



**COST-EFFECTIVENESS OF DOLUTEGRAVIR-
VERSUS EFAVIRENZ-BASED FIRST-LINE
ANTIRETROVIRAL TREATMENTS AND HEALTH-
RELATED QUALITY OF LIFE OF ADULTS WITH
HIV/AIDS IN ETHIOPIA**

Yared Belete [BPharm]

December 2019

Addis Ababa, Ethiopia

Addis Ababa University

College of Health Science

School of Pharmacy

Cost-Effectiveness of Dolutegravir- Versus Efavirenz-Based First-Line
Antiretroviral Treatments and Health-related Quality of Life of Adults
with HIV/AIDS in Ethiopia

Yared Belete [BPharm]

Main Supervisor: Gebremedhin Beedemariam [MSc]

Co-supervisors: Eskinder Eshetu Ali [PhD]

Beate Sander [PhD]

A Thesis Submitted to the Department of Pharmaceutics and Social
Pharmacy in Partial Fulfillment of the Requirements for the Degree of
Master of Science in Pharmacoepidemiology and Social Pharmacy

December 2019

Addis Ababa, Ethiopia

Addis Ababa University

College of Health Science

School of Pharmacy

This is to certify that the thesis is prepared by Yared Belete, entitled: Cost-Effectiveness of Dolutegravir- Versus Efavirenz-Based First-Line Antiretroviral Treatments and Health-related Quality of Life of Adults with HIV/AIDS in Ethiopia, and submitted in partial fulfillments of the requirements for the degree of Master of Science in Pharmacoepidemiology and Social Pharmacy complies with the regulations of the university and meets and accepted standards with respect to originality and quality.

Signed by the Examining Committee:

External Examiner:

Signature _____ Date _____

Internal Examiner:

Signature _____ Date _____

Main Advisor: Gebremedhin Beedemariam (PhD)

Signature _____ Date _____

Co-advisor: Eskinder Eshetu Ali (PhD)

Signature _____ Date _____

Chair of Department or Graduate Program Coordinator

Abstract

Background: In Ethiopia, the dolutegravir (DTG)-based regimen is as of now favored over the efavirenz (EFV)-based regimen in the treatment of patients with human immunodeficiency virus (HIV)/acquired immune-deficiency syndrome (AIDS).

Objective: To determine the cost-effectiveness of DTG- versus EFV-based first-line treatment and health-related quality of life among Ethiopian adults with HIV/AIDS.

Methods: Cost-utility analysis was done using a microsimulation model. The health-related utility value was obtained from adult HIV/AIDS patients receiving antiretroviral treatment at Tikur Anbessa Specialized Hospital. Mann-Whitney U and Kruskal-Wallis tests were done to compare utility values based on patient characteristics. Incremental cost-effectiveness ratio (ICER) was used to determine cost-effectiveness of the proposed regimens and deterministic sensitivity analysis was conducted to assess the parameter uncertainty in cost utility analysis.

Results: Median utility values of HIV/AIDS patients were 0.94 (interquartile range (IQR) =0.87, 1) and 80% (IQR= 70%, 90%) on the EuroQol-5 dimensions (EQ-5D) index and EuroQol-visual analog scales (EQ-VAS) score respectively. Comorbidity, cluster of differentiation 4 and number of medicines were significantly associated with EQ-5D and EQ-VAS values with, $p < 0.001$. Compared to EFV-based regimen, the DTG-based regimen was associated with an expected lifetime cost of 12,709 United States dollar (\$) (versus \$12,701) and expected quality adjusted life month (QALM) gains of 183 (versus 176 QALMs) resulting ICER value of \$1.14 per QALM.

Conclusion: Overall utility value of HIV/AIDS patient is reported as lower than the general population. Replacing EFV- with DTG-based first-line regimen for HIV/AIDS patients in Ethiopian setting was found to be cost-effective.

Key words: cost-utility, dolutegravir, efavirenz, EQ-5D, HIV/AIDS, ICER, utility

Acknowledgement

Above all, my sincerest gratitude goes to the participants of this study primarily patients who were attending ART service in Tikur Anbesssa Specialized Hospital. I am grateful for the cooperation of professionals who were working in ART pharmacy, ART clinic, laboratory service and pharmacy store of Tikur Anbessa Specialized Hospital. I am thankful for the staff who were working at the central office of Ethiopian Pharmaceutical Supply Agency. It is a great honor to thank Addis Ababa University for funding this thesis work. I could not have done this piece of work without the help of my advisors Dr. Gebremedhin Beedemariam, Dr. Eskinder Eshetu Ali and Dr. Beate Sander and I am so thankful for what they did for my successful completion of this project. It is my pleasure to acknowledge Dr. Karen from the University of Toronto for her support in the economic model development and analysis.

Table of Content

Table of Content	iii
List of Tables	v
Abbreviations and Acronyms	vii
1. Introduction.....	1
1.1. Background	1
1.2. Statements of the Problem	3
1.3. Significance of the Study	5
2. Literature Review	6
2.1. The Natural History of HIV Infection.....	6
2.2. Global and National Burden of HIV/AIDS	6
2.3. Advances in HIV/AIDS Treatment.....	9
2.4. Relevance of Outcome Research in HIV/AIDS.....	10
2.5. Relevance of Economic Analysis of HIV/AIDS Medicines.....	13
3. Objectives	16
3.1. General Objective	16
3.2. Specific Objectives	16
4. Methods	17
4.1. Study Area and Period	17
4.2. Study Design	17
4.3. Model Structure for the Economic Analysis.....	17
4.3.1. Health States	18
4.3.2. Treatment Algorithm	19
4.4. Population	20
4.5. Eligibility Criteria	20
4.6. Sample Size Determination and Sampling Technique.....	21
4.7. Data Collection Instrument and Procedures	22
4.7.1. Data Collection Instrument.....	22
4.7.2. Data Collection Procedures	23
4.8. Parameter Inputs for the Cost-utility Analysis.....	23
4.8.1. Probabilities and Tracker Variable	25
4.8.2. Utility Data	26
4.8.3. Cost Data	27

4.9. Study Variables	27
4.10. Data Quality Assurance	27
4.11. Data Analysis	28
4.11.1. Analysis for Health-related Quality of Life study	28
4.11.2. Analysis for Economic Evaluation	29
4.12. Ethical Considerations	30
5. Results	31
5.1. Health-related Quality of life of Patients with HIV/AIDS	31
5.1.1. Demographic and Clinical Characteristics of the Participants	31
5.1.2. Participants' Health Profile	36
5.1.3. Proportion of Reported Health Problems Based on Patient Characteristics	36
5.1.4. Factors Associated with Health-related Quality of life of Patients with HIV/AIDS	37
5.2. Findings of the Economic Evaluation	43
5.2.1. Base Case and Scenario Analysis	43
5.2.2. Sensitivity Analysis	44
6. Discussion	46
7. Strengths and Limitations	51
8. Conclusion	52
9. Recommendations	53
References	54
Annex I: Participant Consent Form and Data Collection Tool	61
Annex II: Sample Tree of the Model	70

List of Tables

Table 1 Model parameter point estimate values and ranges for treatment response, ADE, discontinuation due to ADE and costs	24
Table 2 Socio-demographic characteristics and reported health problem of HIV/AIDS patients, TASH, Ethiopia, 2019 (n=511)	32
Table 3 Clinical characteristics and reported health problem of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511).....	34
Table 4 Socio-demographic factor associated with EQ-5D and EQ-VAS score of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511)	38
Table 5 Clinical characteristics associated with EQ-5D and EQ-VAS score of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511)	40
Table 6 Cost –utility analysis result for DTG-versus EFV-based regimen as a preferred first-line, Ethiopia, 2019	44

List of Figures

Figure 1 Model structure of treatment algorithm and outcome for the cost utility analysis of EFV- versus DTG-based regimens in the Ethiopian context	19
Figure 2 Equation for computing utility score of HIV/AIDS patients, TASH, Ethiopia, 2019.....	28
Figure 3 Frequency of self-reported health profile of HIV/AIDS patients, TASH, Ethiopia, 2019 (n=511)	36
Figure 4 Tornado analysis for cost utility analysis of DTG- versus to EFV- based treatment as first-line treatment for adults with HIV/AIDS, Ethiopia, 2019.....	45

Abbreviations and Acronyms

3TC	Lamivudine
ADE	Adverse drug event
ART	Antiretroviral therapy
ATV	Atazanavir
AZT	Zidovudine
DRV	Darunavir
DTG	Dolutegravir
EFV	Efavirenz
EPSA	Ethiopian Pharmaceutical Supply Agency
EQ-5D	EuroQol-5 dimensions
EQ-5D-5L	EuroQol-5 dimensions-5 levels
EQ-VAS	EuroQol-visual analogue scales
HRQoL	Health-related quality of life
ICER	Incremental cost-effectiveness ration
INSTIs	Integrase strand transfer inhibitors
LPV	Lopinavir
NNRTIs	Non-nucleoside reverse transcriptase inhibitors
NRTIs	Nucleoside reverse transcriptase inhibitors
QALM	Quality Adjusted Life Month
QALY	Quality adjusted life year
r	Ritonavir
TDF	Tenofovir Disoproxil Fumarate
TASH	Tikur Anbessa Specialized Hospital
UNAIDS	United Nations programme on HIV/AIDS
WHO-QoL	World Health Organization Quality of Life

1. Introduction

1.1. Background

Human immunodeficiency virus (HIV)/acquired immune-deficiency syndrome (AIDS) is a major issue of public health relevance globally. The healthcare and economic burdens of the disease are even more daunting in low-income countries, which includes most African nations (Frank *et al.*, 2019; UNAIDS, 2019; UNAIDS, 2015). Despite the significant improvements as a result of increased access to antiretroviral treatment (ART), HIV/AIDS continues to be a significant health concern in Ethiopia with an annual prevalence of 1% and accounting for 19% of the national health expenditure (CDC, 2019; FMoH, 2014). This challenges the progress of Ethiopia to achieve the target aspired by United Nations programme on HIV/AIDS (UNAIDS) to end HIV/AIDS epidemic in 2030 (Girum *et al.*, 2018; UNAIDS, 2014).

Introduction of new and effective treatment is generally recommended to reduce the disease burden on patients (WHO, 2018). Until recently, combinations of two nucleoside reverse transcriptase inhibitors (NRTIs) as the backbone with non-nucleoside reverse transcriptase inhibitors (NNRTIs) or boosted protease inhibitors have been the preferred regimens for the management of HIV. However, these combination therapies have been challenged by resistance, adverse drug events (ADE) and drug interactions (Arts and Hazuda, 2012; WHO, 2016). As a result, second-generation Integrase strand transfer inhibitors (INSTIs) like dolutegravir (DTG) are becoming a preferred first-line treatment instead of NNRTIs like efavirenz (EFV) (Katlama and Murphy, 2012; WHO, 2018). To this effect, the standard treatment guideline of Ethiopia has changed to incorporate these recommendations (FMoH, 2018). Such changes in the treatment guideline call for investigation of the cost effectiveness of the newly introduced regimen as compared to the EFV-based regimen.

Despite advances in the treatment of HIV/AIDS, the currently available medicines cannot cure the disease. Lack of curative therapy for the disease has an impact on the health-related quality of life (HRQoL) and treatment outcomes (Arts and Hazuda, 2012; WHO, 2016). HRQoL helps to measure health-related disability and dysfunctions. It has reliable benefit for chronic conditions (EuNetHTA, 2015) and helps to assess the need and outcome of interventions from the experience of patients (Theofilou, 2013). Several tools have been developed and validated for measuring HRQoL (Hays and Morales, 2001; Janssen *et al.*, 2013; WHO, 1995). In Ethiopia studies have assessed HRQoL of HIV/AIDS patients using World Health Organization Quality of Life in HIV (WHO-QoL-HIV) instrument (Alemayehu *et al.*, 2017; Emamu *et al.*, 2017; Surur *et al.*, 2017). However, there is paucity of studies that employ tools such as the EuroQol-5 dimensions (EQ-5D) that incorporate societal preference and provide effective means to assess the impact of disease across different health states (Devlin and Brooks, 2017). The current study therefore aims to evaluate the cost-effectiveness of DTG- versus EFV-based first-line ART and HRQoL among Ethiopian adults with HIV/AIDS.

1.2. Statements of the Problem

HIV/AIDS has enormous healthcare and economic impacts for the already struggling economies of most African countries. Reports show that the disease reduces countries' average growth rate by up to four percent and this economic burden increases with increase in the prevalence of the disease (Dixon *et al.*, 2002; Essig *et al.*, 2015). In Ethiopia, HIV/AIDS poses a higher financial burden to households compared to other causes of illness. The effect is even more pronounced among poor households (Tekola *et al.*, 2008). HIV/AIDS also takes the largest share of the country's national health expenditure and government was an agent to finance almost two-thirds of the costs of HIV/AIDS care (FMoH, 2014).

The Ethiopian health system is working to introduce different measures that help to curb the health and economic consequences of HIV/AIDS. In an effort to improve treatment of HIV/AIDS, the country currently make a decision to make transition from the existing first-line treatment (EFV-based regimen) to the WHO-recommended DTG-based regimen. The new regimen has demonstrated better clinical evidence on treatment efficacy and rate of treatment failure (WHO, 2018). However, the current price of the new treatment is greater in comparison to the existing regimen (Babigumira *et al.*, 2016). Despite the importance of evaluating whether the added cost of therapy can be justified by the added benefit, the new regimen is being implemented without a proper economic evaluation of its costs and outcomes in Ethiopian context.

Expansion of HIV/AIDS services and maintaining quality of life for the patients were clearly stated in the national guidelines of Ethiopia (FMoH, 2017). Measurement of HRQoL and calculation of utilities can be used to assess the success of the program and generation of more inputs for economic evaluations of interventions (CDC, 2018).

Despite the presence of studies that assessed HRQoL of HIV/AIDS patients in Ethiopia, we still lack well-established utility values for HIV/AIDS patients based on different health states of the disease (Alemu *et al.*, 2013; Deribew *et al.*, 2009; Surur *et al.*, 2017). Utility is a good metrics for comparison of quality adjusted life year (QALY) in economic evaluation of health interventions. Utility study on HIV/AIDS patients use cluster of differentiation 4 (CD4) range for defining health states and these utility values were used for economic evaluation of different ART regimens (Despiegel *et al.*, 2015; Devlin and Brooks, 2017; Tremblay *et al.*, 2018). Consequently, it is crucial to conduct studies that compute utility scores based on different characteristics of HIV/AIDS patients.

We did not find any prior studies which determined the cost-effectiveness of HIV/AIDS treatment regimens using economic analysis in the Ethiopian context. The present investigation, in this way, expected to fill the research gaps in the areas of economic evaluation of treatment interventions and generation of utility scores for HIV/AIDS patients.

1.3. Significance of the Study

This study assessed the cost-effectiveness of DTG- versus EFV-based first-line ART among Ethiopian adults with HIV/AIDS. It also computed the patients' utility scores based on their clinical characteristics. As such, the study helps to describe the HRQoL of HIV/AIDS patients from different perspectives of health domains like physical activity, self-care, usual activities, pain/discomfort, and anxiety/depression. It aids to assess the effect of disease and intervention on each of these domains from the side of patients (Sitlinger and Zafar, 2018). Information on which dimension of a patient's quality of life is truncated would help policymakers on deciding the necessary type of health care program and interventions. Programs that considers patients' perspectives into account would most likely succeed in producing the intended outcomes (Szende *et al.*, 2014).

As this study aims to compute health-related utility value for HIV/AIDS patients based on different health states, the findings will be critical in health economic decision analysis. Without utility evidence, it is hardly possible to conduct a cost-utility analysis (Whitehead and Ali, 2010) hence the utility value generated from this study will help health economists and decision makers.

The distribution of the DTG-based regimen to health facilities in has started in Ethiopia. Examining the cost-effectiveness of replacing the old regimen with a new regimen as a preferred first-line in Ethiopian context, provides an economic case for the decision to include the new regimen. The introduction of technologies, interventions, and programs need economic evaluation to use resources efficiently. Furthermore, this study will serve as a baseline for further studies in the area.

2. Literature Review

2.1. The Natural History of HIV Infection

HIV/AIDS is an infectious disease caused by HIV which mainly targets the immune system. The progress of this infectious disease reduces a patient's CD4 level and leads to AIDS-defining clinical syndromes (Patrikar *et al.*, 2014; WHO, 2007). The main entry for HIV virus is chemokine receptor 5 or chemokine receptor type 4 and the virus mainly targets the immune system of the human body. The gradual reduction of CD4 and increase in viral population leads to advanced condition called AIDS (Nwankwo and Seker, 2013). The decline in CD4 is generally associated with severity of the symptom and increase in probability of opportunistic infection (Frimpong *et al.*, 2017). The deterioration of immunological parameter leads to increase in viral load (Shoko and Chikobvu, 2019).

Immunological and clinical staging are used to depict the HIV/AIDS disease progression. The immunological staging works based on the CD4 count range. A CD4 count of above 500 cells/mm³ is considered as stage one and with the progress of the disease there is a reduction in CD4. The CD4 count ranges from 350-499, 200-349 and those less than 200 cells/mm³ represent stage two, three and four disease, respectively. The clinical staging is based on the symptoms of the disease which progress from no symptoms to severe symptoms as the disease advance (WHO, 2007).

2.2. Global and National Burden of HIV/AIDS

Although reports show that there has been a decline in HIV/AIDS related mortality (from 1.95 million in 2006 to 0.95 million in 2017), the disease the cause of around one million deaths per annum worldwide. Similarly, there is a drop in the incidence of the disease from 2.35 million in 2007 to 1.7 million people in 2018 (UNAIDS, 2019; UNAIDS, 2015). However, the level of disease burden showed regional disparity. The

highest prevalence was recorded in the sub-Saharan Africa region in 2017. More than 70% of HIV cases are in Africa and from these less than 60% of them have access to ART (UNAIDS, 2019; UNAIDS, 2015). The global prevalence of the disease is still high and the burden of the disease is magnified in the younger adult population and low-income countries (Frank *et al.*, 2019). The total number of HIV/AIDS patient is estimated to be 20.6 million in eastern and southern Africa. Annually 800, 000 new infections happened and from this, 710,000 of them were adults. In this region, no more than 14 million people have access to treatment (UNAIDS, 2019).

In addition to morbidity and mortality the disease has a financial burden. From 2000 to 2015 it was estimated that the global community invested around United States Dollar (\$) 562.6 billion for HIV/AIDS. Finance is required for treatment, prevention and strengthening the health care system. The largest share of the resource was spent on care and treatment purpose (Dieleman *et al.*, 2018). In 2020, more than \$26 billion will be required for HIV/AIDS related services (UNAIDS, 2019). HIV/AIDS affects all human development components and as it has a higher burden in Africa, it imposes a significant impact on Africa's economic development. The disease affects a productive portion of the population, as a result, its impact on economic growth is indisputable (Boutayeb, 2009; Dixon *et al.*, 2002).

National prevalence of HIV/AIDS among adult Ethiopians is estimated to be 1% and with the large population size of the country this number is substantial (CDC, 2019). It was reported that 690,000 people were living with HIV/AIDS in 2018 and from these 23,000 of were newly infected. During the same year, 11,000 deaths related to HIV/AIDS were recorded (UNAIDS, 2018). It is estimated that around 20% of HIV/AIDS patients did not know their HIV status. From the HIV/AIDS diagnosed patients, 88% had access for ART (Girum *et al.*, 2018).

The UNAIDS target, 90-90-90 aimed to know the HIV status of 90% of patients with HIV/AIDS, to provide ART for 90% of patients diagnosed with HIV and to achieve viral suppression in 90% of the ART users in 2020. The aspiration of the target is to end HIV epidemics by 2030. The equitable access for high-quality HIV/AIDS treatment and prevention is the mainstay for the target. Achievement of the targets is expected to reduce the social, educational and economic burden of HIV/AIDS (UNAIDS, 2014).

To combat the burden of the disease, Ethiopia adopted the 90-90-90 targets of UNAIDS. From 2008 to 2016 the epidemic was increasing from 0.3 to 0.33 per 1000 population. This 10% rise in incidence of HIV/AIDS indicates that it would be challenging to achieve the aspired goal (Girum *et al.*, 2018). Despite the evidence of resurgence in epidemics, the global disease burden analysis result has shown that Ethiopia is the country that achieved the most rapid decrease in HIV/AIDS related death. With this success rate the country has a high likelihood to achieve the 2030 goal of UNAIDS (Frank *et al.*, 2019).

HIV/AIDS has both health and economic burden, as a result, it is considered as one of the health sector priority in Ethiopia. In the fifth national health account, it was depicted that the total national health expenditure increased from \$248 million in 20008 to \$306.7 million in 2011. From this expenditure, 14.1% was the contribution of government (FMoH, 2014). This low contribution was because of too much dependence on donor financing but recent reports demonstrated there is a decline in the fund from donor countries for HIV/AIDS prevention and care. Ethiopia faced \$66 million financial gap for the health sector in 2018, and this figure is expected to be higher in 2020 because of reduction in external finance and increased demand of ART services. It is recommended to increase domestic financing and reduce reliance on external

financing for HIV/AIDS to maintain the sustainability of the outcome in the prevention and control of the disease (HP+, 2018).

2.3. Advances in HIV/AIDS Treatment

Since the discovery of the first anti-retroviral medicine in 1987, HIV/AIDS treatment has evolved from a single agent based treatment (monotherapy) to combination approaches such as, the dual therapy and the current triple therapy. The advances in the development of the HIV medicines continue to improve effectiveness and reduce ADE and pill burden (Arts and Hazuda, 2012). However, viral resistance to the existing regimens remains to be a challenge. Moreover, long-term toxicities are also a challenge for patients in the face of early initiation of ART for better treatment outcome in terms of quality of life and control of disease progression. So, search for new treatment is continuing (Lange and Ananworanich, 2014).

Nowadays several classes of medicines are available for management of HIV including, chemokine receptor antagonists, fusion inhibitors, NRTIs, NNRTIs, protease inhibitors, INSTIs, Pharmacokinetic boosters and post attachment HIV inhibitor (Arts and Hazuda, 2012; Kwong, 2019). Combination therapy is the successful approach in combating viral replication and restoring immune system of the patients. The backbone of combination therapy is two NRTIs and the third agent from any of the other classes. Until recently the commonly combined third agents were NNRTI or a ritonavir (r)-boosted protease inhibitor. From the NNRTI, EFV is the most popular drug. But now WHO has recommended INSTIs) based combination as a preferred first-line (WHO, 2018).

INSTIs block an HIV enzyme called integrase and this class of drugs showed impressive results in curbing viral resistance. Particularly the second-generation INSTIs like DTG have a superior outcome than NRTIs (Raffi and Wainberg, 2012).

The previous WHO treatment guide for HIV/AIDS stated that Tenofovir Disoproxil Fumarate (TDF) + Lamivudine (3TC) (or Emtricitabine)) + EFV as the first-line combination therapy with a strong recommendation. In this guideline TDF + 3TC (or Emtricitabine) + DTG were considered as an alternative option to initiate ART with conditional recommendation (WHO, 2016).

The latest policy brief of WHO suggested that DTG has advantages in comparison to EFV as the third agent in triple therapy of HIV/AIDS. Lower potential for drug–drug interactions, more rapid viral suppression and a higher genetic barrier to developing ART drug resistance are some of the advantages that DTG got in comparison to EFV (WHO, 2018). In line with WHO’s recommendation, the existing guideline for HIV in Ethiopia acclaimed the combination of 2NNRTIs and one NRTI as a preferred first-line but the updated version recommended the combination of 2 NNRTIs and one INSTIs (FMOH, 2018; FMOH, 2017). Despite their therapeutic advantages, new regimens have a substantial increment in cost than the existing regimens. Regardless of the income, the price of those second-generation INSTI like DTG is 100–500% higher than that of EFV (Sim and Hill, 2018).

2.4. Relevance of Outcome Research in HIV/AIDS

Outcome research focuses on the end result of a public health care intervention that could employ treatment or prevention strategies. It addresses areas related to quality-of-life measures, safety of an intervention, treatment effectiveness, health care cost, equity of services and timeliness of the services (Krumholz, 2008; Jefford *et al.*, 2003). The main focus of an outcome study on chronic disease is reduction in mortality and improvement in quality of life of the patient since those diseases have no curative therapy. Such evidence has a substantial role in decision-making at policymaker, individual practitioner or patient level (Jefford *et al.*, 2003). To improve the efficiency

and safety of health care services, it is imperative to consider patient reported outcome in terms of quality of life or patient preferences (Lavallee *et al.*, 2016).

Quality of life study is one of the outcome studies and it is a subjective evaluation of different aspects of life including physical, mental or economic factors that influence an individual's or a population's functional status. The utility value is country-specific and it is affected by the cultural and value system of an individual or the society. HRQoL is physical or mental health perception and functionality of an individual or community that helps to determine the burden of disease and outcomes of interventions (CDC, 2019; Mahlich *et al.*, 2018; WHO, 1995). In addition to cultural sensitivity, quality of life would be affected by several factors. Previous studies depicted that quality of life of HIV/AIDS patients would be affected by socio-demographic, clinical characteristics and treatment related factors (Karkashadze *et al.*, 2017; Liping *et al.*, 2015; McGowan *et al.*, 2017; Tran *et al.*, 2012).

Several studies assessed quality of life of HIV/AIDS patients as a means to evaluate the success of interventions. Symptoms of HIV/AIDS are associated with low HRQoL. Patients also exhibit reduced functionality in social relationship and psychological wellbeing (Aranda-Naranjo, 2004; Osei-Yeboah *et al.*, 2017). In comparison to the general population, HIV/AIDS patients reported frequent problem on anxiety/depression domain and claimed lower overall utility scores (Miners *et al.*, 2014). Hence, improving the patients' quality of life is considered an important outcome of HIV/AIDS care.

The utility is a numerical presentation of quality of life and represents the strength of preference of an individual for defined health states. Defining and valuing health states can be conducted through the direct and indirect methods (Tolley, 2009). The utility value of one represents the best imaginable health state and zero represents death or the

worst imaginable health state. HIV/AIDS is associated with lower utility scores, which is demonstrated through the patient's claim of lower quality of life. The utility value of patients using ART was reported as 0.85. Less than half of HIV patients perceived their health state as a full health (Keaei *et al.*, 2016; Stalmeier *et al.*, 2005; Miners *et al.*, 2014). Patients on treatment would have better quality of life than treatment naive patients and they have different levels of quality of life in different health domains (Nglazi *et al.*, 2014; Tran *et al.*, 2012).

Despite the absence of studies that compute utility scores of Ethiopian HIV/AIDS patients, a number of studies have been conducted to assess their HRQoL using the WHO-QoL-HIV assessment tool. The findings depicted that HIV/AIDS patients demonstrated good quality of life in the physical domain but they claimed low quality of life scores in the social relation, environmental and spiritual domains. Comorbidities further reduced the quality of life of the patients (Alemayehu *et al.*, 2017; Emamu *et al.*, 2017; Surur *et al.*, 2017). In addition to WHO-QoL-HIV there is other tool like EuroQol-5 dimensions-5 levels (EQ-5D-5L), for assessing the quality of life of patients. The EQ-5D-5L is a generic tool that assesses the quality of life using five dimensions including mobility, self-care, usual activity, pain/discomfort and anxiety depression dimension. The EQ-5D-5L tool was found to be feasible and cultural acceptable for Ethiopian general population and this tool has better applicability for health technology assessment (Welie *et al.*, 2019).

Health outcomes measured in terms of utility or QALY are helpful for economic evaluation of interventions. Globally the EQ-5D is increasingly used to measure the quality of life values, which are incorporated into the economic evaluation health care interventions (Davis *et al.*, 2017; Devlin and Brooks, 2017; Versteegh *et al.*, 2016). The

commonly utilized economic evaluation in health care is a cost-utility analysis, which needs QALY as a measure for the health outcome (Whitehead and Ali, 2010).

2.5. Relevance of Economic Analysis of HIV/AIDS Medicines

With advances in the treatment regimens for HIV/AIDS there is an associated increase in the prices of medicines. For instance, a study in 52 countries depicted that the price of DTG-based regimens is five times higher than EFV-based regimens (Sim and Hill, 2018; Unitaid, 2017). Even with this background on the price of DTG-based regimens, the price of ART medicines is generally low in developing countries as a result of global support and availability of generic products. However, there has been a continuous decline in the amount of support from developed countries and developing countries need to find cost-effective strategies to ensure sustainability of care to patients (Avert, 2019; Rosenberg, 2018). In this regard, Ethiopia is not an exception in terms of facing the challenges of developing countries and it is imperative to strengthen the health system to be able to run HIV prevention and treatment effectively. This is even more relevant as Ethiopia is already facing significant gaps in financing HIV-related services (HP+, 2018). This makes the evidence-based implementation of technology and conducting of economic evaluations for the newly introduced interventions even more important.

Economic evaluation is a worthwhile tool for intervention decision making from different perspectives like health care payer, provider or society. This analysis can be conducted using modeling which is the best way to conduct economic evaluation. The economic model can consider a number of factors including cost of treatment, the effectiveness of medicine and people's preference into account for estimating the input and output of an intervention (Peyasantiwong *et al.*, 2010). Economic analysis of the available interventions would be an indispensable component in decision-making.

Globally, several studies have been conducted to evaluate different interventions of HIV/AIDS using modeling. Those studies consider CD4 count, viral load, disease progression and ADE as a factor to define disease progression and treatment outcomes (Goldie *et al.*, 2006; Soorapanth and Chick, 2010).

In health economics, decision models are used for analysis of treatment approaches and health care programs. Mathematical modeling has reflective use to estimate the population health effect and cost-effectiveness of various HIV/AIDS interventions (Dang *et al.*, 2016; Sonnenberg and Beck, 1993). As evidenced in prior studies, it is possible to use microsimulation modeling (Despiegel *et al.*, 2015), Monte Carlo Simulation (Restelli *et al.*, 2017) and dynamic markov modeling (Tremblay *et al.*, 2018) for evaluating different intervention of HIV/AIDS. With its ability to prevent oversimplification of the reality and capturing the memory of an event microsimulation models have an advantage over markov model (Kuehne *et al.*, 2007).

Different economic evaluations have been conducted to assess the cost-effectiveness of DTG-based regimen in comparison to EFV-based regimen and the findings revealed that DTG-based regimen is a dominant strategy as a first-line treatment regimen (Despiegel *et al.*, 2015; Restelli *et al.*, 2017). The study which compared DTG-based regimen with EFV-, Darunavir (DRV) - and Raltegravir-based regimens depicted DTG-based regimen is a cost-effective regimen (Guillen *et al.*, 2017). Another study which compared DTG with Raltegravir as a third agent in triple combination therapy depicted that DTG produces more life years and QALY (Pialoux *et al.*, 2015).

Despite the fact that the DTG-based regimen is getting preferable over EFV-based regimen in developing countries based on WHO recommendation, the available economic evaluations were conducted in developed countries. We did not come across

with any economic evaluation which attempted to evaluate the economic feasibility of DTG-based regimen over the existing EFV-based regimen in developing countries including Ethiopia. Without contextual evidence on cost-effectiveness of the new regimen, recent guideline for HIV management in Ethiopia recommended DTG-based regimen (WHO, 2018; FMoH, 2018). Therefore, this study demonstrated cost-effectiveness of the new regimen in comparison to the existing regimen in Ethiopian context which would be an input for revision of the HIV guidelines.

3. Objectives

3.1. General Objective

The aim of this study was to determine the cost-effectiveness of DTG- versus EFV-based regimen as a first-line treatment and to assess health-related quality of life of adults with HIV/AIDS in the Ethiopian setting.

3.2. Specific Objectives

- ✓ To assess health related quality of life of adults with HIV/AIDS
- ✓ To identify factors associated with health related quality of life of adults with HIV/AIDS
- ✓ To determine cost-effectiveness EFV- versus DTG-based regimen as a first-line treatment for adults with HIV/AIDS in the Ethiopian setting

4. Methods

4.1. Study Area and Period

The HRQoL study was conducted in Tikur Anbessa Specialized Hospital (TASH), the largest tertiary teaching hospital (under college of Health Sciences, Addis Ababa University) in Ethiopia (AAU/CHS, 2019). The hospital serves more than 500,000 clients a year. It has 800 beds, with 1204 health professionals. ART clinic pharmacy is one of the 12 pharmacy departments within the hospital. Around 4000 patients are served annually by the ART pharmacy. The study was conducted from April to July 2019. As per the evidence from the electronic dispensing tool of the ART pharmacy, the total number of active ART users was 3,828 during the data collection period.

4.2. Study Design

An institution-based cross-sectional study was employed to assess HRQoL of adults with HIV/AIDS. The collected information was used to derive the health-related utility of HIV patients based on different health states. Moreover, a cost-utility analysis using microsimulation model was employed to identify the cost-effective first-line regimen for HIV management by comparing DTG- versus EFV-based regimen in the Ethiopian setting. Based on WHO recommendation, costs and outcomes were discounted at 3% annually. As Ethiopia lacks an established cost-effectiveness threshold value, WHO's recommendation that an intervention with an incremental cost-effectiveness ratio (ICER) value of 1-3xGDP per capita per QALY is a cost effective strategy. Ethiopia's GDP per capita in the year [2019], \$951.1 was considered in interpretation of the results (IMF, 2019; Marseille *et al.*, 2014; WHO, 2003).

4.3. Model Structure for the Economic Analysis

This study assessed cost-effectiveness of newly introduced DTG-based regimen in comparison to EFV-based regimen from health care payer perspective in the Ethiopian

setting. We developed a microsimulation model to simulate the progress of the disease on HIV infected individual over a lifetime time horizon using Tree Age Pro 2019. The detail of the model structure is described as follows.

4.3.1. Health States

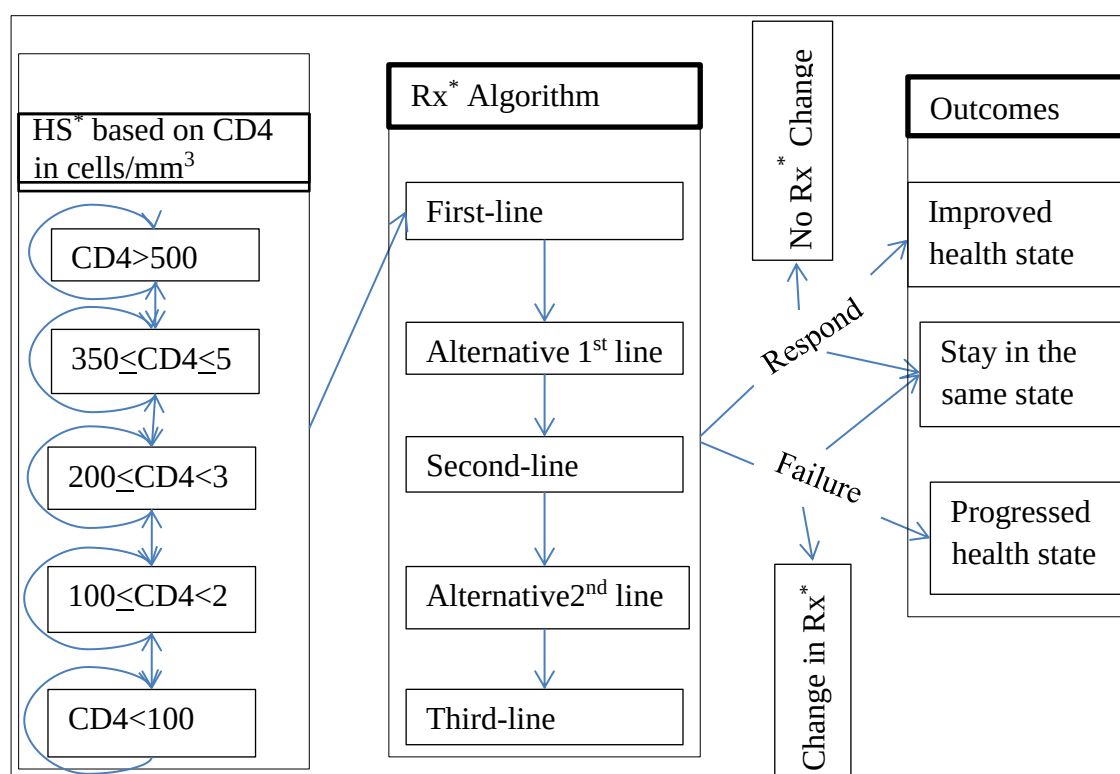
The model considers the disease in five health states based on the CD4 count range. WHO immunological classification of HIV/AIDS with modification was used (WHO, 2007). As part of the modification, one health state with CD4 lower than 100 cells/mm³ was added to account people with lower CD4. As it has been depicted in previous studies the health state with lower CD4 is associated with lower utility value (Despiéglé *et al.*, 2015; Tremblay *et al.*, 2018). Hence, inclusion of health state with lower CD4 range has meaningful implication in economic analysis of HIV/AIDS interventions. Starting health states for individuals were determined randomly by assuming gamma distribution of CD4 with a mean value of 390.2 cells/mm³ and standard deviation (SD) of 232.6 cells/mm³ which was recorded from the HRQoL study of this project.

The change of health states was adjusted based on treatment response and immunological changes. A patient entering the model was defined with their CD4 level and tracked based on the treatment outcomes. CD4 was considered as a tracker variable to determine the transition of a patient from one state to the other. A cycle length of one month was considered for the analysis. An increase in CD4 for treatment response (Kryst *et al.*, 2015; Patel *et al.*, 2014) and a reduction in CD4 for failing regimen (Patrikar *et al.*, 2014) was expected. Move to an adjacent state (improved or progressed health state) or to stay in the same state (Kuhne *et al.*, 2010) was assumed within one cycle. The model supposed a maximum CD4 limit of 1000 cells/mm³ for the

responding regimen which was reported as a maximum CD4 value in healthy Ethiopian individuals (Tsegaye *et al.*, 1999).

4.3.2. Treatment Algorithm

Based on Ethiopian guidelines, five treatment regimens were considered. Patients on DTG-based arm were expected to start a fixed-dose combination therapy with two NRTIs and one INSTI (TDF/3TC/DTG) as the preferred first-line regimen followed by an alternative fixed-dose combination which has two NRTIs and one NNRTI (TDF/3TC/EFV) (FMOH, 2018). Patients on EFV arm are expected to start TDF/3TC/EFV as a preferred first-line followed by an alternative TDF/3TC/DTG.



*Rx: Treatment; *HS: Health state

Figure 1 Model structure of treatment algorithm and outcome for the cost utility analysis of EFV- versus DTG-based regimens in the Ethiopian context

Change in treatment regimen was determined based on treatment response and ADE.

Patients were expected to move to the second-line if they faced treatment failure. For

both arms, preferred and alternative second-line regimens were zidovudine (AZT)/3TC+ (atazanavir (ATV)/r) and AZT/3TC+ (lopinavir/r (LPV)/r), respectively. DRV/r-based regimen (DRV/r + DTG +TDF+3TC) was considered as the third-line (FMOH, 2018). Regimen change to the next treatment option was expected in the case of a treatment failure. Discontinuation related to ADE of the preferred regimen was assumed to result in the use of the alternative regimen. For discontinuation of an alternative regimen, the model assumed the change in the treatment line. All patients in this simulation were assumed to start with first-line treatment (either DTG- or EFV-based regimens).

4.4. Population

For the HRQoL study all patients visiting the ART pharmacy of TASH were considered as a source population while patients visiting the ART pharmacy of the hospital during the data collection period were considered as the study population. The target population of the economic evaluation was Ethiopian adults (>18 years) who are living with HIV/AIDS. This age group comprises more than 90% of the total HIV/AIDS patients in Ethiopia (Girum *et al.*, 2018). The average age of adult HIV patients was estimated from our HRQoL study which was 42 years. The life expectancy of the general population of Ethiopia (i.e., 66 years) was used for the simulation (World Bank, 2019).

4.5. Eligibility Criteria

Participants over 18 years of age during the data collection period were eligible to complete the EQ-5D interview. Participants with incomplete medical chart (absence of CD4 count), who were mentally unstable and with hearing impairment were excluded from the study.

4.6. Sample Size Determination and Sampling Technique

Total number of participants for HRQoL study were estimated based on single proportion formula (Charan and Biswas, 2013). Z-value of 1.96 with 95% level of confidence and 4% of a margin of error were considered. Proportion (P) for sample size estimation was taken from a previous study which assessed the quality of life of HIV/AIDS patients at Gondar university hospital and reported that ~33% of the participants rated their overall perceived HRQoL as good (Surur *et al.*, 2017). The total number of active ART users at TASH was 3,828 during the data collection period.

$$n = \frac{(z\alpha/2)^2 p(1-p)}{d^2}$$

$$n = \frac{(1.96)^2 (0.33) (0.67)}{(0.04)^2} = \sim 560 \text{ (minimum sample size for population above 10,000)}$$

Where: n= sample size desired

$Z \alpha / 2 = 1.96$ (Z=score corresponds to 95% confidence level)

$$p = 33 \%$$

$$d = 0.04 \text{ (Margin of error)}$$

While the total patient who were using ART in TASH were 3828 and then by applying the correction formula we end up with a total sample size of 487.

$$n_f = n / (1 + n/N)$$

$$n_f = 560 / (1 + 560/3828)$$

$$n_f = 487$$

n_f = final sample size

n=sample size for more than 10,000 population

N= population size

And by considering 5% non-response rate the final sample size was estimated to be 511.

We used a convenient sampling method on a ‘first-come first-served’ basis until the sample size was reached.

4.7. Data Collection Instrument and Procedures

4.7.1. Data Collection Instrument

EuroQol introduced the 5-level EQ-5D version in 2009, which has better sensitivity and reduced ceiling effect in comparison to EuroQol-5 dimensions-3 levels. It is used to measure quality of life by considering the five dimensions including, mobility, self-care, usual activities, pain/discomfort and anxiety/depression dimensions. All the dimensions were measured with five levels ranging from no problem to an extremely severe problem or unable to perform any activity. EuroQol-visual analog scales (EQ-VAS) was used to record patient’s self-rated health status on a 20-centimeter vertical scale with endpoints 0 (‘the worst health you can imagine’) and 100 (‘the best health you can imagine’) (EuroQol, 2017).

The Amharic versions of EQ-5D-5L and EQ-VAS were used for collecting HRQoL data. This tool was found to be feasible for general population of Ethiopia (Welie *et al.*, 2019). The tool is able to assess the impact of the disease and its intervention based on different health states. Furthermore, it is able to incorporate societal preferences for health states and is recommended for health technology assessment using different techniques including cost-utility analysis (Devlin and Brooks, 2017). In addition, to EQ-5D-5L and EQ-VAS the data collection tool contained questions related to patients’ socio-demographic characteristics and checklist for recording clinical characteristics from patient chart. Except for the checklist, all the questions were prepared in English and translated to Amharic language (the working language of the country), to ensure understandability by patients. Information in the patient chart was documented in

English. Therefore, using English version of the checklist was found to be suitable for avoiding potential confusion during data collection.

4.7.2. Data Collection Procedures

Data collectors introduced themselves and provided all the relevant information as stated in the Ethical consideration section of this thesis. Face-to-face interviews were carried out on socio-demographic, EQ-5D-5L and EQ-VAS questions. Patients came to the ART pharmacy with their medical chart. Subsequently, the remaining information related to clinical characteristics was copied from the medical records after completion of the interview with patients.

4.8. Parameter Inputs for the Cost-utility Analysis

The parameter input for the modeling were abstracted from primary and secondary data sources. Secondary data was abstracted from PubMed data base by applying appropriate search strategy. Further details of the data used for modeling including probabilities, changes in CD4 count and costs are presented in Table 1.

Table 1 Model parameter point estimate values and ranges for treatment response, ADE, discontinuation due to ADE and costs

Parameters	Base-case analysis	Credible interval	Reference
Probabilities of ADE			(Kanters <i>et al.</i> , 2016)
EFV	0.06	0.04-0.09	
DTG	0.05	0.03-0.07	
ATZ/r	0.06	0.04-0.09	
LPV/r	0.06	0.04-0.09	
DRV/r	0.04	0.02-0.07	
Probabilities of discontinuation due to ADE			
EFV	0.1	0.09-0.16	(Kanters <i>et al.</i> , 2016)
DTG	0.02	0.01-0.03	
ATZ/r	0.1	0.08-0.16	
LPV/r	0.14	0.1-0.18	
DRV/r	0.08	0.05-0.12	
Probabilities of treatment response			
EFV	0.11	0.106-0.112	(Patel <i>et al.</i> , 2014)
DTG	0.16	0.12-0.16	
ATZ/r	0.1	0.08-0.11	
LPV/r	0.09	0.08-0.1	
DRV/r	0.1	0.08-0.12	
Mortality			
HIV related	0.00167	0.00165-0.00168	(Girum <i>et al.</i> , 2018; Indexmundi, 2018)
Other causes	0.000667	0.00066-0.000668	
Monthly CD4 change for first 48 weeks			
EFV	16.3	15.9-16.7	(Kryst <i>et al.</i> , 2015; Patel <i>et al.</i> , 2014)
DTG	20.6	19.2-22.1	
ATZ/r	16.5	15.6-17.4	
LPV/r	17.5	16.1-18.9	
DRV/r	17.7	15.8-19.6	
Monthly CD4 change for second 48 weeks			
EFV	5.6	3.9-7.4	
DTG	10.1	9.6-11.8	
ATZ/r	7.9	7.8-11.6	
LPV/r	8.9	6.8-10.9	
DRV/r	6.7	5-8.1	
Monthly CD4 change after 96 weeks of treatment			

All regimens	-2.32		(Tremblay <i>et al.</i> , 2018)
Monthly CD4 drop for failing regimen	2.9	1.4-7.1	(Patrikar <i>et al.</i> , 2014)
Costs (\$)			
TDF/3TC/EFV	6.24	5.7-6.61	EPISA and TASH
TDF/3TC/DTG	6.87	6.5-7.3	
TDF/3TC+ATZ/r	18.21	17.12-19.3	
TDF/3TC+LPV/r	21.25	19.98-22.5	
DRV/r + DTG +TDF+3TC	64.7	60.8-68.6	
Haematology(CBC)	0.4	0.3-0.42	
Clinical chemistry	0.74	0.7-0.78	
CD4 testing	0.99	0.93-1.1	
Viral load testing	1.95	1.8-2.1	

4.8.1. Probabilities and Tracker Variable

Probabilities of treatment response were estimated based on published systematic review (Patel *et al.*, 2014). Commonly used criterion for considering treatment response for ART is viral load and the viral suppression below 50copies/ml was considered as a treatment success (Meintjes *et al.*, 2017). The annual probability of treatment response was estimated as 0.84 and 0.75 for DTG-based and EFV-based regimen respectively (Patel *et al.*, 2014). These annual probabilities were converted into monthly probabilities. The monthly probabilities were estimated to be 0.16 and 0.11 for DTG- and EFV-based regimen respectively. ADE and discontinuation due to ADE were estimated from the published meta-analysis. Odds ratio of DTG- emergent ADE in comparison to EFV-based regimen was found to be 0.84 and the odds ratio of discontinuation due to the ADE was estimated to be 0.26 (Kanters *et al.*, 2016). These odds ratio values were converted into probability using built in Tree Age functions (TreeAge, 2019).

In addition to probabilities, the microsimulation model has a tracker variable, which served as a memory for an event that determines the change in health state of the patient. The event could be an increase or decrease in CD4 for treatment response or treatment

failure, respectively. This tracker variable value mainly estimated from the systematic review that estimated CD4 cell count. The change in CD4 from baseline was reported as 226.8 cells/mm³ and 179.1 cells/mm³ for DTG- and EFV-based regimens, respectively. These values recorded to occur in 48 weeks after initiation and were transmuted into monthly CD4 change (Patel *et al.*, 2014). Combination of probabilities and tracker variables determine the change in health state of the patient. Since the progress of HIV is determined by change in CD4 and viral load, the microsimulation model accommodated both parameters to determine the disease progress.

The starting CD4 of an individual in the model was determined randomly from the established distribution of CD4. We used the equation “(max (1; min (1000; dist_CD4)))” to decide a maximum limit of CD4. We built equations to accommodate tracker variables. Rapid increase of CD4 was expected at the initial phase of treatment followed by smaller changes. Three phases of changes in CD4 were assumed for responding to regimen (Mauskopf *et al.*, 2012; Stellbrink *et al.*, 2013). We counted the number of cycles that the patient stayed after the treatment response or failure using time tracker. The equation was built to accommodate an event “increase in CD4” and “decrease in CD4”. For treatment failure monthly decline in CD4 without ART intervention was considered (Wolbers *et al.*, 2010). The difference between the death rate of HIV patients and general population was considered as death due to HIV for patients with HIV/AIDS (EPHI, 2017).

4.8.2. Utility Data

CD4 is commonly used as a parameter for defining health states of HIV/AIDS patients (Ghiasvand *et al.*, 2019; Kauf *et al.*, 2008; Shoko and Chikobvu, 2019). This study computed utility value of HIV/AIDS patients who were using ART in TASH hence, the

reported utility values based on CD4 count range were used as an input for the model and for the detail of utility values refer result section.

4.8.3. Cost Data

The cost data of different ART regimens were obtained from EPSA and TASH. EPSA is an agency established for supplying pharmaceuticals for all public health facilities in Ethiopia. Program medicines including, ART, ant-malaria and anti-tuberculosis are exclusively supplied by this agency with collaboration to ministry of health (EPSA, 2019). Per month price of DTG-based regimen and EFV-based regimen was found to be \$6.87 and \$6.24 respectively. Cost related to routine laboratory investigation of the patient was obtained from TASH. In addition to expert interview, invoices and excel documents was referred from EPSA and TASH. Two experts working on HIV program from EPSA and store man in TASH was interviewed. The price estimate of May 2019 was used. The cost data were gathered in Ethiopian birr and converted to United States dollar using the conversion rate of May 2019 (NBE, 2019).

4.9. Study Variables

Due to the nature of the study design, dependent and independent variables can be identified for the HRQoL study only. Accordingly, the level of HRQoL was the dependent variable. Socio-demographic factors including smoking habit, alcohol taking behavior and clinical characteristics including WHO clinical stage of the disease at diagnosis, CD4 count, type of intervention, history of treatment failure, comorbidities, number of medicines that the patient was on at the time of the study and level of treatment adherence were considered as independent variables.

4.10. Data Quality Assurance

The principal investigator conducted half day training on HRQoL data collection for one postgraduate pharmacy student and two pharmacy staff working on ART

pharmacy. Cost data were collected by the principal investigator. All the collected data were checked for their completeness, accuracy and consistency by the principal investigator on the site of data collection. Data coding and data entry template using SPSS version 23 were prepared by principal investigator and the template was reviewed by supervisors. Prior to analysis, data cleaning was done by observing the descriptive statistic output.

4.11. Data Analysis

4.11.1. Analysis for Health-related Quality of Life study

The utility score was calculated using Microsoft excel. Coefficients that represented level specific disutility values obtained from the general population using a hybrid regression model were used for computing utility value. Four dummies were created for each dimension by considering level one as a reference to represent decrease in utility in moving from one level to the other. The 20 parameters reported from the general population for all the five health domains were used (Welie *et al.*, 2019). The utility score was determined using the following equation.

$$\begin{aligned} \text{Utility value} = & 1 - (\text{mo2} * 0.0337341 + \text{mo3} * 0.0644715 + \text{mo4} * 0.2276493 + \text{mo5} * \\ & 0.3598963) + (\text{sc2} * 0.0235125 + \text{sc3} * 0.0394815 + \text{sc4} * 0.1419238 + \text{sc5} * \\ & 0.2223553) + (\text{ua2} * 0.0323013 + \text{ua3} * 0.0482993 + \text{ua4} * 0.1573934 + \text{ua5} * \\ & 0.2721253) + (\text{pd2} * 0.0360808 + \text{pd3} * 0.0515949 + \text{pd4} * 0.2703189 + \text{pd5} * \\ & 0.4063984) + (\text{ad2} * 0.0258862 + \text{ad3} * 0.0848133 + \text{ad4} * 0.2987388 + \text{ad5} * \\ & 0.4577938) \end{aligned}$$

*mo=mobility, *sc=self-care, *ua=usual activity, *pd=pain/discomfort, *ad=Anxiety/depression

Figure 2 Equation for computing utility score of HIV/AIDS patients, TASH, Ethiopia, 2019

For instance, if the patient has mobility problem of level three, would be one and multiplied by the coefficient (0.0644715) that represent the disutility value of mobility problem of level 3. The rest level of mobility would be zero. Descriptive statistics including frequency and percentage were used to describe the health profile of the study population using SPSS version 23. The normality of distribution was checked. Kolmogorov-Smirnov and Shapiro-Wilk test ($p_value < 0.001$) and visual inspection of histogram revealed that the distribution of EQ-5D index value and EQ-VAS score results were skewed and kurtotic. Therefore, we used a non-parametric test for comparing the utility value and EQ-VAS results across groups. Mann-Whitney U test was used for comparing the utility value between two groups including: gender, disclosure status and history of treatment failure. Kruskal-Wallis test was used for the rest of the variables (more than two groups). Median and interquartile range (IQR) were used to characterize the included samples with respect to EQ-5D and EQ-VAS output. In all cases, $p_value < 0.05$ was considered as a cut point for determining statistical significance.

4.11.2. Analysis for Economic Evaluation

For the economic analysis, outcomes including quality adjusted life month (QALM), cost and ICER were computed. ICER was used to compare the two strategies. For the microsimulation analysis, sequencing the analysis result of a different sample size was done to determine the sample size that gives the most stable result. The analysis depicted that, in more than 30,000 simulations, the result was stable and a simulation of 100,000 was conducted to determine the outcome parameters. Base-case analysis with a lifetime horizon was conducted for estimating mean cost, QALM and ICER value per individual for the proposed regimens. Sometimes, policymakers may be

interested in short-term outcome of the interventions (CADTH, 2006). As a result, alternative scenarios with time horizon of five years were conducted.

Deterministic sensitivity analyses using tornado diagram was done to check robustness of the finding. Confidence intervals obtained from the prior studies and assumptions taken from expertise were used for determining parameter range in sensitivity analysis. Variations in price and treatment outcome of the two regimens were considered as a critical parameter, which could affect the ICER value. Furthermore variations in patients' utility values were considered as a sensitive variable.

4.12. Ethical Considerations

Ethical clearance was obtained from the Ethics Review Board of the School of Pharmacy (Ref.No: ERB/SOP/53/03/2019). Permission was also sought from the study hospital. Before data collection, patients were informed of the purpose of the research, confidentiality of data and asked for their consent. Written and verbal consent was obtained from patients. Respondents were informed about their right to refuse or terminate at any point of the interview without any consequence to the treatment they receive at the hospital. Consenting patients were interviewed in a separate place from the waiting area. The confidentiality of information obtained from the study participant was ensured by not collecting personal identifiers in the data collection form and limiting access to participants' information to data collectors and members of the research team.

5. Results

5.1. Health-related Quality of life of Patients with HIV/AIDS

5.1.1. Demographic and Clinical Characteristics of the Participants

The mean age of the participants was found to be 42 years with standard deviation (SD) of 11 years. Majority (325, 63.6%) of the participants were within the age range of 30-49 years and more than half (265, 52.1%) of them were running private business for their living. Over three-quarters (395, 77.3%) of the participant did not drink alcohol and the greater number (496, 97.1%) of them did not smoke cigarette at all (Table 2). Majority (407, 80%) of the participants had a CD4 value of above 200 cells/mm³ and few (22, 4.3%) participants had a CD4 range of below 100 cells/mm³. Majority (440, 86%) of the participants had a viral load below the limit of detection (50copies/ml). TDF/3TC/EFV was found to be the most frequently (297, 58.1%) prescribed ART regimen, which was the preferred first-line in existing guidelines (Table 3).

Table 2 Socio-demographic characteristics and reported health problem of HIV/AIDS patients, TASH, Ethiopia, 2019 (n=511)

Patient Characteristics		Total number of participant n (%)	EQ-5D health dimensions				
			Mobility n (%)	Self-care n (%)	Usual activity n (%)	Pain/ Discomfort n (%)	Anxiety/ Depression n (%)
Gender	Male	202 (39.5)	33 (16.3)	20 (9.9)	41 (20.3)	99 (49)	112 (55.4)
	Female	309 (60.5)	52 (16.8)	21 (6.8)	58 (18.8)	163 (58.2)	170 (55)
Age	18-29	63 (12.3)	4 (6.3)	3 (4.8)	11 (17.5)	38 (60.3)	45 (71.4)
	30-39	141 (27.6)	21 (14.9)	7 (5)	20 (14.2)	63 (44.7)	70 (49.6)
	40-49	184 (36)	28 (15.2)	13 (7.1)	34(18.5)	94 (51.1)	94 (51.1)
	50-59	77 (15.1)	19 (24.7)	9 (11.7)	17 (22.1)	34 (44.2)	41 (53.2)
	>60	46 (9)	13 (28.3)	9 (19.6)	17 (37)	33 (71.7)	32 (69.6)
Marital status	Unmarried	121 (23.7)	17(14)	5 (4.1)	24 (19.8)	63 (52.1)	73 (60.3)
	Married	278 (54.4)	233 (83.8)	25 (9)	48 (17.3)	132 (47.5)	141 (50.7)
	Divorced	47 (9.2)	6 (12.8)	2 (4.3)	11 (23.4)	26 (55.3)	24 (51.1)
	Widowed	65 (12.7)	17 (26.2)	9 (13.8)	16 (24.6)	41 (63.1)	44 (67.7)
Education	No formal education	61 (12)	9 (14.8)	5 (8.2)	11 (18)	39 (63.9)	36 (59)
	Grade(1-4)	88 (17.2)	14 (15.9)	9 (10.2)	23 (26.1)	44 (50)	53 (60.2)
	Grade (5-8)	133 (26)	23 (17.3)	17(12.8)	30 (22.6)	70 (52.6)	73 (54.9)
	High school	132 (25.8)	29 (22)	5 (3.8)	20 (15.2)	66 (50)	71 (53.8)
	TVT /diploma	61 (12)	6 (9.8)	4 (6.6)	10 (16.4)	29 (47.5)	35 (57.4)
	Degree and above	36 (7)	4 (11.1)	1 (2.8)	5 (13.9)	14 (38.9)	14 (38.9)
Occupation	Employed	92 (18.1)	17 (18.5)	8 (8.7)	11 (12)	43 (46.7)	45 (48.9)
	Private business	265(52.1)	33 (12.5)	14 (5.3)	49 (18.5)	132 (49.8)	142 (53.6)
	Pensioner	13 (2.6)	5 (38.5)	4 (30.8)	7 (53.8)	11 (84.6)	11 (84.6)
	Student	17 (3.3)	1 (5.9)	-	2 (11.8)	11 (64.7)	13 (76.5)

Income	Housewife	97 (19.1)	19 (19.6)	10 (10.3)	19 (19.6)	46 (47.4)	54 (55.7)
	Others*	25 (4.9)	9 (36)	5(20)	10 (40)	17 (68)	15 (60)
	<1700 ETB	164 (33.7)	34 (20.7)	15 (9.1)	38 (23.2)	92 (56.1)	95 (57.9)
	1700-5000 ETB	222 (45.6)	33 (14.9)	15 (6.8)	44 (19.8)	123 (55.4)	135 (60.8)
	>5000 ETB	101 (20.7)	11 (10.9)	8 (7.9)	11 (10.9)	38 (37.6)	42 (41.6)
Smoking habit	Daily	2 (0.4)	-	-	-	-	1 (50)
	Occasionally	13 (2.5)	1 (7.7)	-	4 (30.8)	8 (61.5)	9 (69.2)
	Not at all	496(97.1)	84 (16.9)	41 (8.3)	95 (19.2)	254 (51.2)	272 (54.8)
Alcohol taking habit	Never	395 (77.3)	71(18)	35 (8.9)	80 (20.3)	202 (51.1)	211 (53.4)
	Monthly or less	87 (17)	10 (11.5)	4 (4.6)	14 (16.1)	47 (54)	53 (60.9)
	2-4 times a month	24 (4.7)	2 (8.3)	1 (4.2)	3 (12.5)	11 (45.8)	15 (62.5)
	2-3 times a week	5 (1)	2 (40)	1 (20)	2 (40)	2 (40)	3 (60)
Disclosure	Yes	502 (98.2)	80 (15.9)	40 (8)	96 (19.1)	256 (51)	277 (55.2)
	No	9 (1.8)	5 (55.6)	1 (11.1)	3 (33.3)	6 (66.7)	5 (55.6)

*others: Seasonal and unemployed

Table 3 Clinical characteristics and reported health problem of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511)

Patient Characteristics		Number of participant n (%)	EQ-5D health dimensions				
			Mobility n (%)	Self-care n (%)	Usual activity n (%)	Pain/ Discomfort n (%)	Anxiety/Depression n (%)
CD4 (Cells/mm ³)	>500	138 (27)	15 (10.9)	1 (0.7)	11 (8)	40 (29)	39 (28.3)
	350-500	129 (25.2)	22 (17.1)	12 (9.3)	24 (18.6)	65 (50.4)	72(55.8)
	200-350	142 (27.8)	21 (14.8)	14 (9.9)	31 (21.8)	84 (59.2)	95 (66.9)
	100-200	80 (15.7)	22 (27.5)	10 (12.5)	26 (32.5)	59 (73.7)	60 (75)
	<100	22 (4.3)	5 (22.7)	4 (18.2)	7 (31.8)	14 (63.6)	16 (72.7)
WHO clinical stages (at diagnosis)	I	67 (13.3)	16 (23.9)	3 (4.5)	10 (14.9)	40 (59.7)	42 (62.7)
	II	77 (15.2)	11 (14.3)	6 (7.8)	15 (19.5)	40 (51.9)	40 (51.9)
	III	190 (37.6)	28 (14.7)	16 (8.4)	32 (16.8)	83 (43.7)	95 (50)
	IV	171 (33.9)	27 (15.8)	14 (8.2)	40 (23.4)	97 (56.7)	102 (59.6)
Viral load (Copies/mL)	<50 copies/ml	440 (86.1)	70 (15.9)	33 (7.5)	81 (18.4)	217 (49.3)	236 (53.6)
	51-1000 copies/ml	17 (3.3)	3 (17.6)	2 (11.8)	2 (11.8)	9 (52.9)	10 (58.8)
	>1000 copies/ml	54 (10.6)	12 (22.2)	6 (11.1)	16 (29.6)	36 (66.7)	36 (66.7)
Treatment Regimen	AZT/3TC/EFV	30 (5.9)	5 (16.7)	1 (3.3)	4 (13.3)	10 (33.30)	13 (43.3)
	AZT/3TC/NVP	28 (5.5)	4 (14.3)	1 (3.6)	3 (10.7)	14 (50)	13 (46.4)
	TDF/3TC/EFV	297 (58.1)	49 (16.5)	22 (7.4)	51 (17.2)	146 (49.2)	161 (54.2)
	TDF/3TC/NVP	37 (7.2)	4 (10.8)	4 (10.8)	10 (27)	19 (51.4)	19 (51.4)
	ABC+3TC+EFV	40 (7.8)	9 (22.5)	5 (12.5)	8 (20)	28 (70)	27 (67.5)
	TDF+3TC+ATV/r	41 (8)	7 (10.8)	3 (7.3)	12 (29.3)	27 (65.9)	29 (70.7)
	Others *	38 (7.4)	7 (18.4)	5 (13.20)	11 (28.9)	18 (47.4)	20 (52.6)
Number of medicine	1	208 (40.7)	25 (12)	12 (5.8)	25 (12)	88 (42.3)	93 (44.7)
	2	150 (29.4)	26 (17.3)	11 (7.3)	31 (20.7)	84 (56)	90 (60)

	3	91 (17.8)	17 (18.7)	8 (8.8)	21 (23.1)	49 (53.8)	53 (58.2)
	4	43 (8.4)	10 (23.3)	3 (7)	12 (27.9)	27 (62.8)	30 (69.8)
	>4	19 (3.7)	7 (36.8)	7 (36.8)	10 (52.6)	14 (73.7)	16 (84.2)
Duration of treatment	<1 year	4 (0.8)	-	-	-	4(100)	1 (25)
	1-5 years	120 (23.5)	19 (15.8)	8 (6.7)	27 (22.5)	74 (61.7)	77 (64.2)
	>5 years	386 (75.7)	66 (17.1)	33 (8.5)	72 (18.7)	183 (47.4)	203 (52.6)
Adherence	Good	466 (91.5)	77 (16.5)	38 (8.2)	90 (19.3)	236 (50.6)	252 (54.1)
	Fair	13 (2.6)	3 (13.1)	1 (7.7)	-	7 (53.8)	9 (69.2)
	Poor	30 (5.9)	5 (16.7)	2 (6.7)	9 (30)	17 (56.7)	20 (66.7)
History of Rx*	Yes	94 (18.4)	17 (18.1)	9 (9.6)	23 (24.5)	60 (63.8)	62 (66)
	No	417 (81.6)	68 (16.3)	32 (7.7)	76 (18.2)	202 (48.4)	220 (52.8)
Comorbidities	No	349 (68.3)	47 (13.5)	21 (6)	53 (15.2)	156 (44.7)	175 (50.1)
	OIs	41 (8)	5 (12.2)	2 (4.9)	13 (31.7)	25 (61)	28 (68.3)
	Non-OIs	121 (23.7)	33 (27.3)	18 (14.9)	33 (27.30)	81 (66.9)	79 (65.3)

*others: ABC+3TC+NVP, TDF+3TC + LPV/r and AZT+3TC + LPV/r; *Rx: treatment; NVP: Nevirapine; ABC: Abacavir; OIs: Opportunistic infections

5.1.2. Participants' Health Profile

Majority (92%) of the participants reported no problem on self-care dimension followed by mobility in which 83.4% of the participants claimed no problem. The Highest frequency (55.2%) of problems were reported on anxiety/depression dimension followed by pain/discomfort (51.3%). Less than one-fifth of the participants claimed problem on the mobility, self-care or usual activity dimensions. More moderate to severe problems were reported in pain/discomfort and anxiety depression dimension (Fig 2).

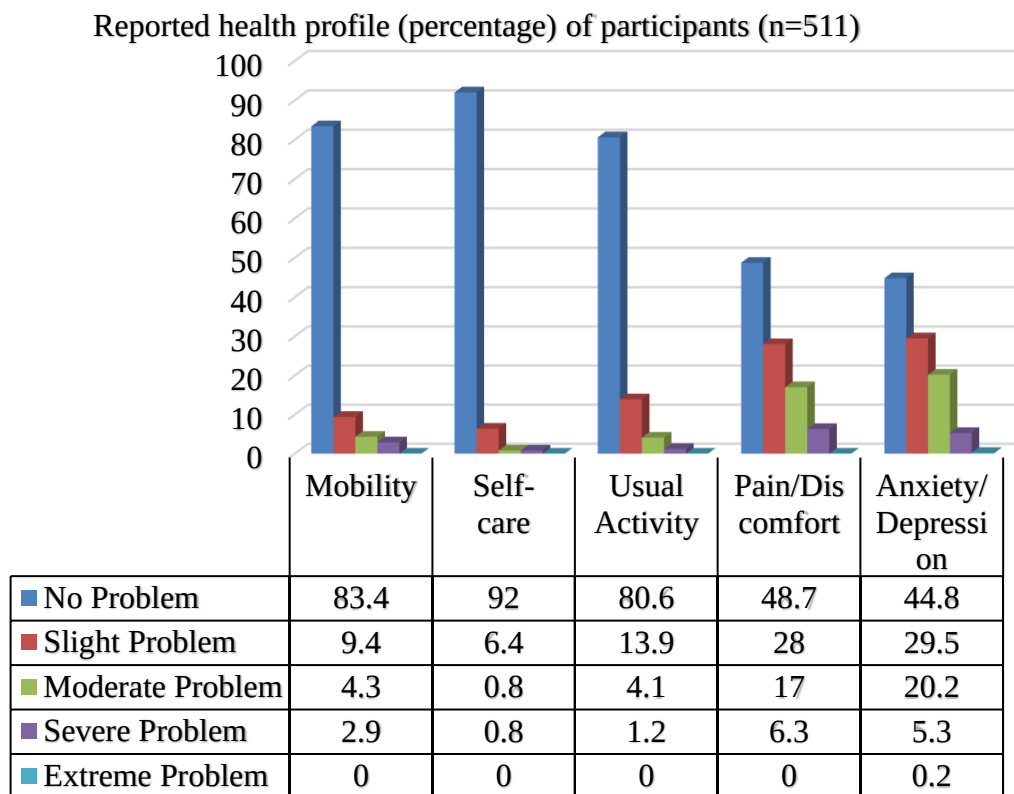


Figure 3 Frequency of self-reported health profile of HIV/AIDS patients, TASH, Ethiopia, 2019 (n=511)

5.1.3. Proportion of Reported Health Problems Based on Patient Characteristics

Irrespective of socio-demographic characteristics, more report of problem was discovered in the pain/discomfort and anxiety/depression dimensions. More than half (163, 58.2%) of female participants reported health problem on pain/discomfort dimension. Nearly similar proportion of male (112, 55.4%) and female (170, 55%)

participants reported problem on anxiety/depression dimension. Higher (45, 71.4%) anxiety/depression problem was reported from the younger age group (18-29 years). Patients who were older than 60 years claimed the highest (33, 71.7%) frequency of problem on pain/discomfort dimension (Table2).

Despite the difference in clinical characteristics of the participant, problems on pain/discomfort and anxiety/depression dimensions were reported most frequently. The proportion of reported health problem on anxiety /depression dimension was (39, 28.3%) and (60, 75%) for CD4 range of > 500 cells/mm³ and 100-200cells/mm³ respectively. Highest proportion of patients on more than four medicines at a time reported problem on pain/discomfort (14, 73.7%) and anxiety/depression (16, 84.2%) dimension (Table 3).

5.1.4. Factors Associated with Health-related Quality of life of Patients with HIV/AIDS

Patient health profile from EQ-5D dimensions were converted into a single index (utility) based on the preference of general population of Ethiopia. EQ-5D index and EQ-VAS score was used to describe the HRQoL of HIV/AIDS patients. Socio-demographic and clinical characteristics associated with patients' HRQoL are described in tables 4 and 5.

Table 4 Socio-demographic factor associated with EQ-5D and EQ-VAS score of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511)

Patient Characteristics		EQ-5D		<i>p-value</i>	EQ-VAS		
		Median [IQR]	<i>Mean Rank</i>		Median [IQR]	Mean Rank	<i>p-value</i>
Gender	Male	0.96 [0.86-1]	261	0.54	85 [70,90]	252	0.65
	Female	0.94 [0.87-1]	253		80 [70-95]	258	
Age	18-29	0.94 [0.84-0.97]	232	0.004*	80 [60-90]	217	<0.001*
	30-39	0.96 [0.88-1]	282		85 [70-95]	284	
	40-49	0.94 [0.88-1]	259		85 [70-95]	271	
	50-59	0.94 [0.86-1]	260		80 [70-90]	250	
	>60	0.89 [0.75-0.97]	192		65 [50-85.5]	177	
Marital Status	Unmarried	0.96 [0.85-1]	253	0.11	80 [70-95]	251	0.26
	Married	0.96 [0.88-1]	268		85 [70-95]	268	
	Divorced	0.94 [0.88-0.97]	250		80 [65-90]	243	
	Widowed	0.92 [0.86-0.97]	216		80 [60-90]	224	
Education	No formal education	0.94 [0.86-0.97]	233	0.27	80 [65-90]	234	0.24
	Grade(1-4)	0.94 [0.86-1]	255		80 [64.75-91.25]	245	
	Grade (5-8)	0.94 [0.88-1]	250		80 [70-90]	246	
	High school	0.94 [0.86-1]	252		80 [70-95]	262	
	TVT /diploma	0.96 [0.88-1]	276		85 [70-95]	280	
	1 st degree and above	0.97 [0.89-1]	301		90 [78.75-95]	293	
Occupational status	Employed	0.97 [0.88-1]	280	0.001*	85[75-93.75]	280	0.008*
	Private business	0.94 [0.88-1]	261		85 [70-90]	255	
	Pensioner	0.85 [0.83-93]	146		70 [45-80]	261	
	Student	0.94 [0.87-0.97]	228		80 [60-85]	194	

	Housewife	0.94 [0.88-1]	258		80 [70-95]	267	
	Others*	0.86 [0.66-0.94]	164		60 [50-95]	196	
Monthly income	<1700 ETB	0.94 [0.85-0.99]	225	0.001*	80 [65-90]	218	0.007*
	1700-5000 ETB	0.94 [0.87-0.97]	233		80 [70-90]	241	
	>5000 ETB	0.97 [0.77-0.97]	299		90 [80-96.5]	293	
Smoking Status	Daily	0.99	388	0.27	-	293	0.49
	Occasionally	0.9 [0.71-1]	215		77.5 [55-92.5]	210	
	Not at all	0.94 [0.87-0.94]	257		80 [70-90]	257	
Alcohol consumption	Never	0.94 [0.88-1]	258	0.77	80 [70-95]	260	0.63
	Monthly or less	0.94 [0.86-0.97]	242		77.5 [70-90]	237	
	2-4 times a month	0.97 [0.8-1]	268		85 [70-90]	256	
	2-3 times a week	0.97 [0.88-1]	275		75	271	
Disclosure status	Yes	0.94 [0.87-1]	257	0.09	80 [70-90]	257	0.35
	No	0.88 [0.67-1]	175		75 [70-90]	211	

* Significant value

*others: Seasonal and unemployed

Table 5 Clinical characteristics associated with EQ-5D and EQ-VAS score of patients with HIV/AIDS, TASH, Ethiopia, 2019 (n=511)

	Patient character	EQ-5D			EQ-VAS		
		Median [IQR]	Mean Rank	p_value	Median [IQR]	Mean rank	p_value
CD4 cells/mm ³	>500	1 [0.94-1]	339	<0.001*	90 [82-99.75]	346	<0.001*
	[350-500]	0.94 [0.88-1]	258		85 [70.25-90]	268	
	[200-350)	0.94 [0.86-0.97]	232		77.5 [65-85]	213	
	[100-200)	0.88 [0.76-0.95]	172		70 [60-85]	184	
	<100	0.88 [0.66-0.96]	184		60 [50-83.75]	166	
WHO clinical stage at diagnosis	I	0.94 [0.85-0.97]	233	0.06	85 [72.5-90]	264	0.08
	II	0.96 [0.87-1]	261		85 [70-95]	266	
	III	0.96 [0.89-1]	273		82.5 [70-95]	265	
	IV	0.94 [0.86-1]	235		80 [65-90]	229	
Viral load	<50 copies/ml	0.95 [0.88-1]	263	0.005*	85 [70-95]	267	<0.001*
	51-1000 copies/ml	0.94 [0.88-1]	257		82.5 [70-95]	260	
	>1000 copies/ml	0.88 [0.7-0.98]	196		70 [60-80]	169	
Type of medicine	AZT/3TC/EFV	0.97 [0.94-1]	309	0.004*	82.5 [70-91.75]	286	0.002*
	AZT/3TC/NVP	0.96 [0.88-1]	271		85 [71.25-90]	278	
	TDF/3TC/EFV	0.96 [0.88-1]	264		85 [70-95]	268	
	TDF/3TC/NVP	0.94 [0.89-1]	269		85 [75-95]	280	
	ABC+3TC+EFV	0.88 [0.82-0.96]	189		70 [60-80]	192	
	TDF+3TC+ATV/r	0.82 [0.77-0.97]	253		70 [51.25-85]	238	
	Others *	0.94 [0.86-1]	205		80 [65-90]	193	
Number of medicine	1	0.96 [0.9-1]	289	<0.001*	90 [70-95]	289	<0.001*
	2	0.94 [0.85-0.97]	240		80 [70-90]	246	
	3	0.94 [0.86-1]	239		80 [65-90]	240	

	4	0.91 [0.83-0.97]	225		75 [60-90]	214	
	>4	0.89 [0.76-0.97]	179		70 [50-80]	144	
Duration of treatment	<1 year	0.96 [0.94-0.96]	49	0.08	85 [72.5-90]	51	0.12
	1-5 years	0.92 [0.86-0.97]	50		80 [66.25-90]	45	
	>5 years	0.96 [0.88-1]	51		82.5 [70-95]	55	
Adherence	Good	0.95 [0.88-1]	259	0.14	80 [70-90]	259	0.08
	Fair	0.93 [0.84-1]	225		72.5[56-93.75]	223	
	Poor	0.89 [0.7-1]	209		70 [60-90]	201	
History of Rx* failure	Yes	0.92 [0.83-0.97]	210	0.001*	70 [60-85]	195	<0.001*
	No	0.96 [0.88-1]	266		85 [70-95]	270	
Comorbidities	No	0.96 [0.88-1]	216	0.001*	85 [70-95]	213	<0.001*
	OIs	0.92 [0.84-0.97]	273		70 [55-90]	274	
	Non-OIs	0.92 [0.8-0.97]	336		80 [65-90]	237	

* Significant value

*others: ABC+3TC+NVP, TDF+3TC + LPV/r and AZT+3TC + LPV/r; *Rx: treatment; NVP: Nevirapine; ABC: Abacavir; OIs: Opportunistic infections

The overall median utility value of HIV/AIDS patients was found to be 0.94 (IQR=0.87, 1) and 80% (IQR=70%, 90%) from EQ-5D index and EQ-VAS result, respectively. There were significant differences in EQ-5D utility index among different age groups, $p=0.004$, with a mean rank utility index of 232, 282, 259, 260 and 192 for the age range of 18-29, 30-29, 40-49, 50-59 and >60, respectively. The finding of this study revealed that the difference in monthly household income showed significant difference in utility index, $p < 0.001$, with mean rank utility value of 225 for <1700 ETB, 233 for 1700-5000 ETB and 299 for >5000 ETB. The Kruskal-Wallis test depicted that age, occupational status, and household monthly income significantly associated with EQ-VAS score with $p < 0.001$, 0.008 and 0.007 respectively. Highest (median=0.94; IQR=0.77-0.97) EQ-5D utility index was recorded from participants with monthly income of greater than 5000 ETB. Participants with the age range of 30-39 years reported higher (median=0.96; IQR=0.88, 1) EQ-5D index (Table 4).

Participant with CD4 range of above 500 cells/mm³ revealed higher (median=1; IQR=0.94, 1) EQ-5D utility index while those with CD4 range of below 100 cells/mm³ depicted lower (median=0.88; IQR=0.66, 0.96) EQ-5D utility index. The EQ-5D utility index (median=0.89; IQR=0.76, 0.97) was obtained for patients who were receiving more than four medicines at a time while the EQ-5D utility index (median= 0.96; IQR=0.9, 1) was drawn for patients on single medicine. A Kruskal-Wallis analysis indicated that there was a statistically significant difference in EQ-5D utility index among patients with different value range of CD4, $p < 0.001$, with a mean rank utility value of 339, 258, 232, 172 and 184 for patients with CD4 range of >500 cells/mm³, 350-500 cells/mm³, 200-350 cells/mm³, 100-200 cells/mm³ and <100 cells/mm³ respectively. Number of medicines and comorbidities were significantly associated with EQ-5D utility index and EQ-VAS score, $p < 0.001$ (Table 5).

5.2. Findings of the Economic Evaluation

5.2.1. Base Case and Scenario Analysis

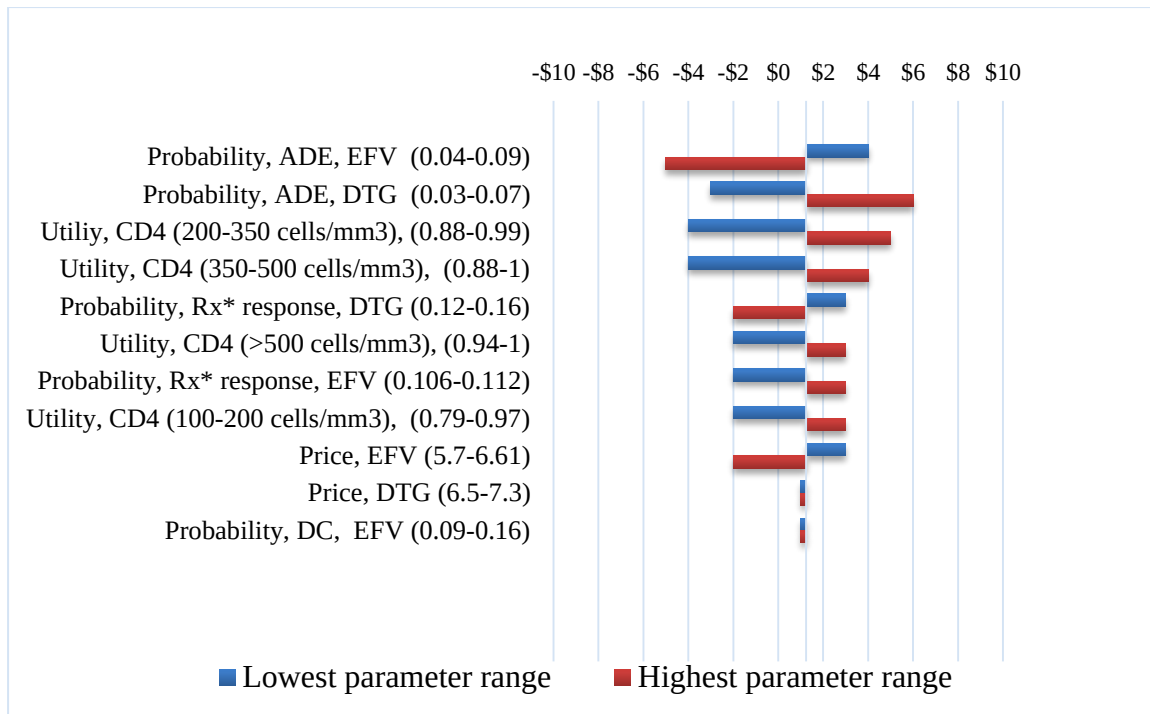
According to the cost-utility analysis, DTG-based regimen was associated with a better QALM in comparison to EFV-based regimen. The base-case analysis revealed that DTG-based regimen was associated with lifetime cost of \$12,709 and expected gains of 183 QALMs while EFV-based regimen incurs a lifetime cost of \$12,701 with expected gains of 176 QALMs per patient. Compared to patients on EFV-based regimen, patient initiated treatment with DTG-based regimen gains 7 extra QALMs for an extra cost of \$8. The ICER of DTG-based regimen in comparison to EFV-based regimen was calculated to be \$1.14 per QALM gained. From the scenario analysis, DTG-based regimen was found to be dominant with expected gains of 2 QALMs at a lower cost (life time cost savings of \$ 1 per patient). The undiscounted analysis depicted that DTG-based regimen is associated with more QALM and lesser cost than EFV-based regimen in both the base-case and scenario analysis (Table 6).

Table 6 Cost –utility analysis result for DTG-versus EFV-based regimen as a preferred first-line, Ethiopia, 2019

Variable	DTG-based regimen	EFV-based regimen	Incremental
Base-case (Discounted at 3%)			
Cost (\$)	12709	12701	8
QALMs	183	176	7
ICER (\$/QALMs)			1.14
Base-case (Undiscounted)			
DTG		EFV	
Cost (\$)	17137	17138	-1
QALMs	246	237	9
ICER (\$/QALMs)			Dominant
Scenario (Discounted at 3%)			
Cost (\$)	3654	3655	-1
QALMs	54	52	2
ICER(\$/QALMs)			Dominant
Scenario (Undiscounted)			
Cost (\$)	3929	3930	-1
QALMs	57	55	2
ICER (\$/QALMs)			Dominant

5.2.2. Sensitivity Analysis

Change in probability of ADE, treatment response or price of both regimens (DTG- and EFV-based) and utility value of different health states of HIV/AIDS have shown effect on ICER value. From the deterministic sensitivity analysis, it was found that with increasing utility score of health state, increase in ICER value detected. Increase in cost of EFV-based regimen, ADE of EFV-based regimen and treatment response of DTG-based regimen reduces the ICER value. The maximum ICER observed is \$6/QALMs in change of any of the sensitive parameter (Figure 3).



*R_x: Treatment

Figure 4 Tornado analysis for cost utility analysis of DTG- versus to EFV- based treatment as first-line treatment for adults with HIV/AIDS, Ethiopia, 2019

6. Discussion

This study assessed the HRQoL of HIV/AIDS patients using EQ-5D and EQ-VAS. The findings demonstrated that a higher proportion of HIV/AIDS patients had reported health problems in anxiety/depression and pain/discomfort dimensions. The lower proportion of patients reported the problem on self-care and mobility dimensions. The CD4-based utility scores calculated in this study were used for the cost-utility analysis that aimed to determine a cost-effective first-line regimen by comparing the existing EFV-based regimen versus the DTG-based regimen. The economic analysis found that the DTG-based regimen is cost-effective as first-line treatment with more QALM and with ICER value of below the estimated cost-effectiveness threshold value of the Ethiopian population.

HRQoL indicator has useful contribution for decision of new and existing interventions (Davis *et al.*, 2017). Evidence related to HRQoL has valuable role for an economic evaluation of health care interventions (Devlin and Brooks, 2017; Versteegh *et al.*, 2016). This study assessed the HRQoL of HIV/AIDS patients using EQ-5D which is a valid tool for HIV patients (Tran *et al.*, 2012). HIV/AIDS patients reported a higher frequency of problem in all five dimensions of EQ-5D than the general population (Welie *et al.*, 2019). This finding is consistent with another previous study, which reported higher frequency of problems on the anxiety/depression dimension (Miners *et al.*, 2014). Henceforward patients with HIV/AIDS needs better health care services than the existing to have reduced health problems.

Higher proportions (45, 71.4%) of younger population depicted anxiety/depression problem. Depression symptoms are reduced with age and it would be common on younger population (McGowan *et al.*, 2017). Thus, younger population needs more psychological support to cope-up with this problem. Anxiety and depression is

significantly associated with fall in level of treatment adherence (Jun *et al.*, 2017). Therefore, it is desirable to intervene the anxiety/depression problem of the patients to improve patient adherence to ART. Almost three-fourth of elder population depicted problem on pain/discomfort dimension. This could be associated with age and comorbidities.

The current study demonstrated overall median EQ-5D utility index of 0.94 (IQR=0.87, 1) while finding from Vietnam (mean=0.65; SD= 0.27) and Colombia (mean=0.85; SD=0.21) depicted lower EQ-5D score (Keaei *et al.*, 2016; Tran *et al.*, 2012). Those utility scores incorporate societal preferences. Utility value could be affected by cultural belief and discrepancies usually occur in the utility scores among participants with different cultural background (Mahlich *et al.*, 2018). The EQ-VAS score of patients living with HIV/AIDS was 80% (IQR=70, 90). It is lower than the value reported from the general population that reported the median value of 90% (IQR=20). Different studies also depicted reduced quality of life in HIV/AIDS patients (Beard *et al.*, 2009; Harding *et al.*, 2014; Surur *et al.*, 2017). Findings from South Africa and Colombia depicted better score with EQ-VAS score (median=90%) and (mean=84.38%) respectively (Keaei *et al.*, 2016; Nglazi *et al.*, 2014). However, Vietnamese HIV/AIDS patients reported lower EQ-VAS (mean=70.3) (Tran *et al.*, 2012). The reported utility value from this study is worthy and it might be the result of efforts made in combating HIV/AIDS burden in Ethiopia. But, further work has to be done to improve the HRQoL of patients since the reported HRQoL of the patients is lower than the general population.

Patients with low income demonstrated lower utility value than the higher income patient population. HIV/AIDS patients and other chronic disease showed better HRQoL with improved economic status (Lemos *et al.*, 2015; Tran *et al.*, 2012). Thus, improved

health outcome is not only achieved through improving health care services rather improving the economic status of the patients should be considered. HIV/AIDS affected the economic status of individuals and families (Boutayeb, 2009). Government, ministry of health and donors should have to give priority for HIV/AIDS patients with low income in creating job opportunity, providing social support. From this study it was found that age, occupational status, and household monthly income were significantly associated with EQ-5D index and EQ-VAS. This revealed the convergent validity of EQ-5D and EQ-VAS as depicted in a previous study from Vietnam (Tran *et al.*, 2012). Participants with CD4 range of above 500 revealed higher utility score while those with CD4 range of below 200 depicted lower utility score. Better quality of life is expected with increasing CD4 (Karkashadze *et al.*, 2017; Liping *et al.*, 2015). In addition to CD4 range, number of medicines and comorbidities were significantly associated with EQ-5D and EQ-VAS score. Viral load and a history of treatment failure were also found to be associated with utility score of the patient. Change in medicine and increase in viral load may cause psychological distress on patients and this would affect utility score of the patient (Weinstein and Li, 2016). Having medicine with better clinical outcome and providing health education for reducing the magnitude of comorbidities has significant role in improving their HRQoL.

From base-case analysis, it was found that DTG-based regimen is more cost effective than EFV-based treatment as a preferred first-line treatment for HIV. DTG is associated with a total gain of 183 QALMs while EFV is expected to yield 176 QALMs. Life time incremental QALMs of 7 per individual was observed in the DTG-based regimen and the finding from this modeling tryout is consistent with previous study which reported six months more in life expectancy from DTG-based regimen than EFV-based regimen

(Despiegel *et al.*, 2015). In Ethiopia it is estimated that around 690,000 people are living with HIV/AIDS and from these adults account for 90% (Girum *et al.*, 2018; UNAIDS, 2018). With this evidence the QALM gain of DTG per-person has profound implication when we account for the total number of adult HIV/AIDS patients at a country level.

DTG-based regimen is associated with incremental cost of \$ 1.14 per QALM gain. If we convert this ICER per QALM into QALY it would be \$13.68 per QALY gain. This value is far below from the threshold value of the country, which is estimated to be \$951.1per QALY (IMF, 2019). Replacing EFV-based regimen with DTG-based regimen is profitable investment in the health care system of Ethiopia. The ICER value of this study is lower than a finding reported from Spain which depicted for every QALY gain DTG saves around quarter million Euro (Guillen *et al.*, 2017). We explored alternative scenario to estimate the cost and effectiveness of the two regimens and it was found that DTG-based regimen is a dominant strategy. This finding is consistent with other previous studies, which revealed better clinical outcome with lower cost for DTG-based regimen (Despiegel *et al.*, 2015; Guillen *et al.*, 2017). Ministry of health and EPSA are promoting the procurement and distribution of DTG-based regimen based on WHO recommendation (PEPFAR, 2018; WHO, 2018). The current economic analysis revealed that the decision made by policymakers in Ethiopia is beneficial for the HIV/AIDS patients. DTG-based regimen is resource-efficient strategy. Hence, it reduces the health and economic burden of the disease with reasonable costs.

Model input parameter including the probability of ADE, treatment response, price of both EFV-and DTG-based regimens and utility value associated with health states were identified as an influential parameter on ICER value. From the deterministic sensitivity analysis it was found that with increasing utility value of health states, increase in ICER value was observed. An increase in price of EFV-based regimen, ADE of EFV-based

regimen and treatment response of DTG-based regimen reduces the ICER value. Maximum ICER observed is \$6/QALMs, which is equivalent to \$72/QALY. Therefore, the finding, which claimed DTG-based regimen as cost-effective first-line treatment in comparison to EFV-based regimen, is robust. DTG-based regimen has better humanistic and economic outcome for Ethiopia as it has been depicted in this microsimulation decision analysis modeling. Subsequently, the decision made by the country is appropriate for the health care system and HIV/AIDS patients in Ethiopia.

7. Strengths and Limitations

This study is the first of its kind to establish the utility value for patients with different health states of HIV/AIDS in the Ethiopian setting. The utility value reported from the current study will be used as an input for conducting an economic evaluation of different HIV/AIDS interventions. The study enrolled large sample size for the HRQoL study. A microsimulation model has been developed for economic analysis that enabled consideration of patient heterogeneity. Economic evaluations of pharmaceuticals prior to making a decision is an unusual practice in Ethiopia and so, this study encourages the application of pharmacoeconomic evaluation in decision making. The participants for utility study was recruited in convenient base and this leads to sampling biases. Therefore the generalizability of the finding should be taken cautiously. The study uses generic tool (EQ-5D-5L) for utility estimation and the tool itself lacks sensitivity to specific disease therefore, the reader should consider the quality of life estimate carefully. The impact of treatment regimens on HRQoL was not considered and the model assumes similar utility value for the proposed regimens. Treatment outcome data were taken from the systematic review and meta-analysis of randomized clinical trials and this may present variation in real-life settings. The treatment algorithm was mainly established based on the treatment guideline and did not accommodate variation in real practice.

8. Conclusion

Finding of the current study elucidated anxiety/depression and pain/discomfort are more frequently reported health problems followed by usual activity and mobility difficulties. The overall utility of patients with HIV/AIDS was 0.94 and 80% from EQ-5D index and EQ-VAS scores, respectively. The utility value of the patients was significantly associated with age, income, CD4, the number of medicine the patient was taking at a time and comorbidities. DTG-based regimen is associated with better monetary value and extra QALM gain. Therefore, this new regimen is a cost-effective strategy to be used as a preferred first-line treatment in the Ethiopian setting. The findings of the economic analysis were robust to changes to any of the key parameters.

9. Recommendations

- ❖ Since the HRQoL of HIV/AIDS patients is lower than the general population service providers including the ministry of health, health facilities and health professionals should improve the counseling and care for the patient.
- ❖ Patients with low-economic status demonstrated lower utility score hence the government and donors working on HIV/AIDS needs to improve the social support services for patients.
- ❖ DTG-based regimen was found to be a cost-effective regimen, so the prescription and dispensing of the regimen should be encouraged by hospital drug and therapeutics committees and managers.
- ❖ Further research that considers the impact of the treatment regimen on HRQoL should be conducted for ensuring the sustainable benefit of the new regimen.

References

- Addis Ababa University (AAU)/College of Health Science (CHS), 2019. College of Health Sciences | Addis Ababa University Sites. <http://www.aau.edu.et/chs/> (accessed 11.11.19).
- Alemayehu, M., Wubshet, M., Mesfin, N., Tamiru, A., Gebayehu, A., 2017. Health-related quality of life of HIV infected adults with and without Visceral Leishmaniasis in Northwest Ethiopia. *Health and quality of life outcomes* 15, 65.
- Alemu, A., Yenealem, A., Feleke, A., Meseret, S., 2013. Health related quality of life assessment and associated factors among people on highly active antiretroviral therapy at Felege Hiwot referral hospital, Bahir Dar, North West Ethiopia. *Journal of AIDS and clinical research* 5, 2–6.
- Aranda-Naranjo, B., 2004. Quality of life in the HIV-positive patient: implications and consequences. *Journal of the Association of nurses in AIDS care* 15, 20S–27S.
- Arts, E.J., Hazuda, D.J., 2012. HIV-1 antiretroviral drug therapy. *Cold Spring Harbor perspectives in medicine* 2(4), 1-24.
- Avert, 2019. Funding for HIV and AIDS. <https://www.avert.org/professionals/hiv-around-world/global-response/funding> (accessed 11.11.19).
- Babigumira, J.B., Jenny, A.M., Bartlein, R., Stergachis, A., Garrison Jr, L.P., 2016. Health technology assessment in low-and middle-income countries: a landscape assessment. *Journal of pharmaceutical health services research* 7, 37–42.
- Beard, J., Feeley, F., Rosen, S., 2009. Economic and quality of life outcomes of antiretroviral therapy for HIV/AIDS in developing countries: A systematic literature review. *AIDS care* 21, 1343–1356.
- Boutayeb, A., 2009. The impact of HIV/AIDS on human development in African countries. *Biomed central public health* 9, S3.
- Canadian Agency for Drugs and Technologies in Health (CADTH), 2006. Guidelines for the economic evaluation of health technologies. https://www.cadth.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf (accessed 11.11.19).
- Centers for Disease Control and Prevention (CDC), 2019. Ethiopia country profile. <https://www.cdc.gov/globalhivtb/where-we-work/ethiopia/ethiopia.html> (accessed 11.11.19).
- Centers for Disease Control and Prevention (CDC), 2018. Health related quality of life concepts. <https://www.cdc.gov/HRQoL/concept.htm> (accessed 11.12.19).
- Charan, J., Biswas, T., 2013. How to calculate sample size for different study designs in medical research? *Indian journal of psychological medicine* 35, 121.
- Dang, A., Likhar, N., Alok, U., 2016. Importance of economic evaluation in health care: An Indian perspective. *Value in health regional issues* 9, 78–83.
- Davis, C., Naci, H., Garpinar, E., Poplavska, E., Pinto, A., Aggarwal, A., 2017. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. *British medical journal* 359, j4530.
- Deribew, A., Tesfaye, M., Hailmichael, Y., Negussu, N., Daba, S., Wogi, A., Belachew, T., Apers, L., Colebunders, R., 2009. Tuberculosis and HIV co-infection: its impact on quality of life. *Health and quality of life outcomes* 7, 105.
- Despiégel, N., Anger, D., Martin, M., Monga, N., Cui, Q., Rocchi, A., Pulgar, S., Gilchrist, K., Camejo, R.R., 2015. Cost-effectiveness of dolutegravir in HIV-1

- treatment-naïve and treatment-experienced patients in Canada. *Infectious diseases and therapy* 4, 337–353.
- Devlin, N.J., Brooks, R., 2017. EQ-5D and the EuroQol group: past, present and future. *Applied health economics and health policy* 15, 127–137.
- Dieleman, J.L., Haakenstad, A., Micah, A., Moses, M., Abbafati, C., Acharya, P., Adhikari, T.B., Adou, A.K., Kiadaliri, A.A., Alam, K., 2018. Spending on health and HIV/AIDS: domestic health spending and development assistance in 188 countries, 1995–2015. *The Lancet* 391, 1799–1829.
- Dixon, S., McDonald, S., Roberts, J., 2002. The impact of HIV and AIDS on Africa's economic development. *British medical journal* 324, 232–234.
- Emamu, S., Sebsebe, F., Bedemariam, G., 2017. (PDF) Quality of life of HIV/AIDS patients on highly active antiretroviral therapy at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Cross-sectional Study. *Clinical research in HIV/AIDS* 4 (2), 1042.
- Ethiopian Public Health Institute (EPHI), 2017. HIV related estimates and projections for Ethiopia. https://www.ephi.gov.et/images/pictures/download2009/HIVestimation_and_projection_for_Ethiopia_2017.pdf (accessed 11.11.19).
- Ethiopian Pharmaceutical Supply Agency (EPSA), 2019. Ethiopian Pharmaceuticals Supply Agency. <https://epsa.gov.et/> (accessed 11.11.19).
- Essig, A., Kang, S. and Sellers, R., 2015. The Relationship between HIV infection rates and GDP per capita in African countries. Georgia Institute of Technology. <http://hdl.handle.net/1853/53303> (accessed 12.08.19)
- European Network for Health Technology Assessment (EuNetHTA), 2015. Endpoints used for relative effectiveness assessment: Health-related quality of life and utility measures. <https://eunethta.eu/endpoints-used-for-relative-effectiveness-assessment-health-related-quality-of-life-and-utility-measures-amended-ja1-guideline-final-nov-2015/> (accessed 11.11.19).
- EuroQol, 2017. EQ-5D-5L. <https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/> (accessed 11.11.19).
- Federal Ministry of Health (FMOH), 2018. National consolidated guidelines for comprehensive HIV prevention, care and treatment. <https://www.afro.who.int/sites/default/files/2019-04/National%20Comprehensive%20HIV%20Care%20%20Guideline%202018.pdf> (accessed 11.11.19).
- Federal Ministry of Health (FMOH), 2017. Ethiopia national guidelines for comprehensive HIV prevention, care, and treatment. https://aidsfree.usaid.gov/sites/default/files/resources/ethiopia_art_guidelines_2017.pdf (accessed 11.11.19).
- Federal Ministry of Health (FMOH), 2014. Fifth health account Federal Ministry of Health, Ethiopia. <https://www.hfgproject.org/wp-content/uploads/2014/04/Ethiopia-Main-NHA-Report.pdf> (accessed 11.17.19).
- Frank, T.D., Carter, A., Jahagirdar, D., Biehl, M.H., Douwes-Schultz, D., Larson, S.L., Arora, M., Dwyer-Lindgren, L., Steuben, K.M., Abbastabar, H. and Abu-Raddad, L.J., 2019. Global, regional, and national incidence, prevalence, and mortality of HIV, 1980–2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the global burden of diseases, injuries, and risk factors study 2017. *The lancet HIV*, 6(12), 831-859.
- Frimpong, P., Amponsah, E.K., Abebrese, J. and Kim, S.M., 2017. Oral manifestations and their correlation to baseline CD4 count of HIV/AIDS patients in Ghana. *Journal of the Korean association of oral and maxillofacial surgeons*, 43(1), 29-36.

- Ghiasvand, H., Waye, K.M., Noroozi, M., Harouni, G.G., Armoon, B., Bayani, A., 2019. Clinical determinants associated with quality of life for people who live with HIV/AIDS: a Meta-analysis. *Biomed central health services research* 19, 768.
- Girum, T., Wasie, A., Worku, A., 2018. Trend of HIV/AIDS for the last 26 years and predicting achievement of the 90–90–90 HIV prevention targets by 2020 in Ethiopia: a time series analysis. *Biomed central infectious diseases* 18, 320.
- Goldie, S.J., Yazdanpanah, Y., Losina, E., Weinstein, M.C., Anglaret, X., Walensky, R.P., Hsu, H.E., Kimmel, A., Holmes, C., Kaplan, J.E., 2006. Cost-effectiveness of HIV treatment in resource-poor settings—the case of Côte d’Ivoire. *New England Journal of Medicine* 355, 1141–1153.
- Guillén, S.M., García, J.E.L., Berenguer, J.B., Sesmero, J.M.M., Gomis, S.C., Graefehain, R., Sánchez-Cambronero, D.L., García, F.J.P., 2017. Cost-utility analysis of the fixed-dose combination of dolutegravir/abacavir/lamivudine as initial treatment of HIV+ patients in Spain. *Farmacia hospitalaria* 41, 601–610.
- Harding, R., Simms, V., Penfold, S., Downing, J., Namisango, E., Powell, R.A., Mwangi-Powell, F., Moreland, S., Gikaara, N., Atieno, M., 2014. Quality of life and wellbeing among HIV outpatients in East Africa: a multicenter observational study. *Biomed central infectious diseases* 14, 613.
- Hays, R.D., Morales, L.S., 2001. The RAND-36 measure of health-related quality of life. *Annals of medicine* 33, 350–357.
- Health policy plus (HP+), 2018. Ethiopia’s emerging HIV financing gap: The need for increased domestic funding. <http://www.healthpolicyplus.com/pubs.cfm?get=10265> (accessed 11.11.19).
- International Monetary Fund (IMF), 2019. World economic outlook (October 2019) - GDP per capita, current prices. <https://www.imf.org/external/datamapper/NGDPDPC@WEO> (accessed 11.11.19).
- Indexmundi, 2018. Ethiopia demographics profile. https://www.indexmundi.com/ethiopia/demographics_profile.html (accessed 11.11.19).
- Janssen, M.F., Pickard, A.S., Golicki, D., Gudex, C., Niewada, M., Scalone, L., Swinburn, P., Busschbach, J., 2013. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *Quality of life research* 22, 1717–1727.
- Jefford, M., Stockler, M.R., Tattersall, M.H.N., 2003. Outcomes research: what is it and why does it matter? What is outcomes research? *Internal medicine journal* 33, 110–118.
- Jun, T.A.O., Han-Zhu, Q., Aaron, M., Yuhua, R., Bryan, E.S., 2017. Effects of depression and anxiety on antiretroviral therapy adherence among newly diagnosed HIV-infected Chinese men who have sex with men. *AIDS (London, England)* 31, 401.
- Kanters, S., Vitoria, M., Doherty, M., Socias, M.E., Ford, N., Forrest, J.I., Popoff, E., Bansback, N., Nsanzimana, S., Thorlund, K., 2016. Comparative efficacy and safety of first-line antiretroviral therapy for the treatment of HIV infection: a systematic review and network meta-analysis. *The lancet HIV* 3, 510–520.
- Karkashadze, E., Gates, M.A., Chkhartishvili, N., DeHovitz, J., Tsertsvadze, T., 2017. Assessment of quality of life in people living with HIV in Georgia. *International journal of STD & AIDS* 28, 672–678.
- Katlama, C., Murphy, R., 2012. Dolutegravir for the treatment of HIV. *Expert opinion on investigational drugs* 21, 523–530.

- Kauf, T.L., Roskell, N., Shearer, A., Gazzard, B., Mauskopf, J., Davis, E.A., Nimsch, C., 2008. A predictive model of health state utilities for HIV patients in the modern era of highly active antiretroviral therapy. *Value in health* 11, 1144–1153.
- Keaei, M., Kuhlmann, J., Conde, R., Evers, S.M., Gonzalez, J., Govers, M., Hiligsmann, M., 2016. Health-related quality of life of patients with HIV/AIDS in Bogota, Colombia. *Value in health regional issues* 11, 68–72.
- Krumholz, H.M., 2008. Outcomes research: generating evidence for best practice and policies. *Circulation*, 118(3), pp.309-318.
- Kryst, J., Kawalec, P., Pilc, A., 2015. Efavirenz-based regimens in antiretroviral-naïve HIV-infected patients: a systematic review and meta-analysis of randomized controlled trials. *Public library of science one* 10(5), 1-23.
- Kuhne, F.C., Chancellor, J., Mollon, P., Myers, D.E., Louie, M., Powderly, W.G., 2010. A microsimulation of the cost-effectiveness of maraviroc for antiretroviral treatment-experienced HIV-infected individuals. *HIV clinical trials* 11, 80–99.
- Kwong, J., 2019. CE: HIV update: an epidemic transformed. *The American journal of nursing*, 119(9), 30-39.
- Lange, J.M.A., Ananworanich, J., 2014. The discovery and development of antiretroviral agents. *Antiviral Therapy*, 19 6:5-14
- Lavallee, D.C., Chenok, K.E., Love, R.M., Petersen, C., Holve, E., Segal, C.D. and Franklin, P.D., 2016. Incorporating patient-reported outcomes into health care to engage patients and enhance care. *Health affairs*, 35(4), 575-582.
- Lemos, C.F., Rodrigues, M.P., Veiga, J.R.P., 2015. Family income is associated with quality of life in patients with chronic kidney disease in the pre-dialysis phase: a cross sectional study. *Health and quality of life outcomes* 13, 202.
- Liping, M., Peng, X., Haijiang, L., Lahong, J., Fan, L., 2015. Quality of life of people living with HIV/AIDS: a cross-sectional study in Zhejiang province, China. *Public library of science one* 10(8), 1-14.
- Mahlich, J., Dilokthornsakul, P., Sruamsiri, R., Chaiyakunapruk, N., 2018. Cultural beliefs, utility values, and health technology assessment. *Cost effectiveness and resource allocation* 16, 19.
- Marseille, E., Larson, B., Kazi, D.S., Kahn, J.G., Rosen, S., 2014. Thresholds for the cost-effectiveness of interventions: alternative approaches. *Bulletin of the World Health Organization* 93, 118–124.
- Mauskopf, J., Brogan, A.J., Talbird, S.E., Martin, S., 2012. Cost-effectiveness of combination therapy with etravirine in treatment-experienced adults with HIV-1 infection. *AIDS* 26, 355–364.
- McGowan, J.A., Sherr, L., Rodger, A.J., Fisher, M., Miners, A., Anderson, J., Johnson, M.A., Elford, J., Collins, S., Hart, G., 2017. Age, time living with diagnosed HIV infection, and self-rated health. *Journal of HIV medicine* 18, 89–103.
- Meintjes, G., Moorhouse, M.A., Carmona, S., Davies, N., Dlamini, S., Van Vuuren, C., Manzini, T., Mathe, M., Moosa, Y., Nash, J., 2017. Adult antiretroviral therapy guidelines 2017. *Southern African journal of HIV medicine* 18(1).
- Miners, A., Phillips, A., Kreif, N., Rodger, A., Speakman, A., Fisher, M., Anderson, J., Collins, S., Hart, G., Sherr, L., 2014. Health-related quality-of-life of people with HIV in the era of combination antiretroviral treatment: a cross-sectional comparison with the general population. *The lancet HIV* 1, 32–40.
- National Bank of Ethiopia (NBE), 2019. National Bank of Ethiopia - commercial banks exchange rate. <https://www.nbe.gov.et/market/banksexchange.html> (accessed 12.24.19).

- Nglazi, M.D., West, S.J., Dave, J.A., Levitt, N.S., Lambert, E.V., 2014. Quality of life in individuals living with HIV/AIDS attending a public sector antiretroviral service in Cape Town, South Africa. *Biomed central public health* 14, 676.
- Nwankwo, N., Seker, H., 2013. HIV progression to AIDS: bioinformatics approach to determining the mechanism of action. *Current HIV research* 11, 30–42.
- Osei-Yeboah, J., Owiredue, W.K., Norgbe, G.K., Lokpo, S.Y., Obirikorang, C., Alote Allotey, E., Gameli Deku, J., Akomanin Asiamah, E., Manaphraim, N.Y.B., Senyo Kwasi Nyamadi, P., 2017. Quality of life of people living with HIV/AIDS in the Ho municipality, Ghana: a cross-sectional study. *AIDS research and treatment* 2017, 1-7.
- Patel, D.A., Snedecor, S.J., Tang, W.Y., Sudharshan, L., Lim, J.W., Cuffe, R., Pulgar, S., Gilchrist, K.A., Camejo, R.R., Stephens, J., 2014. 48-week efficacy and safety of dolutegravir relative to commonly used third agents in treatment-naïve HIV-1-infected patients: a systematic review and network meta-analysis. *Public library of science one* 9(9), 1-10.
- Patrikar, S., Basannar, D.R., Bhatti, V.K., Kotwal, A., Gupta, R.M., Grewal, R.S., 2014. Rate of decline in CD4 count in HIV patients not on antiretroviral therapy. *Medical journal armed forces India* 70, 134–138.
- President's Emergency Plan for AIDS Relief (PEPFAR), 2018. Ethiopia country operational plan (COP/ROP) 2018 Strategic Direction https://et.usembassy.gov/wpcontent/uploads/sites/188/COP18_Standard_FINAL-SDS_Ethiopia_6.14.2018.pdf (accessed 11.11.19).
- Peyasantiwong, S., R Loutfy, M., Laporte, A., C Coyte, P., 2010. An economic evaluation of treatments for HIV-associated facial lipoatrophy: A cost-utility analysis. *Current HIV research* 8, 386–395.
- Pialoux, G., Marcelin, A.-G., Despiéglé, N., Espinas, C., Cawston, H., Finkielsztejn, L., Laurisse, A., Aubin, C., 2015. Cost-effectiveness of dolutegravir in HIV-1 treatment-experienced (TE) patients in France. *Public library of science one* 10(12), 1-14.
- Raffi, F., Wainberg, M.A., 2012. Multiple choices for HIV therapy with integrase strand transfer inhibitors. *Retrovirology* 9, 110.
- Restelli, U., Rizzardini, G., Antinori, A., Lazzarin, A., Bonfanti, M., Bonfanti, P., Croce, D., 2017. Cost-effectiveness analysis of dolutegravir plus backbone compared with raltegravir plus backbone, darunavir+ ritonavir plus backbone and efavirenz/tenofovir/emtricitabine in treatment naïve and experienced HIV-positive patients. *Therapeutics and clinical risk management* 13, 787.
- Rosenberg, 2018. Opinion | H.I.V. Drugs Cost \$75 in Africa, \$39,000 in the U.S. Does It Matter? The New York Times. <https://www.nytimes.com/2018/09/18/opinion/pricing-hiv-drugs-america.html> (accessed 11.11.19).
- Shoko, C., Chikobvu, D., 2019. A superiority of viral load over CD4 cell count when predicting mortality in HIV patients on therapy. *Biomed central infectious diseases* 19, 169.
- Sim, J., Hill, A., 2018. Is pricing of dolutegravir equitable? A comparative analysis of price and country income level in 52 countries. *Journal of virus eradication* 4, 230.
- Sitlinger, A., Zafar, S.Y., 2018. Health-related quality of life: The impact on morbidity and mortality. *Surgical oncology clinics* 27, 675–684.
- Sonnenberg, F.A., Beck, J.R., 1993. Markov models in medical decision making: a practical guide. *Medical decision making* 13, 322–338.

- Soorapanth, S., Chick, S.E., 2010. Cost-utility analysis of behavioral interventions for HIV-infected persons to reduce HIV transmission in the USA, in: Proceedings of the 2010 winter simulation conference. 2433–2443.
- Stalmeier, P.F., Busschbach, J.J., Lamers, L.M., Krabbe, P.F., 2005. The gap effect: discontinuities of preferences around dead. *Health economics* 14, 679–685.
- Stellbrink, H.-J., Reynes, J., Lazzarin, A., Voronin, E., Pulido, F., Felizarta, F., Almond, S., St Clair, M., Flack, N., Min, S., 2013. Dolutegravir in antiretroviral-naïve adults with HIV-1: 96-week results from a randomized dose-ranging study. *AIDS (London, England)* 27, 1771.
- Surur, A.S., Teni, F.S., Wale, W., Ayalew, Y., Tesfaye, B., 2017. Health related quality of life of HIV/AIDS patients on highly active anti-retroviral therapy at a university referral hospital in Ethiopia. *Biomed central health services research* 17, 737.
- Szende, A., Janssen, B., Cabases, J., 2014. Self-reported population health: an international perspective based on EQ-5D. Dordrecht Springer Netherlands.
- Tekola, F., Reniers, G., Haile Mariam, D., Araya, T., Davey, G., 2008. The economic impact of HIV/AIDS morbidity and mortality on households in Addis Ababa, Ethiopia. *AIDS care* 20, 995–1001.
- Theofilou, P., 2013. Quality of life: definition and measurement. *Europe's journal of psychology* 9(1).
- Tolley, K., 2009. What are health utilities? London: Hayward medical communications.
- Tran, B.X., Ohinmaa, A., Nguyen, L.T., 2012. Quality of life profile and psychometric properties of the EQ-5D-5L in HIV/AIDS patients. *Health and quality of life outcomes* 10, 132.
- TreeAge, 2019. User Manual - TreeAge Software. <http://www.treeage.com/support/electronic-help/> (accessed 11.11.19).
- Tremblay, G., Chounta, V., Piercy, J., Holbrook, T., Garib, S.A., Bukin, E.K., Puneekar, Y.S., 2018. Cost effectiveness of dolutegravir as a first-line treatment option in the HIV-1–infected treatment-naïve patients in Russia. *Value in health regional issues* 16, 74–80.
- Tsegaye, A., Messele, T., Tilahun, T., Hailu, E., Sahlu, T., Doorly, R., Fontanet, A.L., de Wit, T.F.R., 1999. Immunohematological reference ranges for adult Ethiopians. *Clinical and diagnostic laboratory immunology* 6, 410–414.
- United Nations Programme on HIV/AIDS (UNAIDS), 2019. Global HIV & AIDS statistics 2019 fact sheet. <https://www.unaids.org/en/resources/fact-sheet> (accessed 11.11.19).
- United Nations Programme on HIV/AIDS (UNAIDS), 2018. Country factsheets, HIV and AIDS estimates, Ethiopia. <https://www.unaids.org/en/regionscountries/countries/ethiopia> (accessed 11.11.19).
- United Nations Programme on HIV/AIDS (UNAIDS), 2015. On the fast-track to end AIDS. <https://www.unaids.org/en/resources/documents/2015/UNAIDSPCB3715-18> (accessed 11.11.19).
- United Nations Programme on HIV/AIDS (UNAIDS), 2014. Fast-track: ending the AIDS epidemic by 2030. Geneva. https://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report (accessed 11.11.19).
- Unitaid, 2017. New high-quality antiretroviral therapy to be launched in South Africa, Kenya and over 90 low- and middle-income countries at reduced price - Unitaid. <https://unitaid.org/news-blog/new-high-quality-antiretroviral-therapy-launched-south-africa-kenya-90-low-middle-income-countries-reduced-price/#en> (accessed 11.11.19).

- Versteegh, M., Knies, S., Brouwer, W., 2016. From good to better: new Dutch guidelines for economic evaluations in healthcare. *Pharmacoeconomics* 34, 1071–1074
- Weinstein, T.L., Li, X., 2016. The relationship between stress and clinical outcomes for persons living with HIV/AIDS: a systematic review of the global literature. *AIDS care* 28, 160–169.
- Welie, A.G., Gebretekle, G.B., Stolk, E., Mukuria, C., Krahm, M.D., Enquoselassie, F., Fenta, T.G., 2019. Valuing health state: An EQ-5D-5L value set for Ethiopians. *Value in health regional issues* 22, 7–14.
- Whitehead, S.J., Ali, S., 2010. Health outcomes in economic evaluation: the QALY and utilities. *British medical bulletin* 96, 5–21.
- World Health Organization, 2018. Policy brief: update on antiretroviral regimens for treating and preventing HIV infection and update on early infant diagnosis of HIV: interim guidance (No. WHO/CDS/HIV/18.19).
- World Health Organization (WHO), 2016. WHO | Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.
- World Health Organization (WHO), 2007. World Health Organization case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.
- World Health Organization (WHO), 2003. World Health Organization guide to cost-effectiveness analysis.
- World Health Organization (WHO), 1995. World Health Organization/quality of life: measuring quality of life. <https://www.who.int/healthinfo/survey/WHOQOL-100.pdf?ua=1> (accessed 11.11.19).
- Wolbers, M., Babiker, A., Sabin, C., Young, J., Dorrucchi, M., Chêne, G., Mussini, C., Porter, K., Bucher, H.C., Collaboration, C., 2010. Pretreatment CD4 cell slope and progression to AIDS or death in HIV-infected patients initiating antiretroviral therapy—the CASCADE collaboration: a collaboration of 23 cohort studies. *Public library of science medicine* 7(2), 1-9.
- World Bank, 2019. Recent development, Ethiopia [http://pubdocs.worldbank.org/en/ 471 041492188157207/mpo-eth.pdf](http://pubdocs.worldbank.org/en/471041492188157207/mpo-eth.pdf) (accessed 11.11.19).

Annex I: Participant Consent Form and Data Collection Tool

Addis Ababa University
College of Health Science
School of Pharmacy

Hello, my name is _____. Currently; we are conducting the study on Health Related Quality of Life of HIV/AIDS patients who are served on Black Lion Hospital. To get adequate evidence for the study, your collaboration is valuable. The interview may take a maximum of 20 minutes and the participation in this study is voluntary based. Participation of this study and refusal to participate in the study has no relation with the service you obtained from the health facility. You have the right to skip any question which is not comfortable for you or you can withdraw from the study at any point; there is no influence that insists you to complete every question, unless you voluntarily confirmed to participate

Your participation and all the information you provided will be confidential. In any condition your name will not be mentioned and the whole data is restricted for access to the data set to the principal investigator and research team. There is no right or wrong answer for the interview question and everything needed is your response and feeling with regard to the questions stated here.

If you have any questions or concern; please contact the principal investigator using the following address.

Persons to contact:

Yared Belete

Mob: 0912854443

E-mail: yared.belete@mu.edu.et/ yaredbeleteb@gmail.com

Are you voluntary to participate? **Yes** ☐ **No** ☐

If the participant agreed to participate and give his/her consent, proceed the interview; if not proceed to the next participant.

Patient Code: _____

Part I: EQ-5D-5L English version

Under each heading, please tick (✓) the one box that best describes your health today

1. Mobility

- | | |
|---|--------------------------|
| I have no problems in walking about | ☐ |
| I have slight problems in walking about | ☐ |
| I have moderate problems in walking about | ☐ |
| I have severe problems in walking about | ☐ |
| I am unable to walk about | ☐ |

2. Self-Care

- | | |
|---|--------------------------|
| I have no problems washing or dressing myself | ☐ |
| I have slight problems washing or dressing myself | ☐ |
| I have moderate problems washing or dressing myself | ☐ |
| I have severe problems washing or dressing myself | ☐ |
| I am unable to wash or dress myself | ☐ |

3. Usual Activities (e.g. work, study, housework, family or leisure activities)

- | | |
|--|--------------------------|
| I have no problems doing my usual activities | ☐ |
| I have slight problems doing my usual activities | ☐ |
| I have moderate problems doing my usual activities | ☐ |
| I have severe problems doing my usual activities | ☐ |
| I am unable to do my usual activities | ☐ |

4. Pain / Discomfort

- | | |
|------------------------------------|--------------------------|
| I have no pain or discomfort | ☐ |
| I have slight pain or discomfort | ☐ |
| I have moderate pain or discomfort | ☐ |
| I have severe pain or discomfort | ☐ |
| I have extreme pain or discomfort | ☐ |

5. Anxiety / Depression

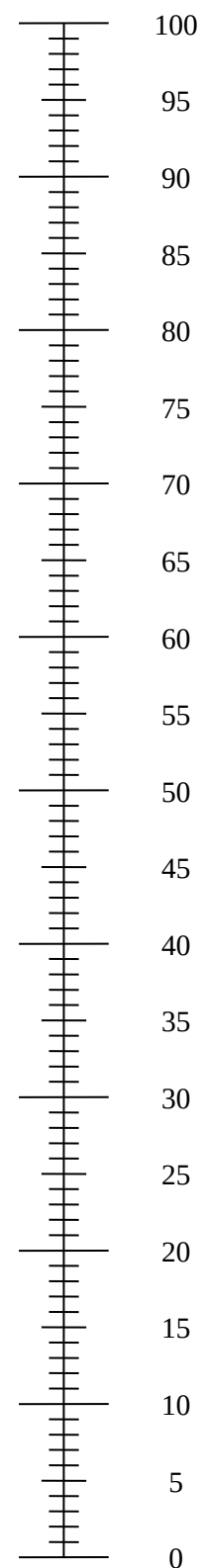
- | | |
|--------------------------------------|--------------------------|
| I am not anxious or depressed | ☐ |
| I am slightly anxious or depressed | ☐ |
| I am moderately anxious or depressed | ☐ |
| I am severely anxious or depressed | ☐ |
| I am extremely anxious or depressed | ☐ |

Part II: Visual Analogue Scale

- We would like to know how good or bad your health Today
- This scale is numbered from 0 to 100
- 100 means the best health you can imagine
0 means the worst health you can imagine
- Mark an X on the scale to indicate how your health is today
- Now, please write the number you marked
on the scale in the box below

YOUR HEALTH TODAY=

The best health
you can imagine



The worst health
you can imagine

Part III: Socio-demographic information

Background information	Answers
1. Gender	1. Male 2. Female
2. Age	____ Years
3. Marital Status	1. Unmarried 2. Married 3. Divorced 4. Widower/widow
4. Education	1. No formal education 2. First cycle primary education (1-4 Grade) 3. Second cycle primary education (5-8Grade) 4. High school (9-12 Grade) 5. Technical and vocational training /college diploma 6. Bachelor degree and above
5. Occupational status	1. Employed (Government or Private organization) 2. Self-employed (Private business) 3. Pensioner 4. Student 5. Housewife 6. Others _____
6. Household monthly income	____ ETB
7. Do you currently smoke	1. Daily 2. Occasionally 3. Not at all
8. How often do you have a drink containing alcohol?	1. Never 2. Monthly or less 3. 2-4 times a month 4. 2-3 times a week 5. 4 or more times a week
9. Have you disclosed your disease status to your family members or significant others?	1. Yes 2. No

Part IV: Checklist of clinical characteristics to be collected from patients' medical records

1. WHO clinical stage of the disease	1. Stage 1 2. Stage 2 3. Stage 3 4. Stage 4
2. CD4 count	_____ cells/mm ³
3. Viral load	_____ copies/mL
4. Current ART regimen	1. AZT+3TC + EFV 2. AZT+3TC + NVP 3. TDF+3TC+EFV 4. TDF+3TC+NVP 5. ABC+3TC+EFV 6. ABC+3TC+NVP 7. TDF+3TC + ATV/r 8. TDF+3TC + LPV/r 9. AZT+3TC + ATV/r 10. AZT+3TC + LPV/r
5. Duration of ART treatment	_____ months
6. History of treatment failure	1. Yes 2. No
7. Presence of comorbidities other than HIV/AIDS	1. Yes 2. No (Skip to question # 10)
8. If the answer for question #7 is "yes", list the types of comorbidities	
9. Total number of medication that the patient is currently on	
10. ART adherence	1. Good 2. Fair 3. Poor

ቅፅ 1: መረጃ ለመስጠት ፈቃደኝነታቸውን የሚገልፁበትና የመረጃ መሰብሰብያ መጠይቅ

አዲስ አበባ ዩኒቨርሲቲ

የጤና ሳይንስ ኮሌጅ

ፋርማሲ ትምህርት ቤት

ጤና ይስጥልኝ እኔ _____ እባላለሁ በአሁኑ ሰዓት በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል ውስጥ በመታከም ላይ በሚገኙ የኤችአይቪ ታማሚዎች ስለህመማቸው ሁኔታ ጥናት እየተደረገ ስለሆነ ለጥናቱ የሚሆን መረጃ ለማግኘት የእረሶ ትብብር ያስፈልገናል። በመሰራት ላይ ያለው ጥናት አላማ ስለእርስዎ ጤንነትና ስለሚደረግልዎት ህክምና ለማጥናት ነው። መጠይቁ ከጊዜዎ ቢበዛ 20 ደቂቃ የሚወስድ ሲሆን በዚህ ጥናት ውስጥ የእርስዎ ተሳታፊነት ሙሉ በሙሉ በእርስዎ ፈቃደኝነት ላይ የተመሰረተ ነው። በዚህ ጥናት ውስጥ ለመሳተፍም ሆነ ላለመሳተፍ መወሰንዎ በሆስፒታሉ ውስጥ በሚያገኙት አገልግሎት ላይ ምንም አይነት ተጽእኖ የማይኖረው ሲሆን ቃለመጠይቁን በማንኛውም ሰዓት ማቋረጥ ወይም ጥያቄዎችን አለመመለስ ይችላሉ። በጥናቱ ውስጥ ለተነሱት ጥያቄዎች የሚሰጧቸው መልሶች ሙሉ በሙሉ በምስጢር የሚጠበቁ ሲሆን የእርስዎም ስም በማንኛውም መልኩ በጥናቱ ውስጥ አይገለጽም፤ እንዲሁም የሚሰጡት ምላሽ ከእርስዎ ማንነት ጋር በማንኛውም መልኩ አይያያዝም። በዚህ መጠይቅ ውስጥ ለቀረቡት ማንኛውም ጥያቄዎች ትክክለኛ ወይም የተሳሳቱ የሚባሉ ምላሾች የሉም። ዋናው የሚፈለገው በእነዚህ ጥያቄዎች ወይም አረፍተኝነቶች ዙሪያ ያሉዎት ምላሽ ነው።

አድራሻ:

ያፌድ በለጠ

ሞባይል: 0912854443

E-mail: yared.belete@mu.edu.et / yaredbeleteb@gmail.com

በጥናቱ ለመሳተፍ ፍፈቃደኝነዎት ?

አዎ ☐

አይደለሁም ☐

ፈቃደኛ መሆናቸውን ካረጋገጡ ቃለመጠይቁን ይጀምሩ

ፈቃደኛ ካልሆኑ ወደሚቀጥለው ተገልጋይ ይሸጋገሩ

የጤና መጠይቅ
የአማርኛ ትርጉም ለኢትዮጵያ

ክፍል አንድ

በእያንዳንዱ ርዕስ ስር፣ እባክዎ ዛሬ ያለዎትን ጤንነት በተሻለ ሁኔታ የሚገልጸው አንድ ሳጥን ላይ ምልክት ያድርጉ፡፡
1. እንቅስቃሴ

የመራመድ ችግር የለብኝም ☐

አነስተኛ የሆነ የመራመድ ችግር አለብኝ ☐

መጠነኛ የሆነ የመራመድ ችግር አለብኝ ☐

ከባድ የሆነ የመራመድ ችግር አለብኝ ☐

ምንም መራመድ አልችልም ☐

2. ራስን መንከባከብ

ለመታጠብም ሆነ ለመልበስ ምንም ችግር የለብኝም ☐

ለመታጠብም ሆነ ለመልበስ አነስተኛ የሆነ ችግር አለብኝ ☐

ለመታጠብም ሆነ ለመልበስ መጠነኛ ችግር አለብኝ ☐

ለመታጠብም ሆነ ለመልበስ ከፍተኛ የሆነ ችግር አለብኝ ☐

ራሴ ልታጠብም ሆነ ልለብስ አልችልም ☐

3. መደበኛ ተግባራት (ለምሳሌ፡- ስራ፣ ትምህርት፣ የቤት ውስጥ ስራ፣

ቤተሰባዊ ወይም የእረፍት ጊዜ ተግባራት)

መደበኛ ተግባራቶቼን ያለ ምንም ችግር አከናውናለሁ ☐

መደበኛ ተግባራቶቼን ለማከናወን አነስተኛ ችግር አለብኝ ☐

መደበኛ ተግባራቶቼን ለማከናወን መጠነኛ ችግር አለብኝ ☐

መደበኛ ተግባራቶቼን ለማከናወን ከፍተኛ ችግር አለብኝ ☐

መደበኛ ተግባራቶቼን ለማከናወን አልችልም ☐

4. የሕመም ስሜት/ምችት ማጣት

የሕመም ስሜትም ሆነ የምችት ማጣት ስሜት የለኝም ☐

አነስተኛ የሕመም ስሜት ወይም የምችት ማጣት ስሜት አለኝ ☐

መጠነኛ የሕመም ስሜት ወይም የምችት ማጣት ስሜት አለኝ ☐

ከባድ የሕመም ስሜት ወይም የምችት ማጣት ስሜት አለኝ ☐

የከፋ የሕመም ስሜት ወይም የምችት ማጣት ስሜት አለኝ ☐

5. ጭንቀት/ደብዳቤ

ጭንቀትም ሆነ ደብዳቤ የለብኝም ☐

አነስተኛ ጭንቀት ወይም ደብዳቤ አለብኝ ☐

መጠነኛ ጭንቀት ወይም ደብዳቤ አለብኝ ☐

ከባድ ጭንቀት ወይም ደብዳቤ አለብኝ ☐

እጅግ ከባድ ጭንቀት ወይም ደብዳቤ አለብኝ ☐

ክፍል ሁለት

- ዛሬ የጤና ሁኔታዎ ምን ያህል ጥሩ ወይም መጥፎ መሆኑን ለማወቅ እንፈልጋለን።
- መለኪያው ከ0 እስከ 100 ድረስ ቁጥሮች አሉት።
- 100 ማለት ሊኖርዎ የሚችለው በጣም ጥሩው የጤና ሁኔታ ነው።
0 ማለት ሊኖርዎ የሚችለው በጣም መጥፎው የጤና ሁኔታ ነው።
- በመለኪያው ላይ ዛሬ ጤንነትዎ ያለበትን ሁኔታ ለማሳየት የ X ምልክት ያድርጉ።
- አሁን፣ከስር ባለው ሳጥን ውስጥ በመለኪያው ላይ ምልክት ያደረጉበትን ቁጥር ይጻፉ።

የዛሬ ጤንነትዎ =

ሊኖርዎ የሚችለው

በጣም ጥሩው የጤና

100

95

90

85

80

75

70

65

60

55

50

45

40

35

30

25

20

15

10

5

0

ሊኖርዎ የሚችለው

በጣም መጥፎው

የጤና ሁኔታ

ክፍል ሶስት

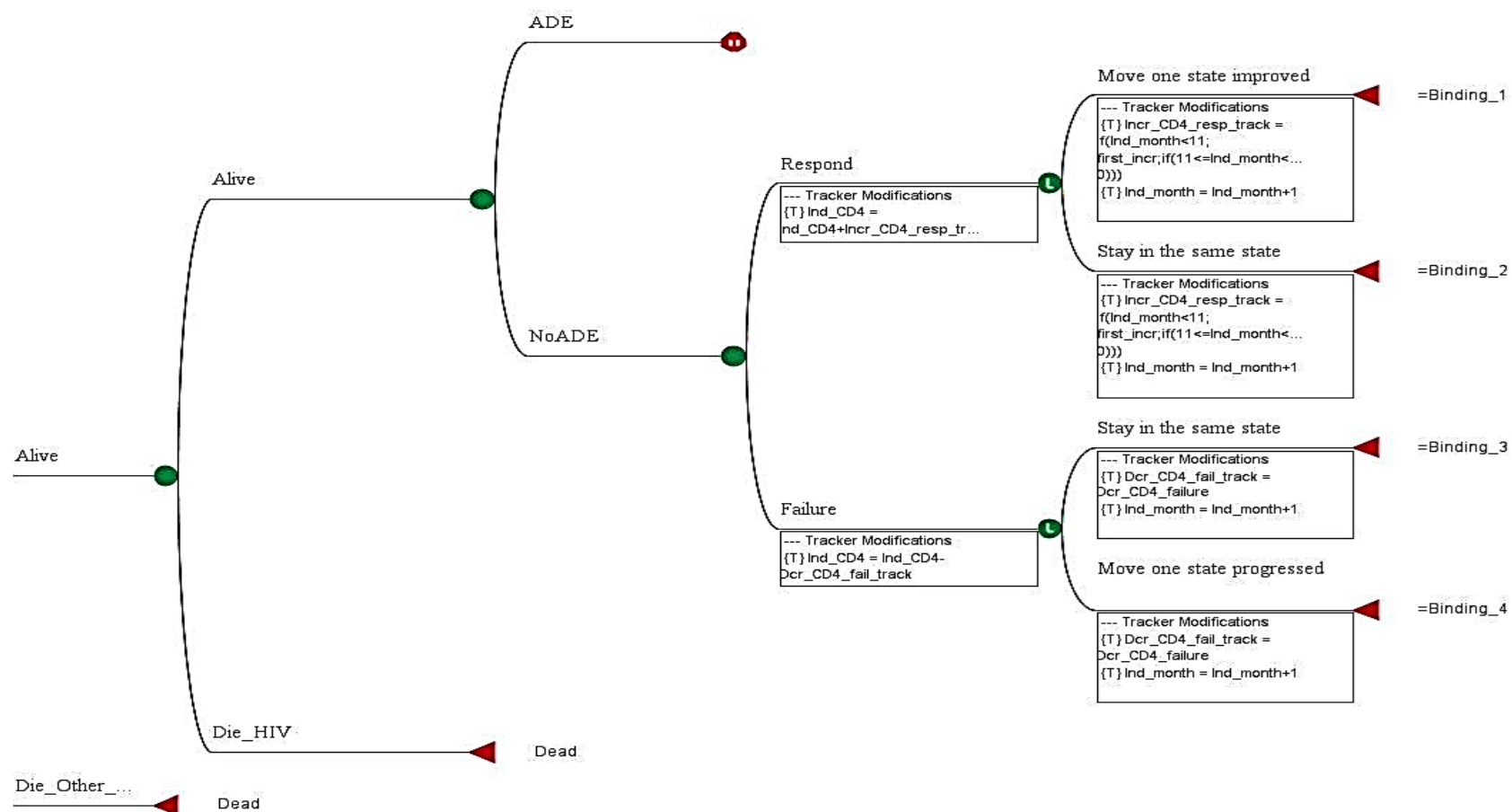
ስለተሳታፊው ጠቅላላ መረጃ

እርስዎን በተመለከተ አጠቃላይ መጠይቅ	መልስ
1. ጾታ	1. ወንድ 2. ሴት
2. እድሜ	ዓመት
3. የጋብቻ ሁኔታ	1. ያላገባች 2. ያገባች 3. አግብቶ/ታ የፈታች 4. የትዳር ጓደኛን በሞት ያጣች
4. የትምህርት ደረጃ	1. መደበኛ ትምህርት ያልቀሰመ 2. ከ 1ኛ-4ኛ ክፍል 3. ከ 5ኛ-8ኛ ክፍል 4. ሁለተኛ ደረጃ/መስናዶ ትምህርት (ከ 9ኛ-12ኛ ክፍል) 5. የተከንክና ሙያ ስልጠና /የኮሌጅ ድረሎማ 6. የመጀመሪያ ዲግሪና ከዚያ በላይ
5. የስራ ቅጥር ሁኔታ	1. ተቀጣሪ 2. የግል ስራ 3. ጡረተኛ 4. ተማሪ 5. የቤት እመቤት 6. ሌሎች፣ይግለፁ _____
6. የቤተሰብ የወር ገቢ	_____ ETB
7. ስጋራ ያጨሳሉ	1. በየዕለቱ 2. አንዳንድ ጊዜ 3. በፍፁም
8. አልኮል ያላቸውን መጠጦች ምን ያህል ጊዜ ይዎስዳሉ	1. በፍፁም 2. በየወሩ ወይም ከዚያ በታች 3. 2-4 ጊዜ በወር 4. 2-3 ጊዜ በሳምንት 5. 5. 4 ወይም ከዚያ በላይ በሳምንት
9. የጤናዎን ሁኔታ ለቤተሰብ ወይም ለፍቅር ጓደኛዎ አሳውቀዋል	1. አዎ 2. አይደለም

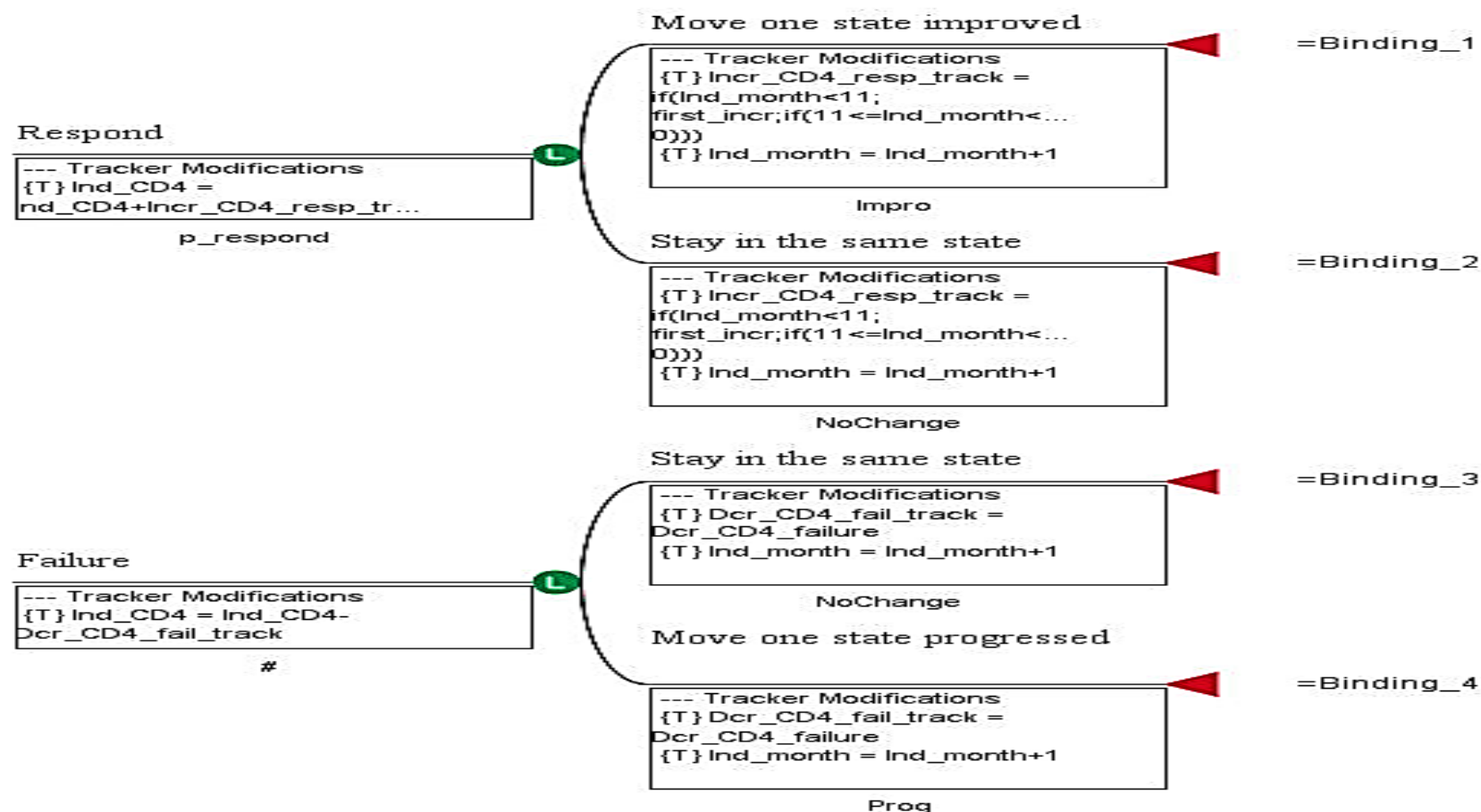
Annex II: Sample Tree of the Model

Here from the available 64 subtree of the model we try to depict one of the tree to show how the patient move through the model.

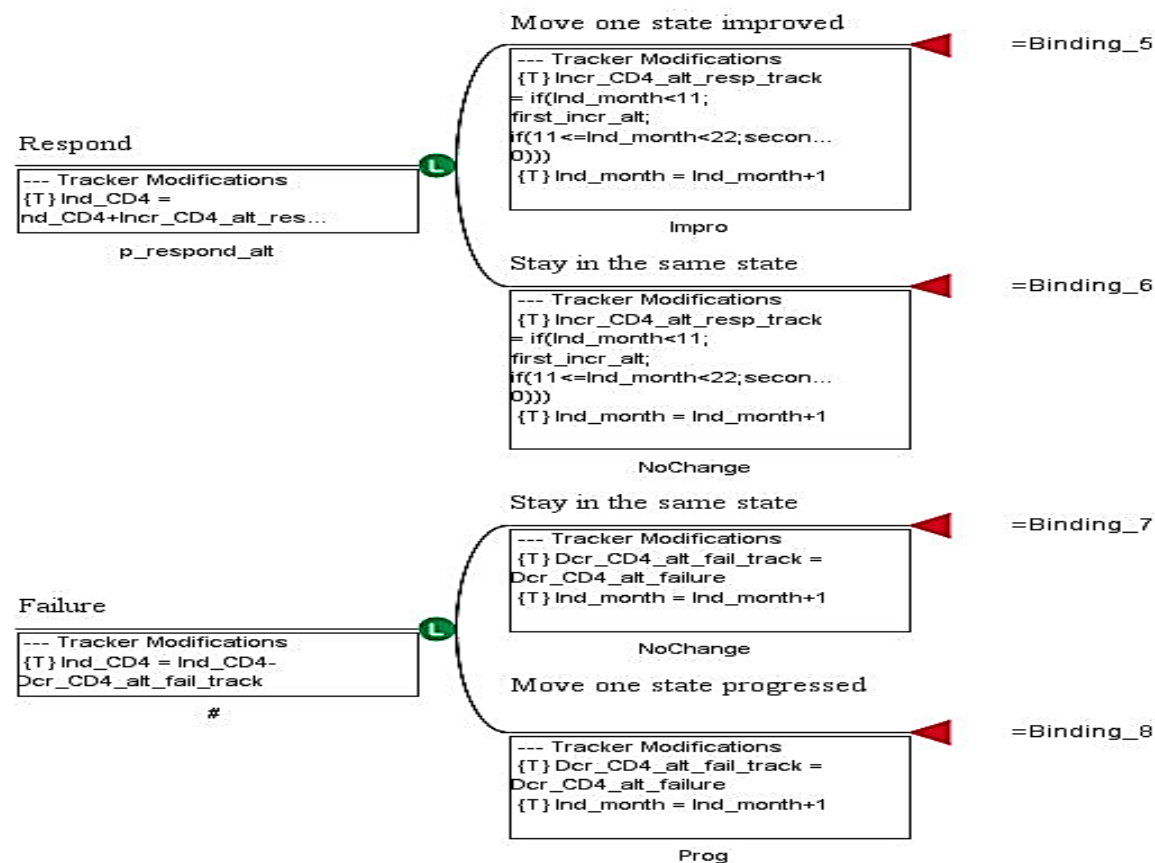
The sample is taken from [State 2 (first-line)] health state of the model. If the patient did not face ADE on first-line his move through model is depicted as follows.



If the patient faces ADE in first line and continue the treatment his path in the model is depicted below



If the patient discontinue treatment his move through the model is presented below



Definitions

Name	State
Binding_1	State 1 (1st Line)
Binding_2	State 2 (1st line)
Binding_3	state 2 (2nd line)
Binding_4	State 3 (2nd line)
Binding_5	State 1 (alternative 1st line)
Binding_6	State 2 (alternative 1st line)
Binding_7	state 2 (2nd line)
Binding_8	State 3 (2nd line)