: European Union
FTC	: Emtricitabine
HIG	: Health Implementation Guide
HIV	: Human Immunodeficiency Virus
INSTI	: Integrase Strand Transfer Inhibitor
LPV	: Lopinavir
MoH	: Ministry of Health
MSM	: Men who have sex with men

MVC	: Maraviroc
NGO	: Non-Governmental Organization
NNRTI	: Non-Nucleotide Reverse Transcriptase Inhibitor
NRTI	: Nucleotide Reverse Transcriptase Inhibitor
NVP	: Nevirapine
OECD	: Organization for Economic Corporation and Development
OOP	: Out-of Pocket
PI	: Protease Inhibitor
PLA	: Positive Living Association
q.d	: Once daily
/r	: ritonavir, low dose
RAL	: Raltegravir
RPV	: Rilpivirine
SSI	: Social Security Institution
TAF	: Tenofovir Alafenamide
TDF	: Tenofovir Disoproxil Fumarate
UNAIDS	: The joint United Nations Program on HIV/AIDS
WHO	: World Health Organization
ZDV	: Zidovudin

1. Introduction

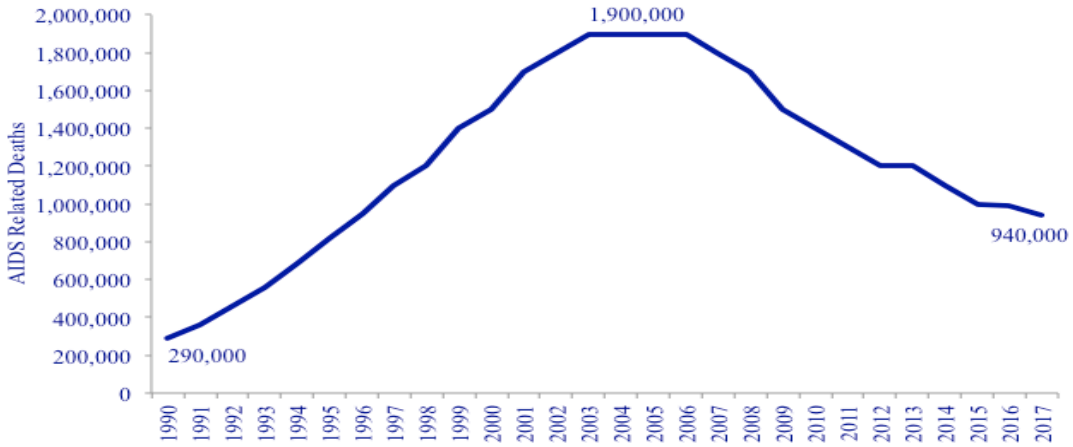
Despite improvements in treatment and in incidence and mortality rates, Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) are still among the major health problems that all health care systems face. According to the World Health Organization (WHO), globally, 36.9 million people lived with HIV/AIDS in 2017 and 940,000 people died of HIV-related illnesses in the same year (https://www.who.int/gho/hiv/en/). HIV/AIDS have become under control since the 2000s with breakthrough innovations in treatment, increased awareness about the disease and global prevention approaches.

There is a global decline in new infections (-18%) and in AIDS related deaths (-34%) since 2010. The HIV incidence per 1000 among 15-49 aged population has declined from 0.85 in 1990 to 0.40 in 2017 (from 0.49 to 0.25 for all ages). The incidence rate has reached to its peak in 1995 with 1.03 per 1000. Since 1995 a steady decline has been observed in the number of new cases https://www.who.int/gho/hiv/en/). This overall decrease in incidence rates can mainly be attributed to global programs to increase HIV/AIDS awareness and health policies developed especially in areas with high infection rates.

Breakthrough treatments introduced for the treatment of the disease since the beginning of the 2000s, have contributed positively to the decline in HIV/AIDS related deaths and have improved longevity and quality of life. Antiretroviral therapies (ART) had impact not only on the viral suppression outcomes but also on patient adherence to therapy as well. Patient adherence has improved especially after the decrease in daily number of pills to be taken. In 2001 a HIV patient had to take 8 pills daily on average, whereas this number has dropped to one pill in 2014 with new treatments (UNAIDS, 2015). In addition to this, the cost of treatment has declined over the years. In 2001 the cost of treatment was 10,000$ compared to 100$ in 2014 (UNAIDS, 2015). All these developments have improved global access to treatment. According to the UNAIDS, 81% of people on ART have achieved viral suppression in 2017 (http://aidsinfo.unaids.org). The number of deaths from the disease has

declined over time (Figure 1) and survival of HIV/AIDS patients have improved with longer life expectancy rates.

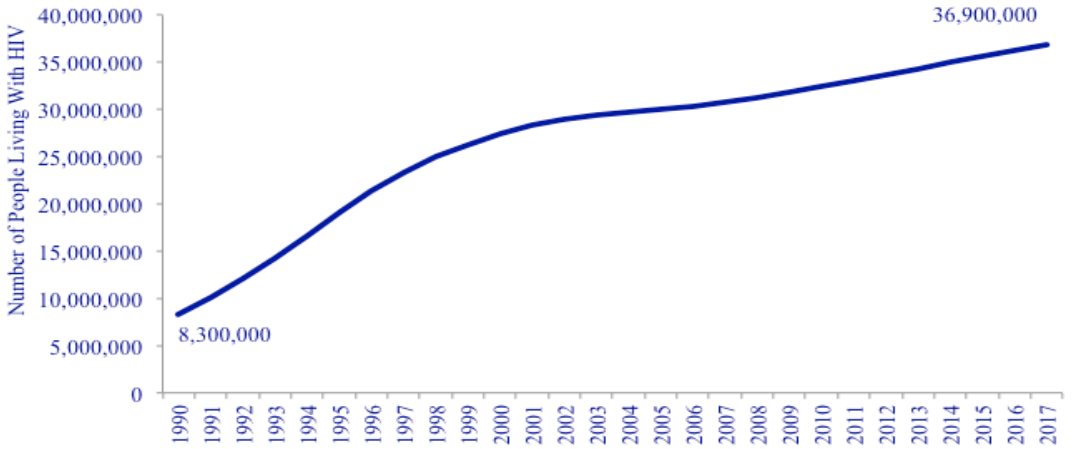
Figure 1: Global AIDS Related Deaths (All Ages)



Source: http://aidsinfo.unaids.org

However, with the current developments in treatment, despite the decrease in incidence rates, the number of people living with HIV at all ages has increased globally due to declined mortality and longer life expectancy (http://aidsinfo.unaids.org) (Figure 2).

Figure 2: Global Number of People Living With HIV



Source: http://aidsinfo.unaids.org

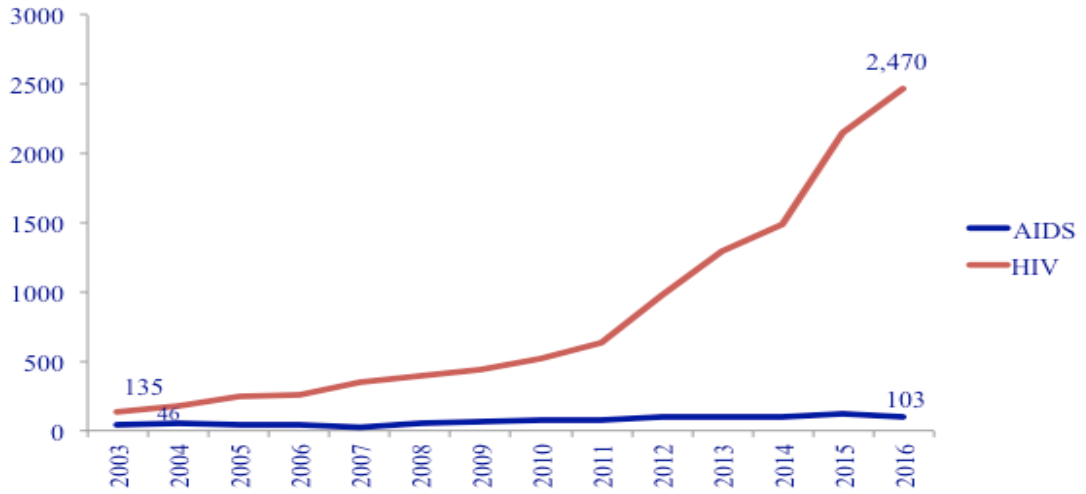
This report aims at drawing the general outlook of HIV/AIDS in Turkey with special reference to access and reimbursement of available treatments. In the following

sections first, the epidemiology of the disease will be presented. The second section will outline the access to HIV/AIDS treatments with special reference to their reimbursement status and rules. The penultimate section will focus on the direct and indirect costs of treatment in Turkey.

2. Epidemiology of HIV/AIDS in Turkey

The first HIV case was diagnosed in 1985 in Turkey and the disease was included immediately on the list of infectious diseases with compulsory notification status. According to the Ministry of Health (MoH) Public Health Institute, 17,884 HIV/AIDS cases were notified between October 1985-December 2017 (http://www.hatam.hacettepe.edu.tr/veriler31Aralik2017.pdf). Of these, 79.7% were male and 71.5% were in the 20-44 age group. Figure 3 below displays the number of new cases in HIV/AIDS in Turkey between 2003-2017.

Figure 3: Number of New HIV/AIDS Cases in Turkey 2003-2017

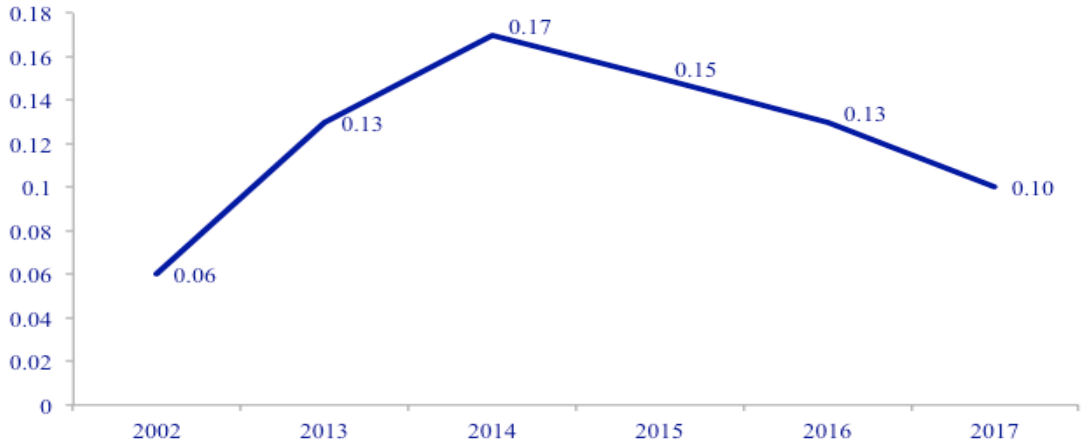


Türkiye Halk Sağlığı Kurumu, 2015

* Data for 2015 and 2016 are from http://www.hatam.hacettepe.edu.tr/veriler31Aralik2017.pdf

Although there seems to be a steady increase in the number of new cases, the incidence rate has started to decline after 2014 (Figure 4). However, all these figures should be approached cautiously as the number of new cases may be underestimated.

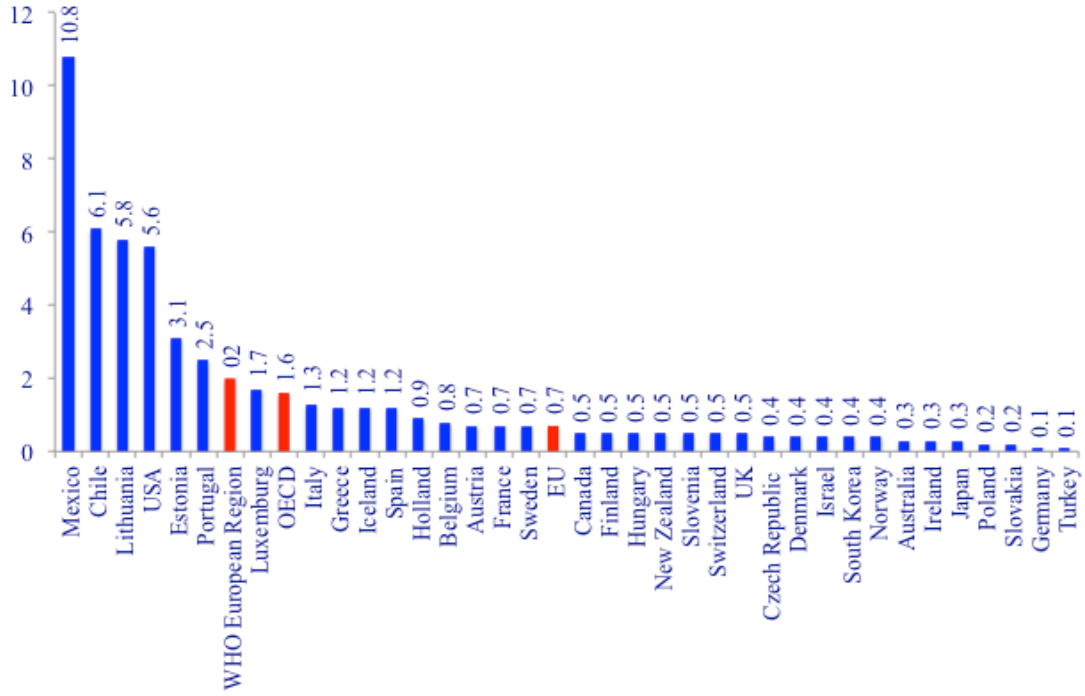
Figure 4: AIDS Incidence in Turkey 2002-2017 (per 100,000 population)



Sağlık Bakanlığı, 2018

Despite the relative increase in number of HIV/AIDS patient figures, Turkey is still among the nations with lowest rates in Europe. The figures below clearly indicate that Turkey has the lowest AIDS incidence among the OECD, WHO European Region and European Union countries (Figures 5 and 6). However, a word of caution is needed, as there might probably be an underreporting problem as well.

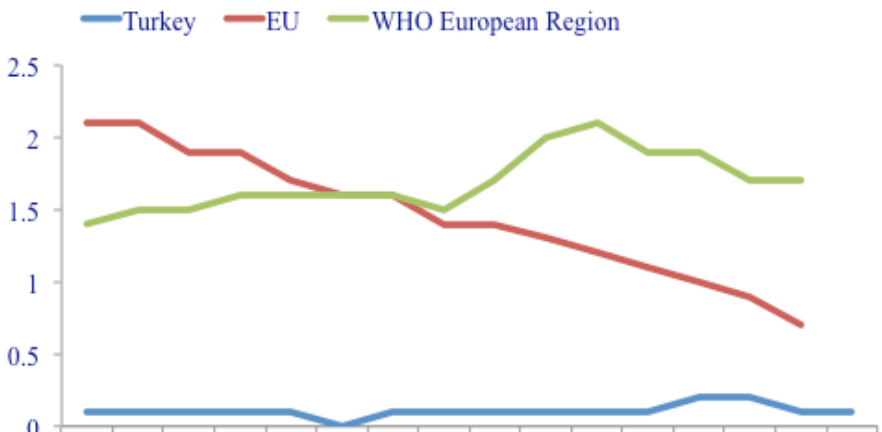
Figure 5: International Comparison of AIDS Incidence (per 100,000) - 2016



The Turkish data are for 2017, others are for 2016 or the nearest year

Sağlık Bakanlığı, 2018

Figure 6: International Comparison of AIDS Incidence (2002-2017) (Per 100,000)



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Turkey	0.1	0.1	0.1	0.1	0.1	0	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.1	0.1
EU	2.1	2.1	1.9	1.9	1.7	1.6	1.6	1.4	1.4	1.3	1.2	1.1	1	0.9	0.7	
WHO European Region	1.4	1.5	1.5	1.6	1.6	1.6	1.6	1.5	1.7	2	2.1	1.9	1.9	1.7	1.7	

Sağlık Bakanlığı, 2018

The transmission route of HIV/AIDS is very important for policy-makers. The following Table 1 presents the national data on transmission routes of HIV/AIDS in Turkey between 1985-2017. As can be seen from the table, the percentage of the 'unknown' category is very high (47.83%) undermining the reliability of the data.

Table 1: Transmission Routes of HIV/AIDS- Turkey (October 1985-2017)

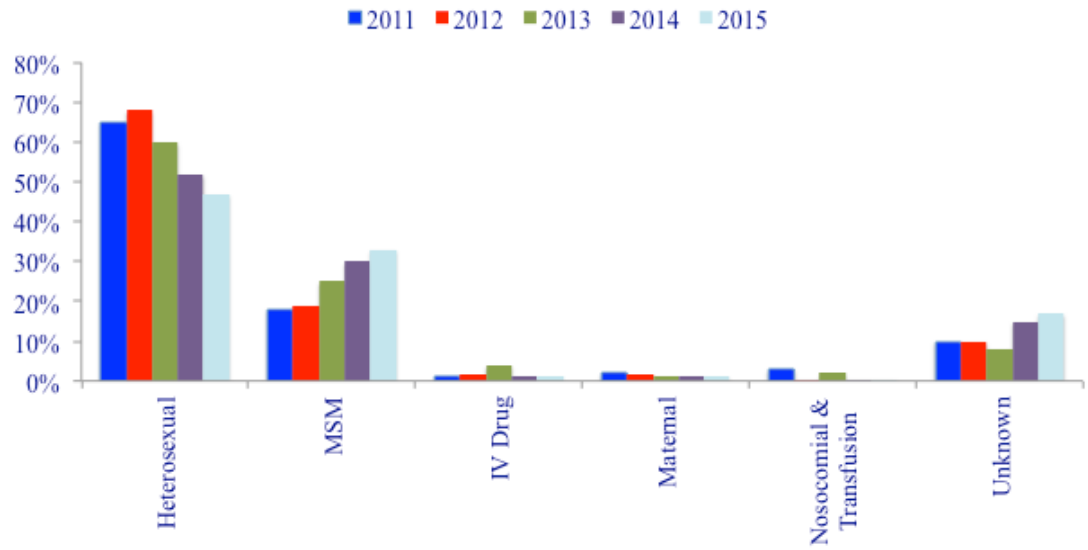
Transmission Route	N	%
Heterosexual Relation	6,403	35.8
Homosexual/Bisexual Relation	2,499	13.97
IV Drug Addiction	245	13.70
Maternal Transition	156	0.87
Hemophilia Patient	23	0.13
Blood and Blood Product Transfusion	97	0.54
Nosocomial infection	78	0.44
Homosexual/Bisexual+Drug Addiction	171	0.96
Unknown	8,554	47.83
Total	17,884	100

http://www.hatam.hacettepe.edu.tr/veriler31Aralik2017.pdf

As Gökengins's (2018) study suggests there is a change in the transmission route of HIV/AIDS over the years. Figure 7 displays the change in transmission route between

2011-2015. As the figures show, a decrease in heterosexual relationship was experienced between 2011-2015 whereas an increase was observed in transmission among men who have sex with men (MSM). However, it should be noted that being in the MSM group is a cause for discrimination and stigmatization in Turkey, enforcing a cautious approach to these figures. Blood transfusion as a transmission way has decreased from 7.1% between 1985-1996 to 0.0% in 2012-2013 (Gülümser, Erbaydar, 2015). This achievement can clearly be attributed to legal arrangements made after the 1990s to regulate the rules for blood and blood products and donors.

Figure 7: Transmission of HIV/AIDS 2011-2015



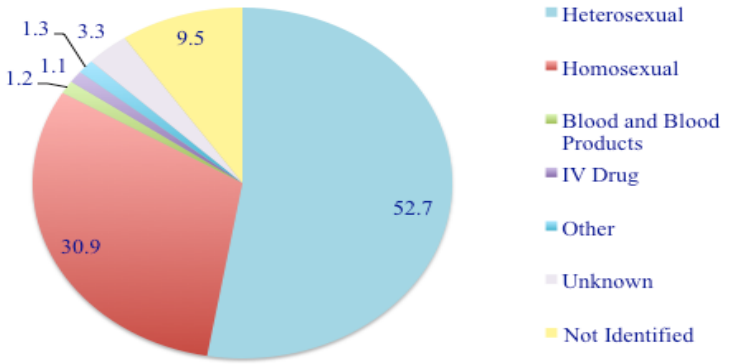
Gökengin, 2018

Along with the national statistics published by national agencies, several single hospital or single province/region studies have been undertaken to discover the demographic and epidemiologic features and transmission route of the disease. In an earlier study analyzing the data from 97 HIV/AIDS patients followed by Ankara Numune hospital between 1993-2006, 72% of the patients were male and average age of 36. Contrary to the belief that the disease was transmitted by homosexual relation, the main transmission route for this cohort was heterosexual relationship (84%). The majority of the male patients (85%) had out of marriage relationship. For the female population in the group, 74% transmitted disease from their husbands (Çelikbaş et al, 2008). This is a common phenomenon for the Turkish female patients observed in

other studies as well. For instance in a study by Alp et al (2011), it was concluded that 92% of female patients' husbands had the disease.

The most comprehensive recent study for HIV/AIDS was undertaken in İstanbul (Yemişen et al 2014). The study analyzed the records of 829 HIV positive patients (700 males) retrospectively. The average age of the patients was 37.5 (± 11.3) and 84% of them were between the 21-50 age group. The education level of the patients was low as 51.2% of them were literate and with primary school education. Figure 8 below shows the transmission routes of the disease in this study.

Figure 8: Transmission Routes of HIV/AIDS in Istanbul Study



Yemişen et al, 2014

Çerçi et al (2016) analyzed the database of the oldest HIV/AIDS Treatment and Research Center in Turkey. The study covered records of 255 cases followed by the Hacettepe University HIV/AIDS Treatment and Research Center (HATAM) between January 1986-January 2013. The mean age of this cohort was 38.0 ± 11.6 (range: 19-80) and 75.6% (n=193) were male. The demographic features of the cohort are presented in Table 2.

In the Hacettepe study, parallel with the findings of the İstanbul study and others, the main transmission route was heterosexual relation (75.8% for females, 59.1% for males). The MSM transmission rate was 17.6%. Again females transmitted the disease mainly from their husbands as 72.3% stated that they only had sexual

relationship with their husbands. Table 3 represents the transmission route of the disease for the Hacettepe cohort.

Table 2: The Demographic Features of the Hacettepe University's HIV/AIDS Cohort (1986-2013)

	Male n (%)	Female n (%)	Total n (%)
Age (n=255)			
19-29	46 (23.8)	20 (32.3)	66 (25.9)
30-39	64 (33.2)	21 (33.9)	85 (33.3)
40-49	49 (25.4)	9 (14.5)	58 (22.7)
>50	34 (17.6)	12 (19.4)	46 (18.0)
Education (n=181)			
Illiterate	-	3 (70.0)	3 (1.7)
Primary	51 (37.0)	15 (34.9)	66 (36.5)
Secondary	36 (26.1)	11 (25.6)	47 (26.0)
University	51 (36.9)	14 (32.6)	65 (35.9)
Nationality (n=255)			
Turkish	165 (85.5)	51 (82.3)	216 (84.7)
Ukraine	-	4 (6.5)	4 (1.6)
Germany	10 (5.2)	1 (1.6)	11 (4.3)
Cyprus	9 (4.7)	2 (3.2)	11 (4.3)
Other	9 (4.7)	4 (6.5)	13 (5.1)
Marital Status			
Single	75 (41.2)	8 (13.6)	83 (34.4)
Married	93 (51.1)	42 (71.2)	135 (56.0)
Divorced/Widowed	14 (7.7)	9 (15.3)	23 (9.5)

Çerçi et al, 2016

Table 3: HIV Transmission Route for the Hacettepe Cohort (1986-2013)

Transmission Route	Male n (%)	Female n (%)	Total n (%)
Heterosexual	114 (54.9)	47 (75.8)	161 (63.1)
Unknown	29 (15.0)	10 (16.1)	39 (15.3)
MSM	34 (17.6)	-	34 (13.3)
Other*	16 (8.3)	5 (8.1)	21 (8.3)

* Blood transfusion, vertical transmission, needle

Çerçi et al, 2016

An interesting finding of the analysis by Çerçi et al (2016) was related with the increasing rate of reports of transmission with MSM (men having sex with men) after 2006 (Table 4).

Table 4: Distribution of MSM Cases by Diagnosis Date- Hacettepe Cohort (1986-2013)

Diagnosis Year	MSM n(%)
1996 and before	2 (5.9)
1997-2005	6 (17.6)
2006 and after	26 (76.5)

* p<0,005

Çerçi et al, 2016

Another important finding of the study was related with the stage of the disease at the time of diagnosis. Before 1996, 55.6% of the patients had CD4 T cell count below 200 whereas this rate has declined to 27.7% after 2006 (Table 5). Figure 9 also displays the HIV/AIDS status of patients before and after 2006. These findings indicate that, currently, HIV/AIDS patients are diagnosed and treated at earlier stages in Turkey.

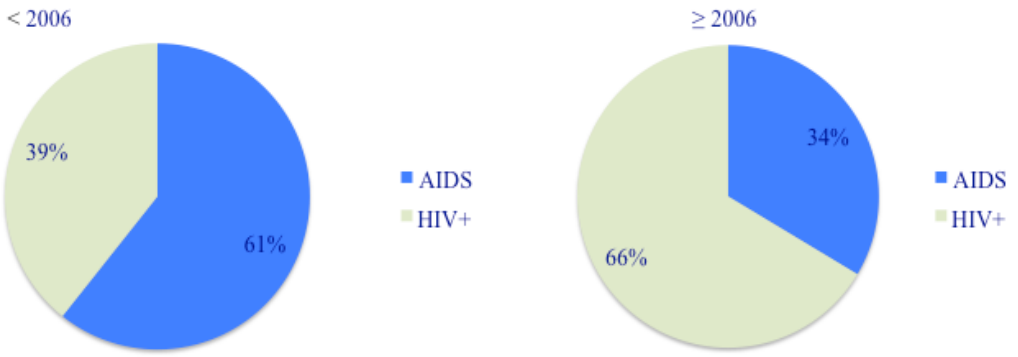
Table 5: Periodical Distribution of CD4 T Cell Counts at the Time of Healthcare Visit

Period	CT4 T Cell Level At the Time of Healthcare Visit			
	<200 n (%)	200-500 n (%)	>500 n (%)	Total n (%)
1996 and before	10 (55.6)	7 (38.9)	1 (5.5)	18 (100)
1997-2005	49 (55.1)	26 (29.2)	14 (15.7)	89 (100)
2006 and after	36 (27.7)*	55 (42.3)	39 (30.0)	130 (100)
Total	95 (40.1)	88 (37.1)	54 (22.8)	237 (100)

* p<0.005

Çerçi et al, 2016

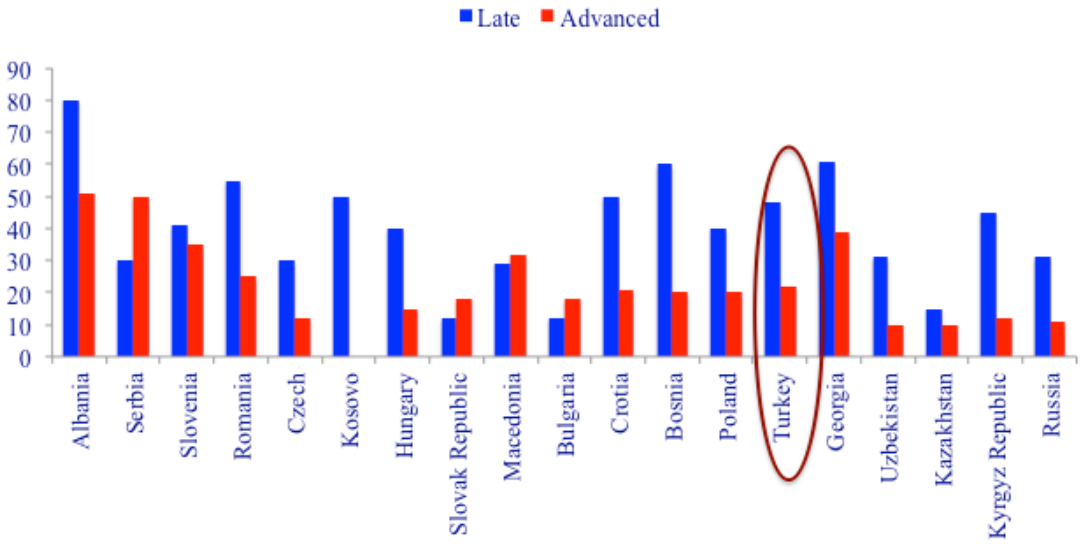
Figure 9: HIV/AIDS Status of Hacettepe Patients Before and After 2006 (1986-2013)



Çerçi et al, 2016

However, despite these improvements over the years, Turkey ranked fifth among the Central and Eastern European countries in estimated percentage of cases diagnosed with late and advanced disease in 2014 (Figure 10).

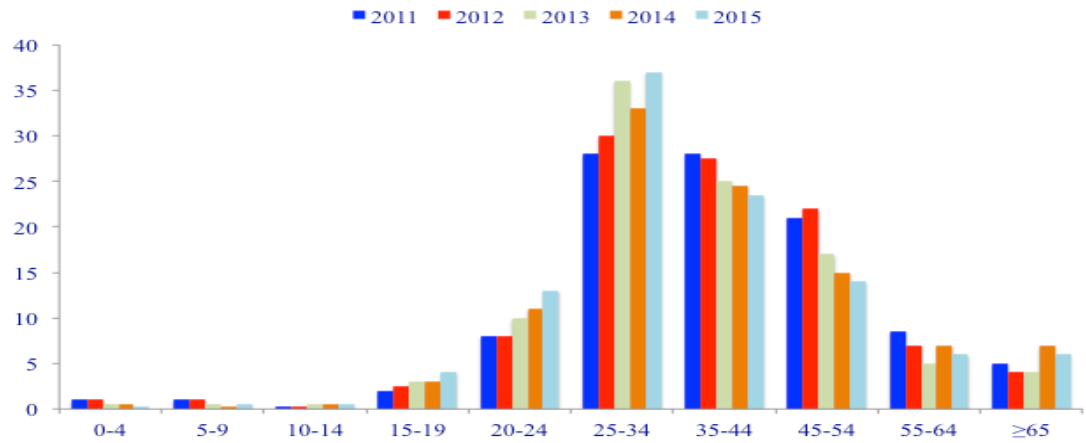
Figure 10: Estimated percentages of Patients Diagnosed with Late* and Advanced* Disease in 2014



Kosovo reported only cases with advanced disease
*Late disease= CD4 T cell count <350 per microliter or AIDS defining illness regardless of the CD4 T cell count
** Advanced disease= CD4 T cell count <200 per microliter or AIDS defining illness regardless of the CD4 T cell count
Gökengin et al, 2018

A last word has to be said about the age distribution of newly diagnosed HIV+ patients (Figure 11).

Figure 11: Age Distribution of Newly Diagnosed HIV+ Patients (2011-2015)- Turkey



Gökengin, 2018

As can be seen from the figure, the rate is highest in the 25-34 group but there is a steady increase in the younger age groups over the years. This age group seems to be the most vulnerable group at risk both in the national data and individual studies.

3. Access to HIV/AIDS Treatment in Turkey.

Development of HIV/AIDS policies in Turkey can be divided into three phases (Çetin, 2017):

1. The first phase: response to the first AIDS case (1985-1992)
2. The second phase: institutionalization and self-organization (1992-2002)
3. The third phase: Health Transformation Program (2002-)

The first phase has commenced with the diagnosis of the first patient in Turkey in 1985. As the patient was also a popular person among the pop music society, the attention of the media and hence the public was immediately drawn to HIV/AIDS. The stigma attached to the disease and to the patient was enormous to the extent that when he died in 1992, his body was washed with bleach and buried in a galvanized coffin. The main outcome of the diagnosis of the first case was increased attention of the MoH to the disease that was believed to occur in other areas of the world but not in Turkey. The MoH has taken HIV/AIDS to the list of diseases to be notified (1985) immediately and additional measures were taken in the following years. This notification is made with a coding system to keep the patient anonymous. HIV

testing of all blood and blood products was introduced in 1986 and disposable injectors became compulsory in all health facilities in 1987. In 1987, a High Advisory Board on AIDS was established with the tasks of collecting information on AIDS, training the healthcare staff and developing measures to curb the spread of the disease. In 1988, HIV testing was introduced for those joining the army for compulsory military service.

The second phase (1992-2002) witnessed the establishment of non-governmental organizations for HIV/AIDS. Two associations, led by medical doctors established in this phase are particularly important. These associations had close relations with the MoH and had high influence on the HIV/AIDS policies. The Association for Combatting AIDS (AIDS ile Mücadele Derneği) was established in İzmir in 1991 and The Association for Battle Against AIDS (İstanbul AIDS Savaşım Derneği) was established in 1992 in İstanbul. These associations mainly had a leading role in increasing the awareness of the public and in education and training of the healthcare personnel. The Family Planning Association founded in 1985, also had active involvement in HIV/AIDS arena supported by its close relationship with international organizations and projects. This Association acted as a mediator between the civil society and the government in developing a united action against the disease. The most important development at this stage can be stated as the establishment of the National AIDS Commission in 1996 with the aim of bringing an intersectoral approach to a disease requiring a collaborative action of various sectors. The responsibility of the Commission was restricted to offering advice and its activities have come to a halt in recent years.

The third phase in HIV/AIDS has commenced with the Health Transformation Program of the new single party government in Turkey from 2002. This period entails the major transformation of the health care system in terms of healthcare delivery system and finance. All developments especially directed to more equal distribution of health care resources and to enhancement of public coverage had a positive impact on the HIV/AIDS patients as well. Access to healthcare services and hence access to HIV/AIDS treatment has also improved during this period. An important development on the societal side of the disease was the establishment of the Positive Living

Association (PLA) (Pozitif Yaşam Derneği) in 2005 in İstanbul. Unlike other existing associations, PLA was primarily established by HIV/AIDS patients and was supported by their families and experts in the field. The underlying reason for the establishment of the Association was to improve support between HIV/AIDS patients, but later the organization has evolved into an influential one backed by patients, families, medical experts and the international community. The Association, in addition to its psychological support to people with HIV/AIDS and their parents, also provides legal and medical advice as well. In 2005, the HIV/AIDS Prevention and Support Program for Turkey was launched with the MoH and the Global Fund. This program, with its intersectoral and nationwide characteristics has initiated an environment with high-level cooperation between the government, NGOs and the medical society. Under this program, a research was undertaken in 2007 in five cities among the high-risk population groups. HIV prevalence was found as 0.8% among unrecorded sex workers, 3.5% among MSM patients and 1.2% in IV drug users.

Loosing anonymity is an undeniable fear of an HIV/AIDS patient due mainly to social problems that might be encountered from the family and society at large. In 2006, the MoH adopted a new policy and established special centres for rapid diagnosis. As the patients applying these centres are coded their unanimity is secured. In their study, Özdemir et al (2018) concluded that establishment of these centres was a turning point and more people were admitted to the hospital at an early stage of disease. Patients can also have free tests at these centres.

a. The Healthcare Delivery System

The MoH dominates the health care delivery system in Turkey at the primary, secondary and tertiary level. There are also university hospitals providing tertiary care and a dynamic private sector active at all three levels of care. Primary care is provided by family practitioners of the MoH and also by private centers and laboratories. The latter has to sign a contract with the Social Security Institution (SSI) in order to be included in the reimbursed health care market. There is no compulsory referral system, so patients can directly visit secondary or tertiary facilities even for minor ailments. The SSI determines reimbursement rules and prices of medical services, pharmaceuticals and medical devices declared in the Health Implementation

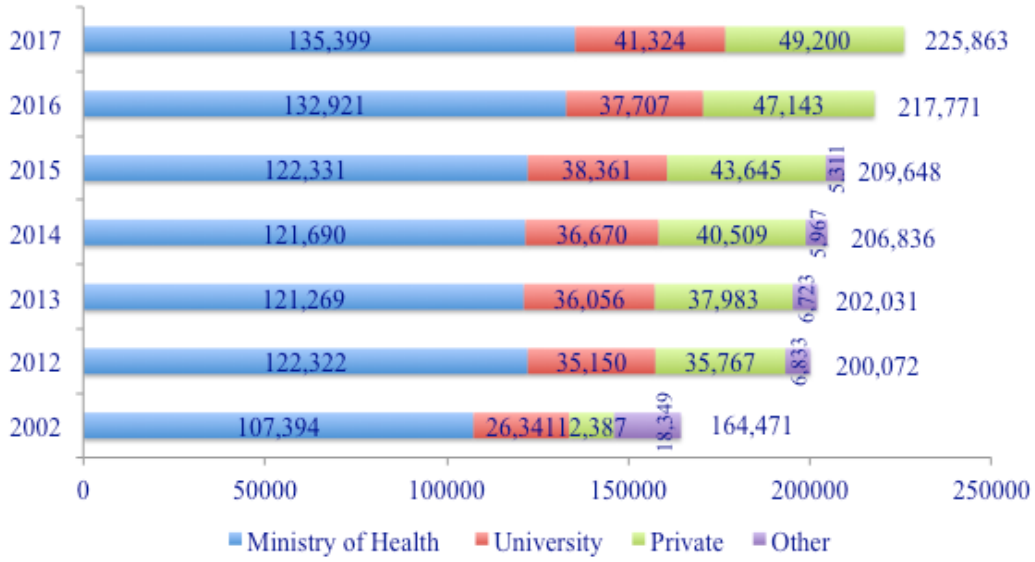
Guide (HIG) (Sağlık Uygulama Tebliği- SUT). Family practitioners can directly prescribe a range of drugs allowed by the HIG. Some others can only be prescribed upon a medical report issued by specialists. In this case, family practitioners can write repeat prescriptions during the validity period of the report. Some group of drugs, including HIV/AIDS drugs cannot be prescribed by family practitioners at all.

At the secondary level, there are MoH hospitals, private hospitals and private centres. MoH facilities are scattered all around the country. After 2003, with the new policies providing incentives for the private sector, the involvement and role of private hospitals have increased in the system. Services of these hospitals are reimbursed by the SSI provided that they have a contract with the institution. Payment rules are the same as public hospitals and are declared in the HIG. The only difference is the special co-payments that private hospitals can ask from patients. The ceiling for this amount is also determined by the government. Currently, private hospitals can ask up to 200% of their bill to the SSI from the patient. Insurance firms were allowed to introduce complimentary insurance for this part of the healthcare expenditures in 2013.

At the tertiary level, there are MoH Education and Training Hospitals, University Hospitals and Private University Hospitals. Same rules for both public and private facilities as above apply for tertiary units as well. Figure 12 displays the distribution of beds in the hospital sector. As can be seen, in 2016, 61.03% of beds were owned by the MoH, 17.08 % were by universities and 21.0% were by the private sector.

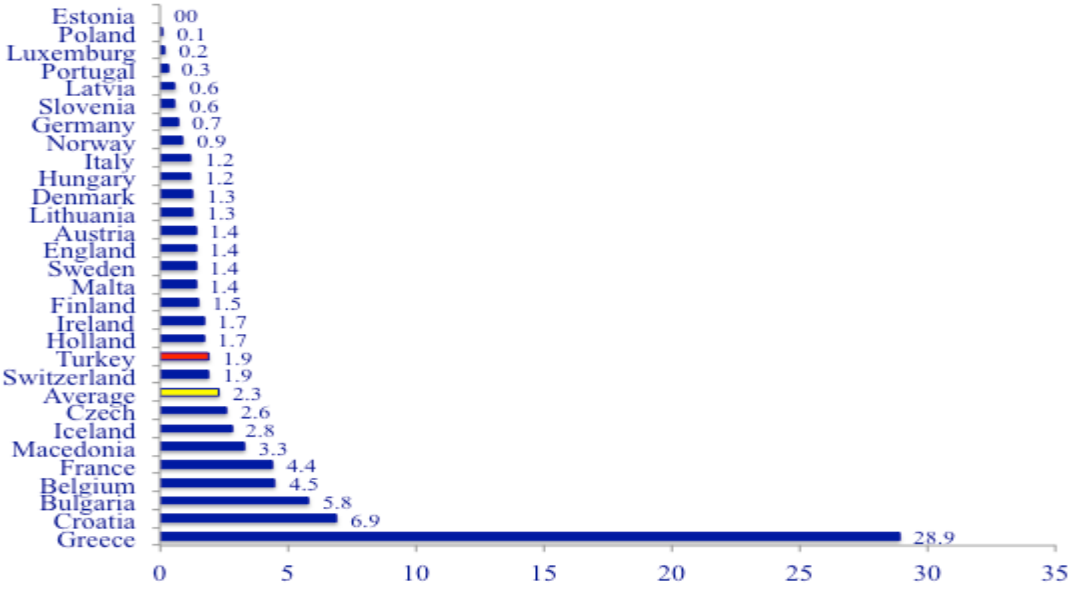
Infection specialists are the key actors in HIV/AIDS management. There were 1,289 specialists in 2013 (1.9 per 100,000) in Turkey. Of these, 844 were working in the MoH facilities, 225 in university hospitals and 220 in the private sector (Yükseköğretim Kurulu, 2015). Figure 13 below compares this figure with EU countries.

Figure 12: Distribution of Hospital Beds in Turkey (2002-2017)



Sağlık Bakanlığı, 2018

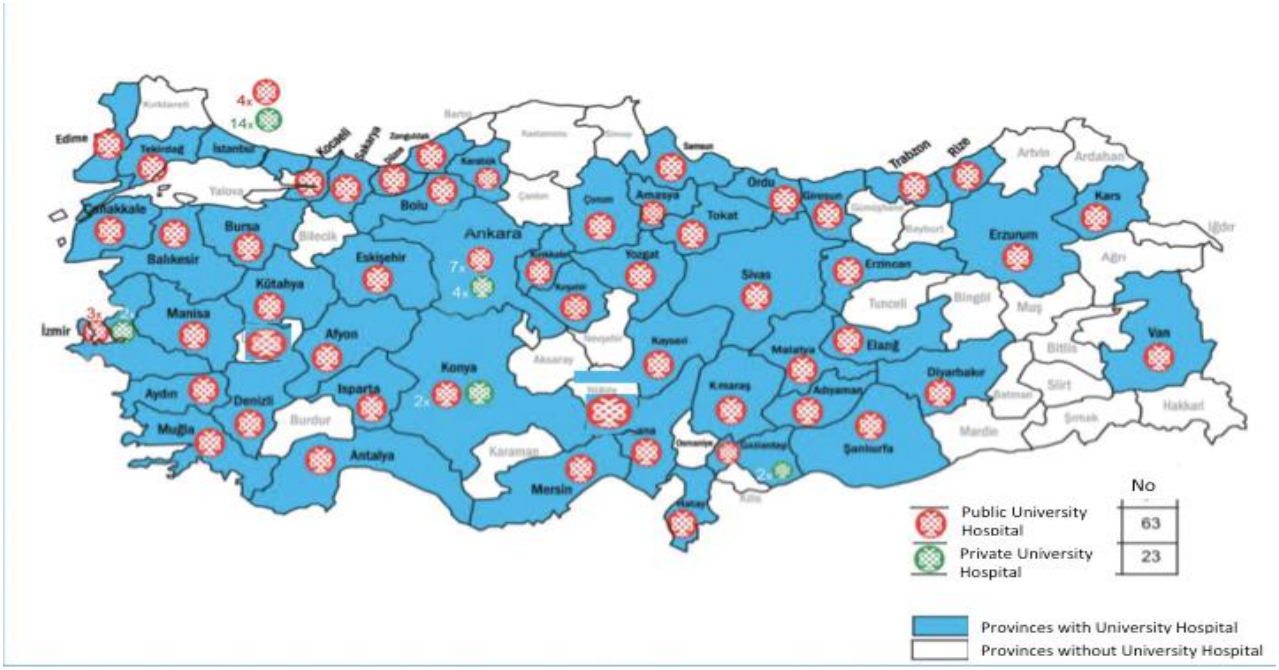
Figure 13: Number of Infection Specialist per 100,000- 2013



Yükseköğretim Kurulu, 2014

HIV/AIDS diagnosis, treatment and monitoring are usually undertaken at tertiary level hospitals. Figure 14 below shows the distribution of university hospitals followed by Figure 15 showing the distribution of MoH tertiary hospitals.

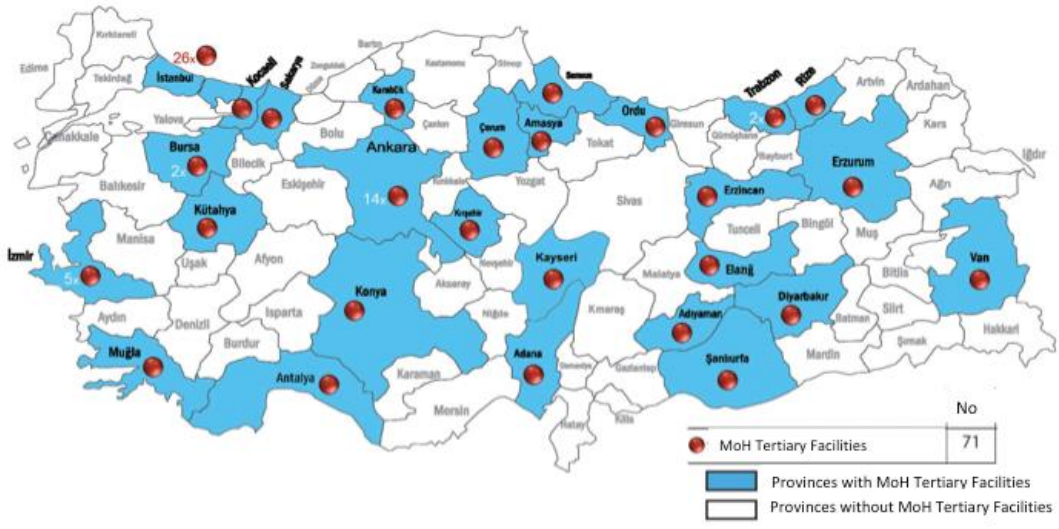
Figure 14: Distribution of University Hospitals in Turkey- 2018



Two provinces (Uşak and Niğde) are added to provinces with public university hospital after the publication of this report. These provinces are included in the map.

Yükseköğretim Kurulu, 2013

Figure 15: Distribution of Ministry of Health Tertiary Hospitals in Turkey- 2013



Yükseköğretim Kurulu 2014

As can be seen from these figures, tertiary units are spread almost evenly except in some parts of the Eastern and Southeastern Anatolia.

b. Financing of HIV/AIDS Patients

The SSI is the main public purchaser of health care services. As the only player in the public sector, it has a monopsonic power and uses this power to regulate the reimbursement rules and prices of the medical goods and services.

Currently, 98.3 % of the population is covered by the SSI making it as the key player in the financing part. Share of public health care spending is higher than the OECD average in Turkey (78% vs. 72% in 2015). Out-of-pocket (OOP) expenditure is lower than the OECD average (16% vs. 20% in 2015). Figure 16 shows the flow of funds in Turkey, followed by Figure 17 outlining the healthcare financing system.

Figure 16: Flow of Funds in the Turkish Healthcare System

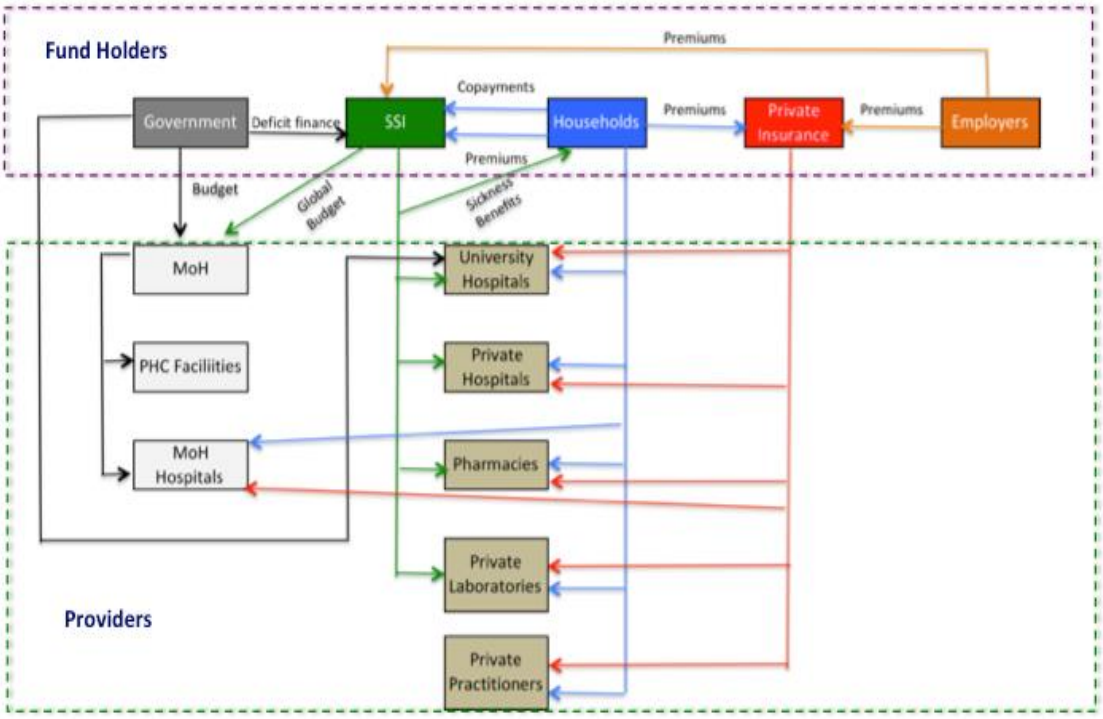
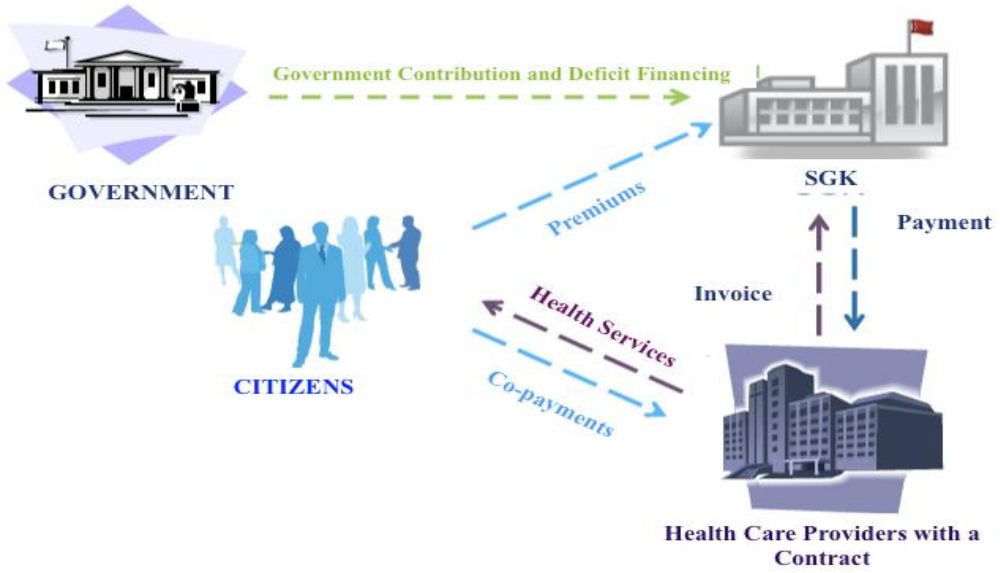


Figure 17: The SSI Flow of Funds



SGK is the Turkish abbreviation for SSI (Sosyal Güvenlik Kurumu)

Financial access to healthcare services for all segments of the population, including HIV/AIDS patients, have improved following the introduction of the General Health Insurance Scheme in Turkey in 2008. People working in public and private sector and their dependents are covered through the employer and employee premiums collected by the SSI. If a person has a job either in the public or private sector, both employee and employer premiums are transferred to the SSI. In this case, both the employee and his/her dependents' health care expenditures are covered automatically. But there are many options for people below a certain income level, unemployed and for people in the vulnerable groups. In addition to this, people without any job and who are not under the income level described as 'poor' can benefit from the general health insurance scheme by paying an affordable premium to the SSI (76.75TRY for 2019). Children under 18 without any coverage from their parents are automatically covered by the SSI. HIV/AIDS patients are exempt from statutory prescription co-payments.

4. Reimbursement Status of HIV/AIDS Treatment in Turkey

a. HIV/AIDS Treatment Guidelines

There are both international guidelines and a Turkish guideline recommending strategies and therapies to screen, treat and monitor HIV/AIDS patients. The common recommendation of international guidelines is to start ART therapy immediately after diagnosis of HIV regardless of the CD4 T counts (European Aids Clinical Society, 2018; Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018; World Health Organization, 2015). The Turkish guideline also adopts this approach as well. Table 6 below presents The European AIDS Clinical Society's (EACS) recommendations for treatment naive patients followed WHO's recommendations.

Table 6: EACS's Recommended ART Regimen for Treatment Naive Patients

Regimen	Dosing	Caution
2NRTIs + INSTI		
ABC/3TC/DTG	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd	Al/Ca/mg- containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before) DTG 50mg bid with rifampicin.
TAF/FTC or TDF/FTC +DTG	TAF/FTC/BIC 25/200/50 mg, 1 tablet qd or TDF/FTC 300/200mg, 1 tablet qd +DTG 50mg, 1 tablet qd	
TAF/FTC/BIC	TAF/FTC/BIC 25/200/50 mg 1 tablet qd	Al/Ca/Mg- containing antacids should be taken 2h after BIC (fasting conditions) whereas Ca, Mg, Fe or multivitamins supplements can be administered simultaneously with food.
TAF/FTC or TDF/FTC +RAL	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg 1 tablet qd +RAL 600 mg 2 tablets qd or +RAL 400 mg 1 tablet bid	Co-administration of antacids containing AI or Mg not recommended. Co-administration of RAL 1200 mg qd with Ca containing antacids or with Ca, Mg, and Fe supplements is not recommended. RAL 400 or 800 mg bid with rifampicin

Table 6: EACS's Recommended ART Regimen for Treatment Naive Patients (…continued)

2 NRTIs +NNRTI		
TAF/FTC/RPV or TDF/FTC/RPV	TAF/FTC/RPV 25/200/25mg 1 tablet qd or TDF/FTC/RPV 300/200/25mg 1 tablet qd	Only if CD4 count>200 and HIV-VL<100,000 copies/mL. PPI contraindicated; H2 antagonists to be taken 12h before or 4h after RPV.
2NRTIs+PI/r or PI/c		
TAF/FTC or TDF/FTC +DRV/c or +DRV/r	TAF/FTC 10/200mg, 1 tablet qd or TDF/FTC 300/200mg, 1 tablet qd +DRV/c 800/150mg, 1 tablet qd or +DRV 800mg 1 tablet qd+RTV 100md 1 tablet qd TAF/FTC/DRV/c 10/200/800/150 mg	Monitor in persons with a known sulfonamide allergy

3TC: Lamivudine, ABC: Abacavir, BIC: Bictegravir, /c: Cobicistat, DTG: Dolutegravir, DRV: Darunavir, FTC: Emtricitabine, INSTI: Integrase Strand Transfer Inhibitor, NRTI: Nucleotide Reverse Transcriptase Inhibitor, NNRTI: Non-Nucleotide Reverse Transcriptase Inhibitor qd: once daily, PI: Protease Inhibitor, /r: Ritonavir, RAL: Raltegravir, RPV: Rilpivirine, TAF: Tenofovir Alafenamide, TDF: Tenofovir Disoproxil Fumarate,

EASC, 2018

Table 7: Preferred and Alternative First-Line Regimens in Adults and Adolescents

Population				Preferred First Line Regimen	Alternative First Line Regimen(s)	Special Situations
Adult men and adolescent boys				TDF+3TC (or FTC) + DTG	TDF+3TC (or FTC) +EFV 600mg TDF+3TC (or FTC) +EFV 400mg	AZT+3TC +EFV 600mg TDF+3TC (or FTC)+PI/r[b]
Adult women and adolescent girls	Pregnant or breastfeeding					
	Not of childbearing potential					
	Of childbearing potential	Offered and using effective contraception	Offered but not using effective contraception or without access to contraception or want to become pregnant	Choose to use DTG after informed choice		
				Choose to use EFV after informed choice	TDF+3TC (or FTC)+ EFV 600mg	TDF+3TC (or FTC) + EFV 400mg TDF+3TC (or FTC) + ATV/r[b]	AZT+3TC + EFV 600mg TDF+3TC (or FTC)+RAL

3TC: Lamivudine, ATV: Atazanavir, AZT: Zidovudine, DTG: Dolutegravir, EFV: Efavirenz, FTC: Emtricitabine, PI/r: Protease Inhibitor/ritonavir, RAL: RaltegravirTDF: Tenofovir Disoproxil Fumarate,

[a]Based on programmatic practicality and uncertainty surrounding possible DTG effects after the neural tube closes at 28 days of gestation as noted by the originator and FDA, previous safe period after 8 weeks is now extended to after the first trimester. In practice the majority of women will not yet know that they are pregnant during the first 8-12 weeks of pregnancy.

[b]If the national prevalence of pre-treatment resistance to EFV or NVP is 10% or higher or if no other alternatives are available.

World Health Organization, 2018

Another guideline to mention is from the US Department of Health and Social Security (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018). However the recommendations of this guideline is not very compatible with the available treatments in Turkey. That is why its recommendations will not be presented here.

The Turkish HIV/AIDS Guideline was published in 2013. Beginning to ART therapy regardless of the CD4 T cell count was advised in this Guideline. Since, then ART therapy is commenced in patients infected with HIV regardless of the CD4 count. This recommendation is in line with international agencies' recommendations. Table 8 presents countries following this advice in Central and Eastern European countries as of 2015.

Table 8: Antiretroviral Treatment Indication Threshold for CD4 T Cell Count According to Income (as of 2015, after the change in major guidelines)

Income	CD4 T Cell <350/mm^3	CD4 T Cell <500/mm^3	Any CD4 T Cell Count
Lower-Middle	Kosovo Uzbekistan	Armenia Kyrgyz Republic Moldova	Georgia
Upper-Middle	Albania Azerbaijan Bulgaria Macedonia Montenegro Serbia	Bosnia and Herzegovina Kazakhstan	**Turkey** Romania
High	Russian Federation		Croatia Czech Republic Estonia Hungary Poland Slovak Republic Slovenia

Gökengin et al, 2018

The advices of the Turkish HIV/AIDS Treatment Guideline (Sağlık Bakanlığı, 2013) are presented in Table 9 below. The following table summarizes the conditions to start ART therapy regardless of the CD4 T cell count.

Table 9: Turkish HIV-AIDS Guideline: Conditions to Start ART Therapy

Clinical Category	CD4 T Cell Count	Recommendation
Symptomatic Patient	Any value	Initiate therapy
Asymptomatic Patient	<350 cell/mm^3	Initiate therapy
Asymptomatic Patient	300-500 cell/ mm^3	Initiation of therapy is beneficial. Patient specific therapy is recommended
Asymptomatic Patient	>500 cell/ mm^3	Treatment can be initiated. If the patient is willing and ready, based on the specific conditions of the patient, treatment can be

Sağlık Bakanlığı, 2013

The Turkish Guideline recommends initiating ART therapy regardless of the CD4 T Cell count under the following conditions (Sağlık Bakanlığı, 2013):

- Patients with rapid risk of progression
  - Rapid decline in CD4 T cell count (>100 cell/ mm^3/year)
- Viral load>100,000 copy/mL
- >50 age
- Existence of chronic hepatitis B or C
- HIV related kidney disease
- High cardiovascular risk
- Presence of opportunistic disease
- Pregnancy
- Presence of malignancy

The Turkish Guideline states the basic principle of ART as to combine two nucleotide reverse transcriptase inhibitors (NRTI) with one non-nucleotide reverse transcriptase inhibitor (NNRTI) or one protease inhibitor (PI) or integrase inhibitor or receptor antagonist. This approach is labeled as combined ART therapy (cART). The recommendations for treatment naïve patients are listed in the Table 10 below (Sağlık Bakanlığı, 2013).

Adherence to ART therapy is essential to achieve therapeutic drug levels, ensure virologic suppression and to reduce drug resistance. As stated earlier, there is no cure for HIV/AIDS, but new therapies improve health status of patients and prolong life expectancy after initial diagnosis. Adherence to any treatment is difficult to measure, as it requires a thorough follow-up of patients continuously for a predetermined time.

Also the reasons for non-adherence are a key to improve the treatment patterns. A comprehensive study on adherence to ART therapy for HIV/AIDS patients in Hacettepe University's hospital was carried out recently by Ceylan et al (2019). As stated earlier, the treatment and research center in the university is the oldest one with comprehensive and reliable data. In the research, 158 patients were asked to answer an individual questionnaire and the Turkish version of the Morisky Medication Adherence Scale. The research concluded that 61% of the patients were highly and 37.9% were moderately adherent to treatment. Adherence was mostly affected by having information on ART. Patients with information about the therapy were more adherent than those without information. The difference was statistically significant. Patients with social support were also more adherent but the side effects of the therapy did not have an influence on the adherence levels.

c. HIV/AIDS Reimbursement in Turkey

The SSI's health benefits package in Turkey is very comprehensive. As stated earlier, the SSI determines the rules and prices of treatments, pharmaceuticals and medical devices to be reimbursed. Companies submit a reimbursement dossier covering the clinical and economic value of their product with a budget impact analysis covering the next three years after launch.

Decreasing the viral load is the main focus of ART treatment and achievement of this ultimate goal depends mainly on early initiation of therapy. Lower levels of viral load not only avoids the progress of the disease but also avoids its transmission by sexual contact. It has been stated that Turkey is in a better position in reimbursement of ART treatment for HIV/AIDS in comparison to Central and Eastern European countries. In 2015, Turkey was among the three countries with reimbursement of all three drugs in the integrase inhibitors group (the other two were Czech Republic and Poland) and the only country among 11 where fixed dose combination containing elvitagravir was reimbursed (Gökengin, 2018). Figure 18 summarizes the general reimbursement rules for antiretrovirals with HIV/AIDS indication followed by Table 11 listing the reimbursed treatments and specific rules in addition to the general rules outlined in Figure 18.

Table 10: Recommended Treatments for Treatment Naive Patients: The Turkish Guideline

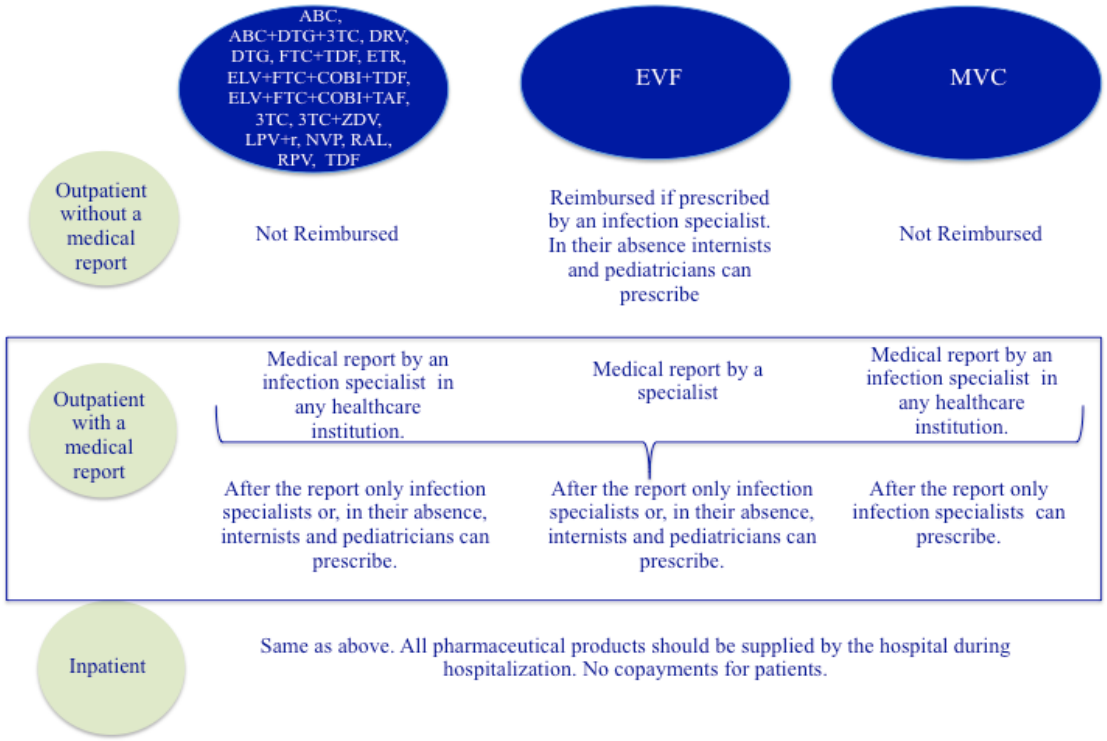
Recommended Combination			
First Choice			
NRTI-NNRTI	Tenofovir/ Emtricitabine+ Efavirenz (TDC/FTC) + EFV		
NRTI-PI	Tenofovir/Emtricitabine (TDF/FTC)	and	Lopinavir/Ritonavir or (LPV/R)
			Darunavir/Ritonavir or (DRV/R)
			Atazanavir/Ritonavir (ATV/R)
NRTI -INSTI	Tenofovir/Emtricitabine +Raltegravir (TDF/FTC + RAL)		
Second Choice			
NRTI-NNRTI	Zidovudin/Lamuvidine (ZDV/3TC)	and	Efavirenz (EFV) or
			Nevirapin (NVP)
	Abacavir[2]/Lamuvidine + Efavirenz (ABC/3TC) + EFV		
	Tenofovir/Emtricitabine + Nevirapin[3] (TDF/FTC) + NVP		
NRTI-PI	Zidovudin/Lamivudine (ZDV/3TC) or Abacavir/Lamivudine (ABC/3TC)	and	Lopinavir/ Ritonavir or (LPV/R)
			Darunavir/Ritonavir or (DRV/R)
			Atazanavir[1]/Ritonavir (ATV/R)
NRTI-INSTI	Zidovudin/Lamivudine/Raltegravir (ZDV/3TC) + RAL		

[1] Atazanavir is not available in Turkey.

[2]Due to ABC high sensitivity, before initiating this therapy non existence of HLA-B*5701b type should be ensured.

3As it causes liver toxicity, NVP should not be used in patients with mild liver failure, in female patients with CD4 T cell count >250 cell/ mm^3 and in male patients with CD4 T cell count >400 cell/ mm^3.

Figure 18: Reimbursement Rules for Antiretrovirals with HIV/AIDS Indication



3TC: Lamivudine, ABC: Abacavir, COBI: Cobicistat, DRV: Darunavir, DTG: Dolutegravir, EFV: Efavirenz, ELV: Elvitegravir, ETR: Etravirine, FTC: Emtricitabine, LPV: Lopinavir, MVC: Maraviroc, NVP: Nevirapine, RAL: Raltegravir, RPV: Rilpivirine,TAF: Tenofovir Alafenamide, TDF: Tenofovir Disoproxil, ZDV: Zidovudine.

Table 11: Reimbursed HIV/AIDS Treatments and Reimbursement Rules in Turkey (April 2019)

Active Ingredient	Brand	Special Condition
Abacavir	Ziagen	-
Abacavir+Dolutegravir+Lamivudine	Triumeq	-
Darunavir	Prezista	Can be used with low dose ritonavir and in combination with other antiretrovirals
Dolutegravir	Trivicay	50mg dose can be used in adults with the following conditions: • Maximum 1x1 dose in HIV-1 infected patients without resistance to integrase class of drugs. • Maximum 2x1 dose when used in combination with efavirenz, nevirapine, tipranavir/ritonavir or rifampicin in HIV-1 infected patients without resistance to integrase class of drugs. • Maximum 2x1 dose in HIV-1 infected patients with resistance to integrase class of drugs. In children over 6 and adolescents infected with HIV and without resistance to integrase class of drugs • The daily dose of dolutegravir per kg is as follows: 20mg for 15-19kg, 25mg for 20-29kg, 35mg for 30-39kg, 50mg for 40kg and over • Twice the daily dose based on weight can be used in combination with efavirenz, nevirapine, tipranavir/ritonavir or rifampicin in HIV infected patients without resistance to integrase class of drugs
Efavirenz	Stocrin	-
Emtricitabine+Tenofovir Disoproxil Fumarate	Hivent, Pernoi, Sidatria, Truvada	Can be used in combination with other antiretrovirals. Tenofovir Disoproxil Fumarate cannot be used with other drugs containing emtricitabine or lamivudine.
Etravirine	Intelence	Can be used in adult patients previously treated with an antiretroviral therapy and developed resistance (virologic non-response [viral load>50 copy/ml] and/or determined by resistance tests).

Table 11: Reimbursed HIV/AIDS Treatments and Reimbursement Rules in Turkey (April 2019) (…continued)

Active Ingredient	Brand	Special Condition
Elvitegravir+Emtricitabine+Cobicistat+Tenofovir alefenamid	Genvoya	-
Elvitegravir+Emtricitabine+Cobicistat+Tenofovir Disoproxil	Stribild	-
Lamivudine	Epivir, Medovir, Micend, Mivux, Zeffix, Zefomen	-
Lamivudine+Zidovudine	Combivir	-
Lopinavir+Ritonavir	Kaletra	-
Maraviroc	Celsentri	Resistant Adult patients with at least 3 different antiretroviral therapies before and only patients infected with CCR5-tropic HIV-1.
Nevirapine	Viramune	-
Raltegravir	Isentress	-
Rilpivirin	Edurant	In treatment naïve adult patients with <100,000 copy/ml viral load
Tenofovir Disoproxil	Abavir, Doro, Evasif, Nefovir, Ovirptoxil, Sotacar, Tenoviral, Tenribel, Ternavir, Veforix, Viread, Virsoem, Virtenix, Voxus, Zenovirt	-

5. Cost of HIV/AIDS in Turkey

Cost of disease studies are rare in Turkey but there are two published studies for HIV/AIDS. The first published study, covering the period between 2001-2012 was conducted by exploring the records of Hacettepe University's HIV/AIDS Treatment and Research Centre. The HIV patients were classified according to their CD4 cell counts. The distribution of patients by CD4 cell counts in the dataset are listed below.

Table 12: Distribution of Patients by CD4 T Cell Counts - Hacettepe Patient Dataset

Classification	CD4 Cell Count (cell/mm^3)	Distribution (n=252)
Group 1	<100	25.3%
Group 2	100-300	29.0%
Group 3	>300	45.7%

Koçkaya et al 2016

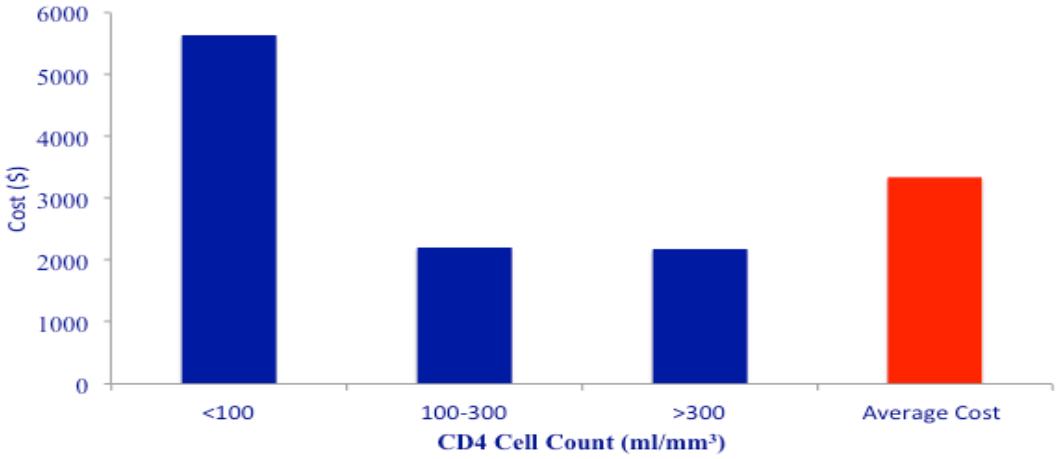
The direct costs of HIV patients in the group are presented in Table 13 and Figure 19.

Table 13: Itemized Direct Costs of HIV/AIDS Patients in the Hacettepe Patient Dataset by Treatment Groups ($ per capita)

Group	Outpatient	Laboratory	Inpatient	Complications	Total
1	192.07	1,297.09	1,888.81	2,259.06	5,637.04
2	82.00	760.04	306.72	1,062.78	2,211.64
3	76.57	773.20	47.36	1,285.20	2,182.35
				Weighted Mean Cost	3,334.64

Koçkaya et al 2016

Figure 19: Annual Cost per Patient in the CD4 Cell Count Classification Groups



Koçkaya et al, 2016

As can be seen from Table 13, treatment cost of complications had the highest share in the overall direct costs and the cost increased with the decreased CD4 cell counts as expected. This data set does not cover the cost of ART treatment that could precede all cost items on the list. That is why the total health care cost per capita should be treated cautiously.

Another study with the patients in the same database was undertaken by Polar Health Economics and Policy in collaboration with the Centre (HATAM). This study explored both direct and indirect costs of the disease. For the direct cost part of the study, an expert panel comprised of five clinical experts from five different HIV/AIDS treatment centres was formed. A questionnaire exploring the types, amount and frequency of resources used in diagnosis, treatment and monitoring of the disease was used to estimate the direct cost of treatment. Tuberculosis, coronary heart disease, Kaposi sarcoma, brain lymphoma, cancer of the cervix, renal failure, depression and dyslipidaemia were selected as the major comorbidities of the disease and separate questionnaires were designed to find out the cost of treatment of these comorbidities. The annual direct cost of treatment per patient, including the cost of treating comorbidities, was found as 14,946.75 TRY (2,346€)[1]. The share of treatment cost of comorbidities in the total cost of treatment comprised approximately 6% of the total cost. Table 14 below presents the direct costs of HIV/AIDS treatment.

Table 14: Annual Direct Cost per HIV+ Patient (Including the treatment cost of co-morbidities)

Treatment	Cost Per Patient (TRY)
HIV	14,075.85
Tuberculosis	209.6
Coronary Artery Disease	91.1
Kaposi Sarcoma	35.1
Renal Failure	250.9
Osteoporosis	72.8
Depression	98.2
Dyslipidaemia	113.2
Total Annual HIV Treatment Cost Per Patient	14,946.75

Tatar et al, 2016a

[1] 1 Euro= 6.37TRY, April 8, 2019

As can be seen from Table 14 the cost of renal failure had the highest treatment cost followed by tuberculosis. The total treatment cost of HIV/AIDS to the SSI was found as 102,968,161 TRY (16,164,546€)[2] for 2015.

If cost of disease studies are rare, studies on indirect costs of a disease is almost non-existent in Turkey. Indirect cost of HIV/AIDS is important, as with the introduction of successful ART therapies both the length and quality of life of patients have improved. Polar Health Economics and Policy and Hacettepe University's HIV/AIDS Treatment and Research Centre have collaborated to explore the indirect costs of HIV/AIDS in Turkey. The study adopted the human capital approach and a questionnaire exploring the number of days lost at work due to the disease and extent of productivity losses was designed. The questionnaire was completed by a telephone interview to the 72 HIV+ patients registered at the treatment and research centre. The indirect costs associated with lost income due to premature death were also collected from the centre's patient database (255 patients).

The annual indirect cost of HIV/AIDS per patient was estimated as 3,560.40 TRY (559€)[3] for 2015. The majority of this cost was due to unpaid work (1,478.4TRY – 232€[3]) and absenteeism due to a disease related visit to a healthcare facility (1,057.92 TRY – 167€[3]) (Table 15, Fig 20).

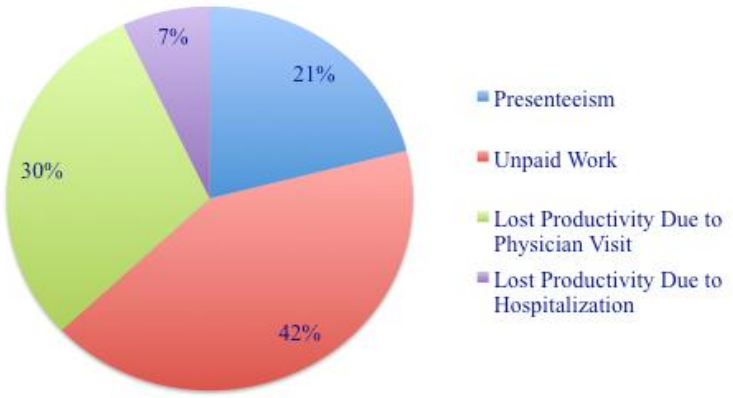
Table 15:Annual Indirect Cost per HIV/AIDS Patient (2015)

Item	Cost (TRY)	Cost (€)[3]
Presenteeism	759.6	119.2
Unpaid Work	1,478.40	232.1
Lost Productivity due to Physician Visit	1,057.92	166.1
Lost Productivity due to Hospitalization	264.48	41.5

Tatar 2016b

[2] 1 Euro= 6.37TRY, April 8, 2019
[3] 1 Euro= 6.37TRY, April 8, 2019

Figure 20: Percentage Distribution of HIV/AIDS Indirect Costs in – 2015



Tatar et al 2016b

The indirect cost of HIV/AIDS in the form of loss of income due to premature death was estimated from the records of the center. Table 16 presents the indirect costs due to life years lost after HIV diagnosis. Income statistics were taken from the Turkish

Statistics Institute and the net present value method was used with 3% discount rate. The following assumptions were made:

1. Maximum years for HIV after diagnosis was estimated as 22 years for males and 23 years for females (Harrison et al, 2010)
2. The retirement age was taken as 60 for males and 58 for females

Table 16: Indirect Costs due to Life Years Lost After HIV Diagnosis:

	Male		Female	
	19-29	30-29	19-29	30-39
Average Age at Diagnosis	25.1	30.65	24.5	30.17
Maximum age for HIV	48.14	53.65	47.5	53.17
Lost Life Year	29.36	23.85	30.0	24.33
Lost Working Year	11.86	6.35	10.5	4.83
Lost Income (TRY)	308,902	221,495	252,344	144,708

Tatar 2016b

Based on these findings, the annual indirect cost of loss of income due to HIV/AIDS for this cohort was calculated as 10,401,595 TRY (1,632,903€[4]) (Tatar, 2016b).

Table 17: Loss of Income due to HIV/AIDS- Hacettepe Cohort

Age Groups	Number of Male Patients	Number of Female Patients	Loss of Income (TRY)	
			Male	Female
19-29	7	2	2,162,314	504,688
30-39	31	6	6,866,345	868,248
Total	38	8	9,028,659	1,372,936
		Total	10,401,595	

Tatar, 2016b

6. Challenges for Future

Given the breadth of the coverage of benefits package of the SSI, the physical access and financial access problems for HIV/AIDS patients should not be high in Turkey, compared to many other parts of the world. However there are certain problems hindering the implementation of sound HIV/AIDS policies in Turkey.

Underreporting is a problem for HIV/AIDS in Turkey. There are statements that the real number of patients is three times the registered ones (https://www.cnnturk.com/saglik/turkiyede-bilinmeyen-aidsli-hasta-sayisi-bilinenlerin-uc-kati). Not being aware of the disease and stigmatization may be the most import reasons for this.

Although an improvement has been achieved in non-stigmatizing of HIV/AIDS patients after the diagnosis of the first case in 1985, this is still a cultural problem hindering the access of infected people to the healthcare system. Köse et al (2012) in their study evaluating the social and health problems of people living with HIV/AIDS in a metropolitan area of Turkey (İzmir) found that the most important problems identified were society and work related problems and access to health services. The study covered not only the patients but their family members as well. Opinions of the participants related to stigma are presented in Table 18.

[4] 1 Euro= 6.37TRY, April 8, 2019

Table 18: Opinions of Patients and Relatives Related to HIV/AIDS Stigma – İzmir

Stigma Item	% Agreed Patients	% Agreed Relatives
I have heard of an HIV+ person being refused health treatment	43.3	30.0
I have heard of an HIV+ person being excluded from society	65.5	70.0
I have heard of an HIV+ person exposed to violence for this reason	60.0	70.0
I am worried about transmitting the virus to others	83.3	-
HIV+ health personnel should not care for patients	41.4	30.0
An HIV positive person should not have sexual intercourse	36.7	30.0
I have support for my disease from those close to me	76.7	-
I am not invited to social events because I am HIV+	16.7	
If an HIV+ person has their status revealed they will loose their job	60.0	44.4
I feel guilty for being HIV+	48.3	-
I have never been ashamed for being HIV+	51.7	-
Many people feel uncomfortable around and HIV+ person	86.7	77.8
I believe I have been discriminated against	58.6	57.1
Some people stopped seeing me once they found out I was HIV+		
A doctor should provide information to those closed to a person diagnosed with HIV	75.9	80.0

Köse et al 2012

The table shows that, despite the policies to improve overall access to healthcare services in Turkey, HIV/AIDS patients still experience refusal to healthcare treatment. The stigma attached to the disease and discrimination problems can clearly be seen from the survey results.

The findings of Köse et al's (2012) study was confirmed by a recent study using 'People Living with HIV Stigma Index' (Gökengin et al, 2017). HIV related stigma/discrimination and violation of human rights were found as 23.1% and 30% respectively. Loosing job is a phenomenon attached to the stigma and 30% of the participants in the survey lost their jobs for this reason. A more alarming result of the survey was related to the access problems to healthcare services because of stigmatization. The survey concluded that 20% of the participants were denied health care services because of HIV positivity (Gökengin et al, 2017).

Extending anonymous tests especially to the population under risk is a key to success in avoiding stigma attached to the disease. If the patient uses the SSI system, his/her national identity number has to be imputed in the system, hence anonymity is not

secured. This hinders the use of the system by HIV/AIDS patients as the risk of loosing jobs or social status may become higher.

The epidemiological profile of the patients show that the disease is common among people with lower education levels. This indicates a need to develop awareness policies targeting mainly this group of population. In addition to this, the wives of HIV/AIDS patients are highly at risk as the majority of women have been infected by their husbands.

As a last word, it can clearly be stated that, despite improvements in access to healthcare services and a comprehensive benefits package, there are still problems in diagnosing, monitoring and treating the disease. A strong intersectoral collaboration mechanism covering the NGOs, medical experts, government agencies and the private sector will help to clarify the problems faced by HIV/AIDS patients. Strong and valuable policies can only be developed after the outcomes of this process.

References

Alp, E et al (2011), 'Epidemiological and Clinical Characteristics of HIV/AIDS Patients Followed-up in Cappadocia Region: 18 Years Experience', Mikrobiyoloji Bülteni, 45(1): 125-136.

Ceylan, E et al (2019), 'Determination of Medication Adherence and Related Factors Among People Living with HIV/AIDS in a Turkish University Hospital', Turkish Journal of Medical Sciences, 49: 198-205.

Çelikbaş, A et al, (2008), 'Epidemiologic and Clinical Characteristics of HIV/AIDS Patients in Turkey, Where the Prevalence Is the Lowest in the Region', J Int Assoc Physicians Aids Care, 7(1).

Çerçi, P et al (2016) ' Evaluation of 255 HIV/AIDS cases: Hacettepe cohort, Ankara, Turkey', Mikrobiyol Bul 50(1): 94-103.

Çetin, Z (2017), Intertwined Movements, Interwoven Histories: HIV and AIDS in Turkey. Disentangling European HIV/AIDS Policies: Activism, Citizenship and Health (EUROPACH) Working Paper No. 17-001/2. Available at: europach.phils.uj.edu.pl/project-outcomes/library/workingpapers/

European AIDS Clinical Society (2018), Guidelines. Version 9.1, October 2018.

Gökengin D, (2018), 'HIV infection in Turkey: How close are we to the target?'. Klimik Derg. 31(1): 4-10. (Turkish).

Gökengin, D et al (2017), 'Analysis of HIV/AIDS-Related Stigma and Discrimination in Turkey: Results of the People Living With HIV Stigma Index', Klimik Dergisi, 30(1): 15-21 (in Turkish).

Gökengin D et al (2018), 'HIV Care in Central and Eastern Europe: How Close are we to the Target? International Journal of Infectious Diseases. https://doi.org/10.1016/j.ijid.2018.03.007

Gülümser, Ç, Erbaydar T (2015),' HIV/AIDS epidemic in Turkey and use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants', Turk J Obstet Gynecol, 12: 192-198.

Harrison KM et al (2010), 'Life Expectancy after HIV Diagnosis Based on National HIV Surveillance Data From 25 States, United States. J Acquir Immune Defic Syndr. 2010; 53(1): 124-30.

http://aidsinfo.unaids.org (accessed in March 2019).

(https://www.cnnturk.com/saglik/turkiyede-bilinmeyen-aidsli-hasta-sayisi-bilinenlerin-uc-kati) (accessed in March 2019).

http://www.hatam.hacettepe.edu.tr/veriler31Aralik2017.pdf (accessed in March 2019).

https://www.who.int/gho/hiv/en/ (accessed in March 2019).

Koçkaya, G et al (2016), 'Analysis of the Treatment Costs of HIV/AIDS in Turkey', Farmeconomia. Health economics and Therapeutic Pathways,17(1): 13-17.

Köse, S et al (2012), 'The Social and Health Problems of People Living with HIV/AIDS in Izmir, Turkey' The European Journal of Medicine, 44: 32-39.

Özdemir, B et al (2018), 'Evaluation of Epidemiological, Clinical, and Laboratory Features and Mortality of 144 HIV/AIDS Cases in Turkey, HIV Clinical Trials, DOI: 10.1080/15284336.2018.1453990.

Panel on Antiretroviral Guidelines for Adults and Adolescents, (2018), Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services.
http://www.aidsinfo.nih.gov/ContentFiles/ (Accessed, March 2019).

Sağlık Bakanlığı (2013), HIV/AIDS Tanı ve Tedavi Rehberi, Ankara.

Sağlık Bakanlığı (2018), Sağlık İstatistik Yıllığı 2017, Ankara.

Tatar, M et al (2016a), 'Direct Cost of HIV/AIDS in Turkey', Value in Health, 19(7): A411-A412.

Tatar, M et al (2016b), ' Indirect Cost of HIV/AIDS: Results of A Survey From A Turkish Research Center', Value in Health, 19/7): A411.

Türkiye Halk Sağlığı Kurumu (2015), *Faaliyet Raporu 2014*. Ankara.

UNAIDS (2015), Fact Sheet: 2014 Statistics

World Health Organization, (2018), Recommendations on First-Line and Second-Line Antiretroviral Regimens and Post-Exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV, December 2018.

Yemişen, V et al (2014), 'Epidemiological Profile of Naïve HIV-1/AIDS Patients in Istanbul: The Largest Case Series from Turkey', Current HIV Research, 12(1).

Yükseköğretim Kurulu, (2013), Türkiye'de Sağlık Eğitimi ve Sağlık İnsangücü Durum Raporu, YÖK Yayın No 2014/1, Eskişehir