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# DETERMINING THE DRIVERS OF QUALITY OF LIFE IN HIV PATINTS TREATED WITH ANTIRETROVIRAL THERAPY IN SUBSAHARAN AFRICA

OUBOTE SANGBANA

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DETERMINING THE DRIVERS OF QUALITY OF LIFE IN HIV PATIENTS TREATED WITH  
ANTIRETROVIRAL THERAPY IN SUB-SAHARAN AFRICA

by

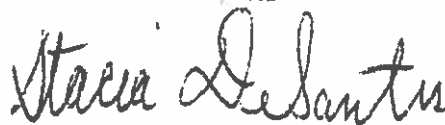
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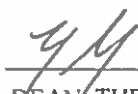
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## DEDICATION

To Kondé and Alimatou Sangbana

To Dr. Tométo Kalhoulé

To Prof. James A. Egan

To Ahmed and Aicha

To Daniela and Sahana

To Ella and her little sister

DETERMINING THE DRIVERS OF QUALITY OF LIFE IN HIV PATIENTS TREATED  
WITH ANTIRETROVIRAL THERAPY IN SUB-SAHARAN AFRICA

by

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## PREFACE

I dearly thank Dr Tométo Kalhoulé for inspiring me to pursue a doctoral degree in epidemiology. In 2009, Dr Kalhoulé reminded me of the paucity of US-trained PhDs in public health in western Africa, and he encouraged me to pursue a career in this field to contribute to the health improvement of our fellow Africans. He made me realize the positive impact I could have in the public health field in western Africa and he later influenced my choice to conduct research on HIV/AIDS, an epidemic sweeping the African continent. Dr Kalhoulé is no longer with us today, but I hope to relentlessly attempt to fulfill his visions for improving public health in Africa and continue to believe in the ideals he passionately shared with me. Merci Docteur.

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I would like to thank my academic advisor and committee chair, Dr. Charles Darkoh, who has patiently mentored me through my years as a doctoral student, during both the simple and difficult moments of my journey. Your advice allowed me to find the appropriate path corresponding to my scientific aspirations and help me place innovation at the heart of my research projects. I also thank my entire dissertation committee for their invaluable guidance, advice and support: Dr. Patrica Dolan Mullen, Dr. Stacia DeSantis, Dr. Sheryl McCurdy and Dr. Christine Markham.

I also deeply thank the staff members of Espoir Vie Togo, particularly Jean Marie, Docteur Nina, Emmanuel, and all the patients who participated in the study, for welcoming me in their family and allowing my research plans to become reality.

I am thankful to my friends and peers at UTHHealth, who underwent the same journey and with whom I often spent long days and nights studying: Peter Elyanu, who contributed to the systematic review of this dissertation, Aleisha Elliot, Jun Xu, Tao Xu, Boomadevi Narendran and Yunju Yang. We collaborated as students and I sincerely hope we will collaborate as researchers in the future. Akira Look, thank you for your precious support. I see you.

My father, Konde, my mother, Alimatou, my sister, Aicha, my brother, Ahmed, and my daughter, Ella, I want to thank you all for the unconditional support during this journey. Each of you, in your own way, have contributed to my academic advancement and I am very grateful.

# DETERMINING THE DRIVERS OF QUALITY OF LIFE IN HIV PATIENTS TREATED WITH ANTIRETROVIRAL THERAPY IN SUB-SAHARAN AFRICA

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During the last decade, HIV in sub-Saharan Africa has shifted from a fatal disease to a chronic condition thanks to the expansion of antiretroviral therapy (ART). As a result, the focus of care has transitioned from survival to quality of life (QoL), and the latter has become a significant outcome measure during patient follow up. Yet, the determinants of QoL among HIV patients in western and central Africa are not well known.

The objective of this dissertation was to determine the main factors associated with QoL among ART-treated HIV adult patients in western and central Africa to ensure healthcare providers and stakeholders use the most relevant, up-to-date evidence when designing and implementing interventions that help patients effectively stay in care and remain asymptomatic.

We first performed a systematic review to synthesize known determinants of QoL in sub-Saharan Africa. Leveraging the findings of the systematic review, we conducted a cross-sectional survey at Espoir Vie Togo (EVT), a patient-oriented community health clinic in Lomé, Togo, to measure QoL and determine which factors previously identified in the systematic review were associated with physical and mental domains of QoL in this

population. We also interviewed EVT patients to better understand their life experiences and potentially uncover novel factors associated with QoL.

The systematic review included 41 observational studies conducted in 14 countries and we found that QoL was most frequently influenced by sociodemographic factors such as age, education, gender, employment, social or family support, as reported in nine or more studies; by clinical factors including mental health and CD4 count; and treatment-related factors such as treatment duration.

At EVT, the mean (SD) physical health summary (PHS) and mental health summary (MHS) scores of 147 ART-treated patients were 80.7 (13.9) and 66.7 (11.1), respectively, on a 0-100 scale. Younger age, male gender, food security, the absence of side effects and self-evaluated “excellent” or “very good” health status were associated with higher PHS scores. Male gender, a higher level of education, food security, family or social support and self-evaluated “excellent”, “very good” and “good” health status were associated with higher MHS scores. Finally, in qualitative interviews with 12 ART-treated EVT patients, patients described good QoL as being in good health and being physically and mentally functional. Family, social and community support, the presence of a supporting individual, being on ART and food security were factors influencing QoL. In this cohort, participants experienced difficulties accepting their positive status, and often faced perceived or enacted stigma.

The QoL of people living with HIV in western and central Africa is driven by multiple sociodemographic, clinical and treatment-related factors that have been summarized in this dissertation. These findings provide stakeholders with valuable evidence to optimize patient care and management. Future research will focus on pediatric populations and compare

treatment satisfaction between patients receiving care in non-governmental organizations and in public healthcare facilities.

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## **BACKGROUND**

The HIV/AIDS epidemic has been a major public health challenge in sub-Saharan Africa for several decades. At its peak in 2005, the number of AIDS-related deaths in sub-Saharan Africa was 2.4 million, and in 2002, only 50,000 individuals were receiving life-saving antiretroviral therapy.<sup>1,2</sup> However, the launch of the “3 by 5” initiative in 2003 by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) set out to provide 3 million doses of life-saving antiretroviral therapy (ART) to people living with HIV (PLHIV) in low- and middle-income countries by the end of 2005.<sup>3</sup> That initial campaign and subsequent ambitious treatment goals led to a significant increase in the number of HIV positive individuals receiving ART, as well as a decrease in AIDS-related deaths and consequently, an increase in HIV prevalence.<sup>4</sup> In fact, an estimated 15.4 million PLHIV in Africa were receiving ART in 2017 and 670,000 died from AIDS-related causes, representing a 42% reduction in AIDS-related mortality from 2004 to 2017 in eastern and southern Africa, and a 24% reduction in western and central Africa.<sup>5,6,7</sup>

Thus, HIV has shifted from a fatal disease to a chronic condition, and as the life expectancy of PLHIV continues to increase and becomes similar to that of the general population in some cases, quality of life (QoL) is emerging as a significant medical outcome in HIV management.<sup>8</sup> WHO defines QoL as “an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.”<sup>9</sup> In the context of HIV as a chronic disease, QoL has become an essential part of follow up assessments. Measuring QoL is key to documenting the burden of disease, monitoring changes in health, evaluating the efficacy of ART, and analyzing the cost-effectiveness of ART programs.<sup>10</sup> Ultimately, HIV patients with higher QoL scores are

more likely to adhere to treatment<sup>11</sup> and thus reduce virologic failure and drug resistance, which have been shown to be associated with poor adherence to ART.<sup>12</sup>

## **HIV Infection: Epidemiology, Pathogenesis and Treatment**

**Epidemiology:** An estimated 37.9 million people were living with HIV globally in 2018, and 1.7 million were newly infected.<sup>13</sup> In low- and middle-income countries, 62% of adults and 54% of children living with HIV were receiving life-saving ART.<sup>13</sup> The most affected region is the WHO African region, with 25.7 million PLHIV and approximately two thirds of new HIV infections globally.<sup>13</sup>

HIV results from the animal-to-human (zoonotic) transfer of a simian immunodeficiency virus.<sup>15</sup> There are two main types of HIV. HIV type 1 (HIV-1) is the most common type, and it is classified into four subtypes. Subtype M (major) is responsible for the global HIV epidemic. Within subtype M, there are nine genetically distinct strains (A, B, C, D, F, G, H, J, K), which are found in different geographic areas. Nearly fifty percent of all PLHIV globally have strain C, and it is highly prevalent in eastern and southern Africa.<sup>15</sup> The subtypes N (new), O (outlier) and P are uncommon and restricted to western and central Africa. In Togo, 99.1% of PLHIV have HIV type 1.<sup>58</sup>

HIV-2 is mainly prevalent in western Africa. It causes an illness similar to HIV-1 but it is less infectious, and an HIV-2 infection progresses more slowly and results in fewer deaths.<sup>15,16</sup> The different HIV types found in western and central Africa compared to eastern and southern Africa thus result in differential risks of transmission, disease progression and quality of life between these sub-Saharan Africa regions.

HIV infection is mainly acquired through unprotected sexual intercourse, mother-to-child transmission, and exposure to infected blood through needles, syringes, or transfusion.<sup>14</sup> The dominant modes of transmission differ according to geographical regions. In high-income countries, male-to-male sexual contact is the main mode of transmission whereas vaginal intercourse and mother-to-child transmission are dominant in developing countries.<sup>15,16</sup> Individuals at increased risk for HIV infection (i.e. key populations) include men who have sex with men, injection drug users, inmates, sex workers and transgenders.<sup>13</sup> Prevention and treatment are the two current strategies for dealing with the epidemic. Successful prevention consists of persistent and continuous behavior change interventions, especially in key populations; a clear understanding of the needs of target populations; and empowering individuals most at risk.<sup>14</sup> There is currently no cure for HIV, but ART effectively controls the virus and prevents transmission by reducing the viral load to an undetectable level, and it is increasingly becoming accessible to HIV patients in developing countries.

***Pathogenesis:*** HIV is a retrovirus belonging to the lentivirus genus.<sup>14</sup> Its genome is less than 10 kilobases and although it only encodes 16 viral proteins, it is able to successfully counter the human immune system.<sup>17</sup> Like most viruses, HIV uses host cells to replicate itself and produce new HIV copies. HIV's life cycle lasts one to two days, and consists of seven well-documented stages:<sup>14-17</sup>

**Binding:** HIV's main envelope proteins, glycoprotein (gp)-120 and gp41, bind to CD4 receptors on the surface of T lymphocytes (also known as T cells) or macrophages, both of which are HIV's main target cells. HIV enters the target cell via interactions with CD4 and chemokine

coreceptors (i.e. **CCR5** when the target cell is a macrophage, or **CXCR4** when the target cell is a T cell).

Fusion: HIV's membrane fuses with the target cell's membrane and HIV releases its viral RNA, reverse transcriptase, integrase, and protease into the cell's cytoplasm.

Reverse transcription. Reverse transcription mediated by viral reverse transcriptase begins and allows viral RNA to be converted into single-stranded DNA, then into double-stranded DNA after replication.

Integration: Viral DNA enters the cell's nucleus and is inserted into the cell's DNA by viral integrase.

Replication: The newly formed DNA produces messenger DNA that initiates the synthesis of HIV proteins, which are building blocks for the formation of more HIV.

Budding: Viral RNA, HIV proteins and components needed to make new viruses gather at the cell's membrane and push out of the cell to form virions, immature HIVs that contain all the components necessary to infect new target cells after maturation.

Maturation: Viral protease cuts HIV proteins into smaller functioning proteins, which combine to form the viral core of the virus. The virus is now mature and can infect other cells.

***Stages of Infection***: Without treatment, HIV-infected individuals naturally progress through three stages of disease, which correspond to the level of viral replication.<sup>18</sup>

Stage 1 - Acute HIV infection: Infected individuals may experience a flu-like illness within two to four weeks after infection. This illness may last for several weeks and it corresponds to the immune system's response to the infection. The immune system is not yet producing HIV antibodies. At this stage, plasma viremia is high, and the risk of transmission is the highest.

Stage 2 - Clinical latency: HIV infection is chronic or asymptomatic for most patients, and HIV replicates at low levels. Without treatment, this stage may last a decade or more although some individuals may progress faster. Individuals may not show signs of illness or have any symptoms. Patients under ART are virally suppressed and are less likely to transmit the infection. The end of this phase is characterized by an increasing viral load and a decline in CD4+ cell count.

Stage 3 - Acquired immunodeficiency syndrome (AIDS): HIV patients are diagnosed with AIDS when their CD4 count is  $\leq 200$  cells/mm<sup>3</sup> or when they acquire AIDS-defining conditions (also known as opportunistic illnesses) such as Kaposi sarcoma, Burkitt lymphoma, or recurrent pneumonia. The immune systems of AIDS patients are highly damaged, and they have high plasma viremia with high rates of HIV replication. They are also highly infectious and may experience symptoms such as swollen lymph nodes, weight loss, and weakness. Without treatment, the life expectancy is three years.

***ART and current treatment options:*** There is currently no cure for HIV, however, antiretroviral medications are available to help patients live healthier and longer lives. In fact, standard ART, if taken correctly and regularly, prevents or slows the progression of HIV, and leads to a significant reduction in HIV morbidity and mortality.<sup>14</sup>

The therapeutic goals of ART include long-term suppression of HIV replication, immune function restoration, and improvement in quality of life.<sup>14</sup> Treatment efficacy is measured through the reduction of opportunistic illnesses, the increase of CD4+ cell count and the decrease of viral load.<sup>14</sup>

HIV patients may experience treatment failure, in which case the combination of antiretroviral medications is changed according to guidelines.

ART is given daily as a combination of different classes of antiretroviral agents capable of stopping HIV at different key steps of its life cycle. The initial regimen usually includes three antiretroviral drugs from at least two different drug classes.<sup>19</sup>

There are seven antiretroviral drug classes, classified according to how they interfere with the virus:

- 1) **nucleoside reverse transcriptase inhibitors** (NRTIs) block reverse transcriptase and prevent the transcription of viral RNA into DNA.<sup>19</sup>
- 2) non-nucleoside reverse transcriptase inhibitors (NNRTIs) also block reverse transcriptase.
- 3) **protease inhibitors** (PIs) block viral protease and prevent new HIV maturation.
- 4) **fusion inhibitors** block HIV from fusing with CD4 cells hence prevent HIV from entering the cell.
- 5) **CCR5 antagonists** block the CCR5 coreceptors on the surface of T cells.
- 6) **post-attachment inhibitors** block HIV from binding to CCR5 and CXCR4 coreceptors.
- 7) **integrase strand transfer inhibitors** (INSTIs) block viral integrase thus prevent viral DNA from inserting into the host cell's DNA.

WHO's current recommendations are to start HIV-infected individuals on ART as soon as possible after diagnosis.<sup>20</sup> The most current WHO standard guidelines, dated July 2019, are based on accumulated scientific evidence and experience from diverse HIV programs worldwide. They recommend starting newly-infected adults and adolescents initiating first-line ART on **dolutegravir** (DTG) in combination with two optimized NRTIs (**tenofovir** [TDF] + **lamivudine**

[3TC] (or **emtricitabine** [FTC])). An alternative first line regimen is **efavirenz** [EFV] 400 mg in combination with TDF + 3TC.<sup>21</sup>

When failing a first-line DTG-based regimen, **atazanavir/ritonavir** (ATV/r) or **lopinavir/ritonavir** (LPV/r) in combination with two optimized NRTIs (**zidovudine** [AZT] + **lamivudine** [3TC]) is recommended for second-line ART. An alternative second-line regimen is DTG in combination with AZT + 3TC or with TDF + 3TC (or FTC), if DTG was not taken as a first-line drug.<sup>21</sup>

First- and second-line regimens differ for children and neonates, for whom approved DTG dosing may not be available.

## Literature Review

Previous research assessing the QoL of HIV patients treated with ART exists, however, most studies quantitatively assess QoL scores without searching for potential factors affecting those scores.<sup>22,23</sup> Studies that do investigate the predictors of QoL among PLHIV have been mostly conducted in high-income countries (in the US, Finland, Spain, Ireland, South Korea, and Iran) and in eastern and southern Africa (in Rwanda and Uganda).<sup>24-32</sup> In those regions, several determinants of improved QoL have been identified, including socio-demographic factors (i.e. male gender, younger age, high socioeconomic status, being employed) and clinical factors (i.e. lower viral load, higher CD4 cell count).<sup>24-32</sup> Those studies also suggest that taking ART and treatment adherence remain the two key factors associated with improved QoL.<sup>33</sup>

There is a lack of evidence on the determinants of QoL in western and central Africa, where HIV prevalence and incidence rates are significantly lower compared to eastern and southern Africa, mainly because of historical, religious, and cultural differences, but also because

of the difference of HIV type associated with the epidemic that results in a differential progression of the disease.<sup>14,34,35</sup> In 2017, of the 25.7 million PLHIV in sub-Saharan Africa, 19.6 million (77%) lived in eastern and southern Africa (out of an estimated population of 597 million)<sup>36</sup> while 6.1 million (33%) lived in central and western Africa (estimated population of 436 million).<sup>36</sup> Moreover, there were 800,000 new HIV infections in eastern and southern Africa, compared to 370,000 in western and central Africa.<sup>35</sup> Thus, generalizing findings from studies conducted in eastern and southern Africa to western and central Africa may not be appropriate, and it is preferable to assess trends and patterns in each region separately in order to better interpret and understand research findings.

Because of the aforementioned historical, cultural and religious particularities, as well as specificities of the epidemic and the paucity of research, there is a need for a comprehensive assessment of factors affecting QoL in central and west African HIV patients.<sup>34</sup> A previous cross-sectional study evaluated QoL and depression in 200 ART-treated Senegalese patients but did not search for an association.<sup>37</sup> Another cross-sectional study investigating QoL among 158 HIV-positive patients in rural Ghana found that being a female, sexually active, asymptomatic and treated with ART were associated with higher QoL scores.<sup>38</sup> Further, a cross-sectional study of 491 Nigerian PLHIV found that being  $\geq 40$  years old was associated with the environment and spirituality domains of QoL, being married with social relationship, self-reporting a “good” or “very good” health status with all domains, a CD4 cell count  $\geq 350$  cells/mm<sup>3</sup> with the physical, psychological and level of independence domains, and being on ART for more than 18 months with the psychological, level of independence and spirituality domains of QoL. Unfortunately, this study did not adjust for confounders and results should be interpreted with caution.<sup>39</sup>

What these studies have in common is that they used previous literature as the source of risk factors for their investigation. Although it is common practice in epidemiological research, this results in the same demographic and clinical variables being repeatedly assessed, and this does not allow new factors to be investigated. A systematic review can be used to synthesize and systematically identify risk or protective factors from diverse and scattered publications, then analyze them comprehensively. This method will help detect under-investigated yet significant factors associated with QoL.

In 2014, Degroote conducted a literature review to identify determinants of QoL in PLHIV in high-income countries and although a few studies drew conflicting results, the author reported that overall, certain socio-demographic characteristics (i.e. male gender, younger age, a stable relationship, employment, and higher education) were associated with higher QoL.<sup>40</sup> Moreover, clinical factors such as better virological status, starting ART at CD4 <200 cells/ $\mu$ l, early HIV stage, and the absence of HIV-related symptoms or comorbidities were also associated with higher QoL. Finally, psychological factors including depression, anxiety, HIV status disclosure and stigma were negatively associated with QoL whereas social support was positively associated. Although Degroote identified several factors associated with QoL, their review may not be generalizable to sub-Saharan Africa, which is fundamentally different from high-income countries in many aspects, notably in the social and molecular epidemiology of the epidemic.<sup>41</sup>

Two systematic reviews geographically restricted to sub-Saharan Africa analyzed QoL among PLHIV receiving ART. One (Beard 2009) assessed the effect of ART on QoL, mental health, labor productivity, and economic wellbeing.<sup>42</sup> This review found ART to be associated with significant improvements in daily function, and physical, emotional and mental health

domains of QoL. Concerning work-related outcomes, performance improved, and absenteeism decreased in patients receiving ART. Unfortunately, factors associated QoL other than ART were not investigated. The other review (Robberstad & Olsen 2010) first reported a synthesis of eight studies quantitatively assessing QoL in PLHIV for economic evaluations purposes, then described the findings of a focus group of HIV clinicians on EuroQol-5D (EQ-5D), a QoL instrument measure, and its use in low-income settings.<sup>43</sup> The authors did not seek to identify factors associated with QoL.

Hence, a systematic review summarizing risk or protective factors associated with QoL among sub-Saharan African populations would address the current gap in knowledge. Subsequently determining which of these factors is associated with QoL would help improve patient wellbeing, and more importantly improve ART adherence, given that treatment adherence is a key factor associated with higher QoL, as previously mentioned.<sup>33</sup> Given the current importance of QoL in HIV management, healthcare professionals can benefit from additional insight on the risk factors causing HIV patients to fall out of care. The consequences of loss to follow up due to poor QoL among patients who started ART are detrimental, not only for the patients themselves but also in terms of potential spread of the infection and in the success of ART programs in sub-Saharan Africa.<sup>44</sup>

In addition to investigating the relationship between risk or protective factors and QoL, this dissertation attempted to further examine the qualitative aspect of QoL research among PLHIV in western and central Africa. Several qualitative studies have been conducted in this region to better understand perceptions of QoL among PLHIV, and we believed that including a qualitative component to this dissertation may contribute to gain additional knowledge on factors influencing QoL in the region. In a qualitative study conducted in Uganda, Mutabazi-Mwesigire

(2014) interviewed HIV patients and asked them to define QoL, and what their perception of QoL was.<sup>45</sup> The author reported that their description was similar to that of the World Health Organization. More interestingly, her research allowed for the discovery of indicators of QoL as perceived by HIV patients, such as happiness, food availability, shelter or availability of money. A similar approach can be undertaken in our dissertation to allow participants to discuss QoL issues that may affect their lives, and potentially lead to the discovery of indicators of QoL in the social and cultural context of western and central Africa.

### **Public Health Significance**

The management of HIV as a chronic disease requires lifelong therapy and sustained care, mainly to ensure continued adherence to ART and rapid adjustments as treatment failure arises.<sup>46</sup> This requires well-honed and well-resourced healthcare delivery systems, which are often lacking in sub-Saharan Africa. However, the lack of efficient healthcare systems at the national level can be balanced by excellent patient care at the community clinic level. Knowing that over 1.1 million individuals in sub-Saharan Africa were newly infected in 2017, treating those individuals early and retaining them in care would contribute to their achievement of viral suppression, which is one of the key steps of UNAIDS's 90-90-90 treatment target to end the AIDS epidemic by 2020 (i.e. by 2020, 90% of PLHIV will know their HIV status, 90% of those infected will receive sustained ART and 90% of those receiving ART will have viral suppression).<sup>35,47</sup> Retaining patients in care is a major challenge in sub-Saharan Africa, and one significant way to overcome it is to ensure patients maintain a high QoL as they cope with their disease. It is therefore crucial to determine the major modifiable factors associated with QoL to

allow healthcare providers and stakeholders to act upon them and ensure patients effectively stay in care, remain asymptomatic and do not transmit the infection.

### **Specific Aims**

The following aims will help determine the main factors associated with QoL in ART-treated PLHIV in west and central Africa.

**Aim 1:** Conduct a systematic review to identify the main factors associated with standardized quality of life measures in ART-treated HIV adult patients in sub-Saharan Africa.

**Aim 2a:** Measure the quality of life of HIV patients receiving long-term ART in a community health clinic in Togo.

**Aim 2b:** Assess the association between main socioeconomic, clinical and treatment-related factors identified in the systematic review and physical and mental domains of QoL in patients of a community health clinic in Togo, after adjusting for demographic variables.

**Aims 3:** Identify indicators of quality of life as described by ART-treated HIV patients of a community health clinic in Togo during qualitative interviews.

## METHODS

### **Aim 1.**

#### ***Study Design***

The first part of this dissertation was a systematic review with the aim to identify key risk or protective factors associated with QoL in sub-Saharan Africa.

#### ***Prior Systematic Reviews and Registration***

Prior systematic reviews on this topic were searched for, first on the Texas Medical Center library website using the following search term: (hiv OR aids) AND (“Quality of Life” OR QOL OR HRQoL) AND (sub-Saharan Africa) AND (“systematic review” OR “meta-analysis”), second on Medline, by combining the following search terms: (hiv OR human immunodeficiency virus OR aids OR acquired immunodeficiency syndrome), (quality of life OR health-related quality of life OR QOL OR HRQoL), exp “Africa South of the Sahara”/ and (systematic review OR meta-analysis), and finally on PubMed using search terms similar to Medline’s.

An additional search was conducted on PROSPERO, the international database for registering systematic reviews. To ensure the most comprehensive and complete search possible, only “HIV” was used for the search. 33 HIV-related reviews were found. We reviewed them individually to assess whether a review of the association between risk or protective factors and QoL in HIV patients was already registered. No previous review matching our methodology was found therefore we registered our proposed systematic review (PROSPERO CRD42019136202).

## ***Participants***

Study participants for the systematic review were sub-Saharan HIV-positive individuals aged 18 years or older who were taking antiretroviral therapy. Following the **PICOTS** principle, **participants** were “HIV-positive individuals aged 18 years or older”, **intervention** was “antiretroviral therapy”, **comparator** was “any” or “none”, **outcome** was “any quality of life assessment obtained using a standardized questionnaire or instrument (such as World Health Organization Quality of Life-HIV [WHOQOL-HIV], Medical Outcomes Study HIV Health Survey [MOS-HIV], EQ-5D, 36-Item Short Form Survey [SF-36], etc...), including an adjusted analysis assessing an association between risk or protective factors and QoL”, **time** was “any”, **setting** was “sub-Saharan Africa” and **study design** was “randomized or non-randomized controlled trial (any phase), observational studies (comparative or non-comparative), and pooled analyses”.

## ***Search Strategy***

Our systematic review was conducted following Methodological Expectations for Cochrane Intervention Reviews (MECIR) standards.<sup>48</sup> A systematic search from inception to May 2019 was conducted on **Medline**, **PubMed**, **Embase** and **PsycINFO** to identify studies for inclusion. In addition, non-databases sources, including GreyNet, Grey Literature Report and BIOSIS Previews, were searched for grey literature such as meeting abstracts, posters and unpublished articles.

Our search strategy was tailored for each database. It combined HIV, quality of life and sub-Saharan Africa terms as shown in Appendix A for Ovid Medline, Appendix B for PubMed, Appendix C for Embase and Appendix D for PsycINFO.

### ***Study Selection***

Two independent screeners (Oubote Sangbana, Peter Elyanu) performed a **title/abstract screening** in order to exclude studies not meeting the pre-determined criteria.

Exclusion reasons during screening were age <18 years old, not HIV-positive, not in sub-Saharan Africa, does not include ART, does not include QoL outcomes, does not include a standardized QoL instrument, not an original study, not a clinical study, animal study, or *in vitro* study. Cohen's Kappa was calculated to assess interrater reliability, and areas of disagreement between the two screeners was resolved by consensus. Following the title/abstract screening phase, a **full text review** phase was performed in order to select studies reporting outcomes of interest. The primary outcome was a QoL assessment from a previously validated questionnaire (eg. WHOQOL, MOS-HIV, EQ-5D, SF-36). The secondary outcome was any risk or protective factor reported in the study to be associated ( $p < 0.05$ ) with improved or reduced QoL, after adjustment.

### ***Data Collection***

A brief data collection form was created after selecting studies meeting the inclusion criteria. One reviewer (OS) extracted all data of interest listed in the form using an excel spreadsheet. A second reviewer (Akira Look) reviewed the extracted data for errors. Disagreements were resolved by consensus. Per Cochrane recommendations, items to collect from each selected study included data related to the source, eligibility, methods, participants, interventions, outcomes, and key findings.<sup>49</sup> Most importantly, it included the factors associated with improved or reduced QoL. A risk or protective factor was selected and retained for the second part of this dissertation if was statistically significantly associated ( $p < 0.05$ ) with overall QoL or domains of QoL, after adjustment, in three or more studies.

An evidence table was created to summarize and present characteristics and key findings from each study. It included the author's name, country, study dates, sample description, QoL instrument, risk or protective factors, and key findings.

### ***Preliminary rapid scoping review***

To assess the feasibility of our systematic review, we conducted a preliminary rapid scoping review, and 12 studies meeting our inclusion criteria were identified (data not shown). Potentially extractable risk or protective factors affecting QoL are shown in table 1.

Table 1. Potential variables of interest from a preliminary focused literature review.

Variable	Format
<b><i>Demographics</i></b>	
Gender	Male, Female
Age	Continuous (years) or Categorical
Education Level	None, Primary, Secondary or more
Employment Status	Student, Employed, Unemployed, Other
Marital Status	Single, Married or Partner, Separated/Divorced, Widowed
<b><i>Health-Related</i></b>	
Duration of treatment	Continuous (months) or Categorical
Regimen	1 <sup>st</sup> Line, 2 <sup>nd</sup> Line, >=3 <sup>rd</sup> Line
Treatment adherence	Yes, No
Social Support	Yes, No
Alcohol Use	Yes, No
Drug Use	Yes, No
Sexually Active	Yes, No
Self-Perceived as Healthy	Yes, No
Time Since HIV	Continuous (months)
<b><i>Clinical</i></b>	
Viral Load	Continuous (copies/mL) or Categorical
CD4+ count	cells/mm <sup>3</sup>
HIV/TB co-infection	Yes, No
Treatment-related adverse events	Yes, No
HIV Serostatus	Symptomatic, Asymptomatic, AIDS

## ***Risk of Bias***

The risk of bias for each included study was assessed using National Institutes of Health (NIH)'s 14-item quality assessment tool for observational cohort and cross-sectional studies.<sup>50</sup>

The 14 questions were:

1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified and defined?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
5. Was a sample size justification, power description, or variance and effect estimates provided?
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

12. Were the outcome assessors blinded to the exposure status of participants?
13. Was loss to follow-up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

For each item, possible choices were “yes”, “no” or “other” (i.e. “cannot determine”, “not applicable” or “not reported”).

After completion of the systematic review, several demographic, socioeconomic, clinical and treatment-related factors associated with QoL in ART-treated sub-Saharan HIV adult patients were identified, and the second part of the dissertation was initiated.

## **Aim 2.**

### ***Study Design***

The second part of this dissertation was a cross-sectional study with the aim to measure the QoL of HIV patients receiving long term-ART in a community health clinic in Togo (Aim 2a), and assess the association between key risk and protective factors and QoL (Aim 2b).

### ***Study Setting***

The study was conducted at Espoir Vie Togo (EVT), a community health clinic in Lomé, Togo. EVT is a non-governmental organization created in 1995 and its mission is to treat and provide social support to PLHIV in Togo. A team of 79 healthcare providers (physicians, medical assistants, nurses, midwives, etc.) at three locations in the country (Lomé [Togo's capital], Aného, Sokodé) manages about 3,500 PLHIV, and this number has been steadily increasing over the last two decades.<sup>51</sup>

### ***Sampling Strategy***

The study's target population was western and central African PLHIV. Lomé university hospital, Centre Hospitalier Universitaire (CHU) Sylvanus Olympio, refers patients to EVT, which accepts all referred patients without exclusion. Patients come from various socioeconomic backgrounds and they are representative of urban HIV patients in west and central Africa.

### ***Study Subjects***

Participants were consecutive men and women HIV patients who visited the outpatient community clinic in July and August 2019. Participants were given a 500 CFA (~ US \$0.85)

token as reimbursement for travel expenses (Appendix L). Eligibility criteria were as follows:  
≥18 years, a confirmed HIV diagnosis and currently taking ART.

### ***Ethical Approval***

Ethical approval was obtained from the Comité de Bioéthique pour la Recherche en Santé (031/2019/CBRS) in Togo (Appendix J), and from the University of Texas Health Science Center at Houston's Committee for the Protection of Human Subjects (HSC-SPH-19-0357) (Appendix K). All participants provided verbal informed consent.

### ***Sample Size Calculation***

We estimated the sample size based on a fixed model and R-squared increase for linear multiple regression. We assumed a medium population effect size (i.e. 0.15; corroborated by a previous study conducted in China)<sup>53</sup>, a power of 80%, a significance level of 5%, and 15 predictors. Using G\*Power software Version 3.1.9.4, a sample size of 140 was generated.<sup>52</sup>

### ***Data Collection***

Two study investigators (Oubote Sangbana [primary investigator]; Jean Marie Atsou-Alley [secondary investigator and EVT's clinical psychologist and patient coordinator]) collected data before or at the end of patients' doctor visits. The clinic's primary physician (Nina Dapam) asked patients if they were interested in participating in the study and, in case of a positive response, they were directed towards the study investigator. The investigator explained the objective of the study following a verbal script (Appendix E), then sought verbal informed consent. If verbal informed consent was obtained, data collection proceeded, in two phases. First, basic demographic and socioeconomic characteristics were collected from the patient's medical records (Table 2, Appendix F). Questions related to the risk or protective factors

identified during the systematic review were also collected directly by asking patients. Overall, the characteristics collected were: gender, age, education level, employment, marital status, body mass index (BMI), HIV status disclosure, social or family support, alcohol use, food insecurity, serostatus, CD4 count, viral load, treatment duration, ART regimen, line of treatment, adherence, and side effects. Second, participants were administered the French version of the MOS-HIV survey (Appendix G,H). Survey questions were digitalized beforehand: rather than being in a paper form, the questionnaire was entered on the Qualtrics application on an Apple iPad and the investigators read the questions to the patients and recorded the answers directly on the Qualtrics application.

Table 2. Collectable data from EVT patients' visit cards.

Variables	
Page 1	Page 2
Temperature	<u>Opportunistic Infections (Type)</u>
Pulse	Opportunistic Infections (Treatment)
Blood Pressure	Side Effects
Weight	TB Test Requested
Height	<u>Suspected TB (Yes, No)</u>
<u>Age</u> †	<u>Confirmed TB (Yes, No)</u>
Status (Well, Can Move, In Bed)	Date TB Confirmed
Pregnant	TB Treatment
<u>CD4+ count   Date Collected</u>	Other Concomitant Diseases
<u>Viral Load</u>	<u>Adherence to ART (Yes, No)</u> †
ART Status (Start, Continued, Change, Stop)	Number of Doses Omitted in the Last Week
Reason for Changing ART <sup>a</sup>	<b>Hemoglobin Level</b> *
Reason for 2 <sup>nd</sup> Line ART	<b>ALT or SGPT</b> <sup>b</sup>
Reason for Stopping ART	<b>Creatinine</b>
ART (Original 1 <sup>st</sup> Line, Switched 1 <sup>st</sup> Line, 2 <sup>nd</sup> Line	<b>Blood Sugar</b>
Concomitant Medication	<b>Triglycerides</b>
<u>Duration of Treatment</u>	<b>Cholesterol</b>
Treated for Opportunistic Infections	<b>Amylase</b>
Co-trimoxazole Prophylaxis	<b>Lipase</b>
	<b>CPK</b>

<sup>a</sup> Antiretroviral Therapy; <sup>b</sup> Alanine transaminase or serum glutamic-pyruvic transaminase; \* Bolded variables indicate the latest data available; † Underlined variables indicate variables of interest; † Defined as attending doctor appointment.

## ***MOS-HIV***

The survey administered was the MOS-HIV (Appendix G,H). It is a previously validated instrument that produces an overall QOL profile specific to HIV patients. It assesses health transition and 10 dimensions of QoL: general health perceptions, pain, physical functioning, role functioning, social functioning, energy/fatigue, mental health, health distress, cognitive functioning, quality of life (Figure 1).<sup>54,55</sup>

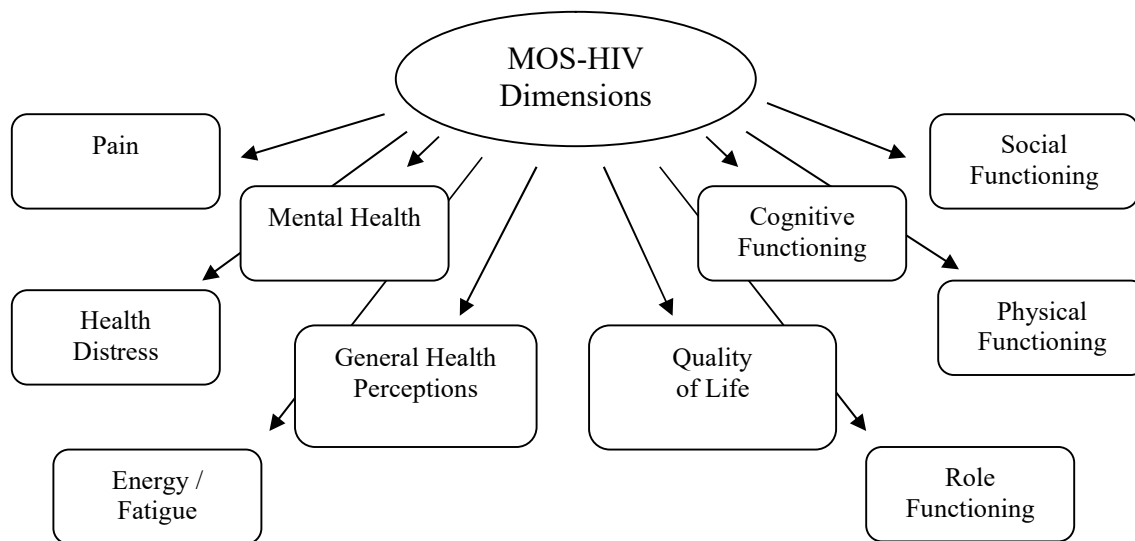


Figure 1. Dimensions of the MOS-HIV health survey.

The MOS-HIV is a disease-specific instrument and contains 35 items. Items are scaled on a 3, 5 and 6-point Likert scale without weighting of items. After linear transformation, the scores range from 0 to 100, where higher scores indicate better QOL. Guidelines for calculating the scores for each dimension are provided with the survey upon request.

The French version of the MOS-HIV and permission to use the questionnaire were obtained by submitting a request on the dedicated website supported by Mapi Research Trust.<sup>56</sup>

## ***Data Analysis***

### ***Aim 2a: MOS-HIV Scores***

Per scoring guidelines, 11 of the 35 items were recoded to reverse their directionality.

Items composing each scale were summed up to compute raw scores, as shown in Table 3. Raw scores were transformed linearly to a 0-100 scale according to the following formula:

$$[(\max_{\text{new}} - \min_{\text{new}}) / (\max_{\text{old}} - \min_{\text{old}})] \times [(v - \max_{\text{old}}) + \max_{\text{new}}]$$

where  $\max_{\text{new}}$  and  $\min_{\text{new}}$  are 0 and 100, respectively,  $\max_{\text{old}}$  and  $\min_{\text{old}}$  are the item's minimum and maximum boundaries, and  $v$  is the observed value.

Then, a physical health summary (PHS) score and a mental health summary (MHS) score were computed using a factor analysis with oblique rotation, as described by Revicki (1998).<sup>57</sup> All coding and computation were performed using SAS software, Version 9.4, SAS Institute Inc.<sup>59</sup>

Table 3. Equations to compute MOS-HIV dimensions scores.

Domain	Equation*
General health perceptions	Q1 + Q11a + Q11b + Q11c + Q11d
Physical functioning	Q4a + Q4b + Q4c + Q4d + Q4e + Q4f
Role functioning	Q5 + Q6
Social functioning	Q7
Cognitive functioning	Q10a + Q10b + Q10c + Q10d
Pain	Q2 + Q3
Mental health	Q8a + Q8b + Q8c + Q8d + Q8e
Energy/Fatigue	Q9a + Q9b + Q9c + Q9d
Health distress	Q9e + Q9f + Q9g + Q9h
Quality of life	Q12
Health transition	Q13

\*Raw scores are subsequently linearly transformed to a 0-100 scale

### ***Aim 2b: Multiple Linear Regression***

Two multiple linear regression analyses, one with PHS as the dependent variable, and the other with MHS as the dependent variable, were fitted to determine the factors associated with QoL. The independent variables were gender, age, education level, employment, marital status, BMI, HIV status disclosure, social or family support, alcohol use, food insecurity, serostatus, viral load, treatment duration, ART regimen, line of treatment, adherence, self-evaluated health status and side effects. All analyses were performed using SAS software Version 9.4.<sup>59</sup>

***Data Preparation.*** After data cleaning, independent variables were inspected for multicollinearity using correlation matrices. In case of highly correlated variables, one variable was dropped.

***Preliminary Models.*** For each health summary score (PHS and MHS), a preliminary model was fitted using the domain score (continuous) as the dependent variable and risk or protective factors (continuous, binary or categorical) as the independent variables.

***Diagnostics.*** All linear regression assumptions were assessed, and remedial measures such as variable transformation were applied in case of assumptions' violations.

***Model Selection.*** Stepwise model selection was performed to determine the subset of variables best defining the relationship between the independent variables and the specific health summary score under investigation.

***Model Validation.*** The most parsimonious model selected during the model selection phase was validated using the data splitting approach (or cross-validation). The dataset was randomly split into two equal sets. One set was used as the model-building (training) set. The other set was used as the validation set. Estimated  $\beta$  coefficients obtained in the training set were used to predict

estimates in the validation set, and the agreement between estimated  $\beta$  coefficients and standard errors between the two sets was assessed.

Potential influential points were then analyzed in the model-building set.

Results from the model selection were reported in a table showing the dependent variable (PHS and MHS), the independent variables selected during model selection, the  $\beta$  coefficients, the 95% confidence intervals and the p-values. The directionality of variables statistically significantly associated with QoL after adjustment was recorded.

### **Aim 3.**

#### ***Study Design***

The third part of this dissertation was a qualitative assessment of ART-treated HIV patients with the aim to understand patients' definitions of QoL, identify and gain additional knowledge on underlying and undiscovered indicators of quality of life, and better understand the life experiences of HIV patients in this population.

#### ***Data Collection***

Every day, one patient visiting the outpatient clinic was asked to participate in the qualitative assessment, in addition to being administered the MOS-HIV survey, before or after the doctor visit. Face-to-face individual interviews took place before administering the survey to ensure participants' responses were not limited by the constructs and dimensions used in the survey. Participants were given a 500 CFA (~ US \$0.85) token as reimbursement for travel expenses (Appendix L). Eligibility criteria to be interviewed for the qualitative assessment were being 18 years or older, having a confirmed HIV diagnosis and currently taking ART more than six months.

The primary investigator (OS), assisted by a clinical psychologist with qualitative interview experience (JMAE), conducted the interviews, which were held in a private consultation room to ensure patient's confidentiality. All interviews were held in French, the official language and first language of most participants. No time limit was predetermined but the interviews lasted approximately 15 minutes. The interview was recorded on a digital audio recorder, and written notes were also taken by the study investigator during the discussion. No participant refused to be recorded. The discussion felt relatively informal and this allowed

participants to engage in a conversation rather than a question-answer session. This approach also encouraged participants to give honest answers.

Based on an interview guide specifically developed for this study, a series of open-ended questions were asked:

1. a) What is a good quality of life for you?  
b) How is that different or similar to what others experience?
2. a) How have your ideas of a good quality of life changed after HIV?  
b) What was it before and how has that changed over time and in relation to what?
3. Are there things or people that put your quality of life at risk? Please tell me about them.

The questions were open-ended, and the investigator discussed risk and protective factors more in depth as deemed necessary. The overall aim was for participants to share their definition of QoL and describe the factors improving or impeding their quality of life in the context of HIV.

### ***Ethical Approval***

Ethical approval was obtained from the Comité de Bioéthique pour la Recherche en Santé (031/2019/CBRS) in Togo (Appendix J), and from the University of Texas Health Science Center at Houston's Committee for the Protection of Human Subjects (HSC-SPH-19-0357) (Appendix K). All participants provided verbal informed consent.

### ***Data Analysis***

Audio recordings were fully transcribed and translated from French to English. Hand-written notes were typed and translated in English. Data analysis was performed using OpenCode version 4.0.<sup>60</sup> Data were analyzed following a thematic analysis. Transcripts were read multiple times to become familiar with the content. The primary investigator (HS) used an

open coding approach to capture the participants' life experience and perception of QoL. After coding several transcripts, a set of codes were defined and subsequently used for similar recurring concepts. Additional codes were incorporated into the analytical framework as they were identified in subsequent transcripts. Several themes emerged and were examined at the latent level: the investigator sought to detect underlying ideas and concepts by analyzing patients' words beyond what was said verbatim during the interviews. All themes were reviewed by an experience researcher who did not take part in the interviews (SM)

## **Human Subjects, Animal Subjects, or Safety Considerations**

This dissertation included the use of the MOS-HIV, a previously validated questionnaire, for the assessment of QoL in human subjects. The latter consisted of HIV patients treated at Espoir Vie Togo, a community clinic in Lomé, Togo. Data collection took place during a one-month period and involved 147 patients. Each patient was assessed only once, and the survey was completed in approximately 10 minutes. Participants were given a 500 CFA (~ US \$0.85) token as reimbursement for travel expenses. Verbal informed consent was sought to access patients' medical records in order to collect demographic data and the most recent clinical data prior to the assessment. Patients were clearly informed of their right to not participate in the study and of their ability to withdraw from the study at any time if they chose to do so. Proper ethical approvals were requested from UTHHealth's Committee for the Protection of Human Subjects (CPHS) and the Togolese Comité de Bioéthique pour la Recherche en Santé. A letter of support was obtained from Espoir Vie Togo since it does not have an ethics committee (Appendix I).

The main risks incurred by study participants were breach of confidentiality and loss of privacy since the investigators (Oubote Sangbana [primary investigator]; Jean Marie Atsou-Alley [secondary investigator and EVT's clinical psychologist and patient coordinator]) accessed private information included in patients' medical records. This risk was mitigated by accessing the record in front of the patient, only for a brief period and only to record the few demographic and clinical variables necessary for the completion of the study. No personal identifying information was collected. Moreover, the primary investigator completed Collaborative Institutional Training Initiative (CITI) training for the protection of human subjects and ethical conduct and followed all standard practices to maintain patient privacy. The secondary

investigator, who is in contact daily with the clinic's patients, was previously trained on-site by local administrators to maintain patient privacy and protect human subjects.

The Apple iPad used for the questionnaire assessment was password-protected and only the two study investigators knew the password. It was not connected to the internet. All data collected on the iPad were deleted once transferred to the primary investigator's password-protected laptop computer for analysis.

In summary, the benefits of the findings of this study exceeded the risk incurred, and the study protocol was consistent with sound research procedures and did not expose patients to unnecessary risks.

## **JOURNAL ARTICLE 1**

**Drivers of Quality of Life in HIV Patients Treated with Antiretroviral Therapy in Sub-Saharan Africa: A Systematic Review.**

**AIDS and Behavior**

## **Abstract**

As HIV evolved from a fatal infection to a chronic disease, quality of life (QoL) has emerged as a significant medical outcome. The objective of this systematic literature review was to identify key risk or protective factors associated with QoL in sub-Saharan Africa. We searched Medline, PubMed, Embase, and PsycINFO from inception to May 2019 and GreyNet and International AIDS Conference archives for original publications. Two screeners independently reviewed titles and abstracts, and full texts of relevant articles for factors statistically associated with QoL. In all, 41 observational studies with multivariate analyses conducted in 14 countries met eligibility criteria. As reported in 9 or more studies, higher QoL was associated with sociodemographic factors: younger age, employment, higher education level, male gender, and social or family support; and a treatment-related factor: longer treatment duration. Lower QoL was associated with clinical factors: mental health and lower CD4 count. This review summarizes the evidence in the literature and highlights key factors affecting the QoL and well-being of ART-treated people living with HIV in sub-Saharan Africa.

## Introduction

In the last decade, the scale-up of antiretroviral therapy (ART) has changed the course of the HIV/AIDS epidemic in sub-Saharan Africa, with an estimated 40% reduction in HIV-related mortality from 2010 to 2018 (1). Although there were an estimated 470,000 HIV-related deaths in 2018, HIV has shifted from a fatal disease to a chronic condition and the HIV care continuum and management approach have evolved to meet the demands of this new paradigm (2). As a result, quality of life (QoL) has emerged as a significant outcome during follow-up for those receiving ART (3,4). Measuring QoL is key to documenting the burden of disease, monitoring changes in health, evaluating the efficacy of ART, and analyzing the cost-effectiveness of ART programs (5). Moreover, patients who maintain a good QoL as they cope with their disease are more likely to adhere to treatment and thus reduce virologic failure and drug resistance (6,7). It is therefore crucial to determine the main factors associated with QoL to ensure healthcare providers use the most relevant, up-to-date evidence in implementing interventions that help patients to effectively stay in care and remain asymptomatic.

An increased research interest in the determinants of QoL has been observed in low-income countries in the last decade, and yet, a synthesis of recent findings on the topic has to be published. This gap is especially important for sub-Saharan Africa, where the course of the disease is unique due to its historical, religious, and cultural singularities. The profile of the epidemic also differs from other regions because of the diverse distribution and prevalence of HIV subtypes across countries in sub-Saharan Africa (8,9,10). There is a need for a region-specific review to capture this part of the African experience and provide a comprehensive overview of the available data on risk and protective factors influencing QoL in this region. The

objective of this review was to identify and summarize the factors associated with QoL among sub-Saharan adult HIV patients treated with antiretroviral therapy.

## **Methods**

This systematic review was conducted following Methodological Expectations for Cochrane Intervention Reviews (MECIR) standards and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11,12). The protocol was registered with the international prospective register of systematic reviews (PROSPERO CRD42019136202) and can be accessed on PROSPERO's website.

## **Inclusion criteria**

Inclusion criteria followed a pre-specified PICOTS framework (13). The population was HIV patients aged 18 years or older under treatment with ART or highly active antiretroviral therapy (HAART) for any duration; independent variables were any sociodemographic, clinical, behavioral or treatment-related variables, the outcome of interest was any quality of life assessment obtained using a standardized questionnaire or instrument (e.g. World Health Organization Quality of Life-HIV [WHOQOL-HIV], Medical Outcomes Study HIV Health Survey [MOS-HIV], EuroQol-5D [EQ-5D]). Any publication date was accepted, the setting was a sub-Saharan country, and all quantitative study designs were considered. In addition, studies had to include an adjusted analysis assessing an association between QoL and risk or protective factors. There were no language restrictions.

## **Search strategy**

We searched Medline, PubMed, Embase, and PsycINFO from inception to May 2019 to identify studies investigating the QoL of ART-treated sub-Saharan African HIV patients. Non-

database sources including GreyNet and the international AIDS conference archives were searched for abstracts, presentations and unpublished articles. The following concepts were tailored for each database: HIV/AIDS, ART, quality of life and sub-Saharan Africa. The search query for Medline is available in the supplementary material (Supplementary Table 1), and others from HS. All citations found through searches were stored on RefWorks (ProQuest, Michigan, USA). Search results were tracked and managed using an Excel workbook designed for this purpose (14).

### **Study Selection**

Two authors (HS, PE) independently screened all titles/abstracts. Prior to screening, the authors reviewed a random sample of 76 titles/abstracts to assess interrater reliability (Cohen's kappa [standard error] = 0.86 [0.076]) (15). Disagreements were resolved by consensus. Subsequently, full texts of relevant studies were reviewed independently (HS, AL) and disagreements were also resolved by consensus.

### **Data collection**

One reviewer (HS) used a standardized data collection form to extract the following data items from each included study: author's name, publication year, country, study design and duration, sample size, population characteristics, ART regimen, QoL instrument, and risk or protective factors whose association with improved or reduced QoL was investigated through an adjusted statistical analysis. We collected all statistically significantly associated ( $p < 0.05$ ) variables. A second reviewer (AL) reviewed the extracted data for errors.

## **Risk of bias assessment**

One reviewer (HS) assessed the likelihood of bias in each included article using National Institutes of Health's 14-item quality assessment tool for observational cohort and cross-sectional studies (16). For each item, possible choices were “yes”, “no” or “other” (i.e. “cannot determine”, “not applicable” or “not reported”). According to the tool, studies were categorized as “good”, “fair” or “poor”, and a second reviewer (AL) reviewed all ratings. Disagreements were resolved by consensus.

## **Results**

From all sources, 795 unduplicated records were identified, and 41 studies met inclusion criteria (Figure 1). Main reasons for exclusion were: ART was not the intervention of interest, risk factors were not investigated, and analyses were not adjusted.

## **Description of studies**

Included studies were published from 2007 to 2019 and conducted in 14 sub-Saharan African countries. Ethiopia (k= 10), Uganda (k= 7), Nigeria (k= 5) and South Africa (k= 5) were the most frequent countries of research. All studies were observational, including 27 (66%) cross-sectional surveys. The total sample size was 18,055. Ten different QoL instruments were used, including WHOQOL, MOS-HIV, 36-Item Short Form Survey (SF-36), EQ-5D, and the HIV/AIDS-Targeted Quality of Life Instrument (HAT-QoL). Moreover, nine studies reported associations with QoL as an overall score while 32 studies assessed associations with specific domains of QoL. Study characteristics and main findings are shown in the supplementary material (Supplementary Table 2).

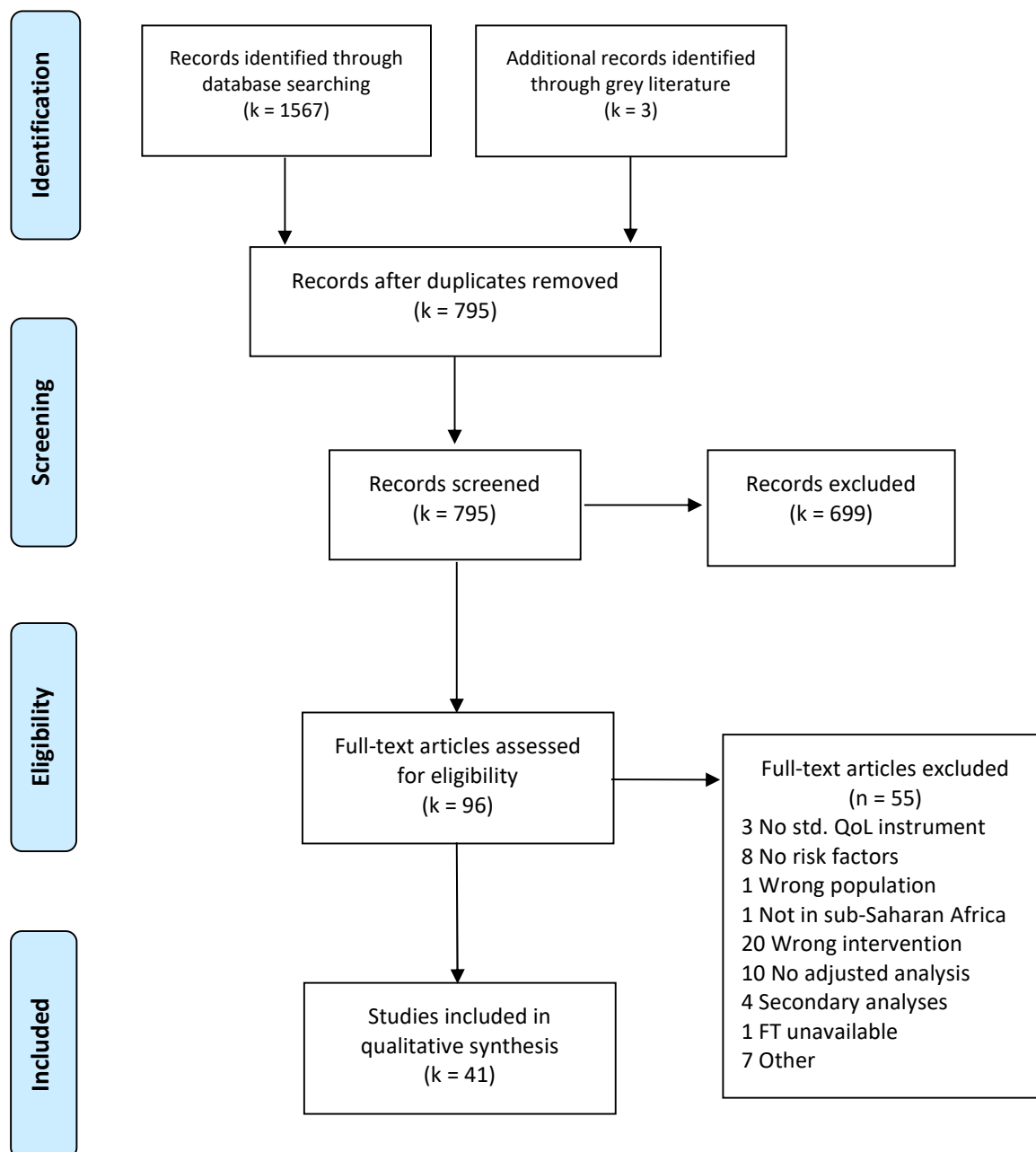


Figure 2. PRISMA flow diagram of the selection process of relevant articles

## **Quality of individual studies**

Twenty-seven studies demonstrated an overall strong internal validity and were rated as good. These studies were conducted based on a robust methodology, and no significant flaws in the conduct of the study or the statistical analyses were identified. Twelve studies were rated as fair, as they presented one or several weaknesses increasing the risk of bias such as the method of selection of participants or confounding. Lastly, six studies overall were rated as poor because of a high risk of bias, notably in the statistical analyses or in the methodology related to the measure of the risk factors or the measurement of QoL.

## **Heterogeneity across studies**

When assessing heterogeneity across studies, we found several differences in the methods. Ten different instruments were used across studies to measure QoL and this diversity may impact the overall joint evidence since QoL domains vary across instruments. For example, MOS-HIV is always summarized into two domains (physical and mental health summaries) for analyses purposes, while WHOQOL-HIV is more comprehensive and measures six domains (physical, psychological, level of independence, social relationships, environment, spirituality/religion/personal beliefs). Lastly, both generic and disease-specific instruments were used across studies. On one hand, generic instruments assess QoL changes resulting from overall clinical features and they are designed for use across different patient populations. On the other hand, disease-specific instruments are generally more sensitive and better designed to measure QoL variations related to specific disease characteristics (17).

Table 4. Factors associated with quality of life identified in 41 studies.

Characteristic	Number of studies reporting an association with quality of life*
<b>Sociodemographic Factors</b>	
Age	16
Employment/Income/SES	14
Education Level	10
Gender	10
Social/Family Support	9
Marital Status	7
Region/Residence (Urban/Rural)/Type of clinic	6
Food security/Diet diversity	6
Knowledge of partner's HIV status/Disclosure of status	4
High risk sexual behavior/Sexual activity/Number of partners	4
BMI/Body fat redistribution/Abdominal obesity	3
Stigma	3
<b>Clinical Factors</b>	
Depression/Psychological distress/Mental disorder/PTSD	13
CD4 Count	9
WHO Stage	7
Symptoms	5
Health Status/Illness (self-evaluated)/Hospitalization	4
Baseline QoL/Domain of QoL	4
Tuberculosis	3
Viral Load/Plasma HIV copies	3
NCD/Chronic disease/Comorbidity	3
<b>Treatment-Related Factors</b>	
Treatment Duration/Follow up time	11
ART/Type of regimen	4
Adherence	4
Side Effects/Toxicity	3

\*Overall quality of life or domains of quality of life.

All associations statistically significant at  $p < 0.05$ .

SES: socioeconomic status, BMI: body mass index, PTSD: post-traumatic stress disorder, NCD: non-communicable disease,

ART: antiretroviral therapy, QoL: quality of life.

## Factors associated with QoL

Factors associated with QoL were grouped into three categories: sociodemographic, clinical and therapy-related factors. Only one study did not find any statistically significant association between risk factors and QoL (44). Table 1 shows the frequency of studies reporting

statistically significant associations between QoL and risk or protective factors, after adjustment. A summary of these factors and their positive or negative impact on QoL is found in table 2.

### **Sociodemographic factors**

Age was the most frequently reported factor: most studies found that older age was associated with poorer QoL (27,28,35), especially the physical domain (19,33,41,45,49). Level of education was also frequently reported. Specifically, QoL was higher when patients were literate or educated (23,26,44), and when patients had reached a secondary level of education or higher (18,33,41). Being employed or having a regular or high source of income were associated with higher QoL (28,34,37), specifically the physical, mental, psychological, and social domains (19,23,24,27,41). Women experienced poorer QoL in the physical, mental, and social relationships domains (19,32,39,56). Regarding marital status, higher scores were measured in married patients or patients cohabiting with or having a stable partner (21,33,35). Similarly, receiving social or family support was associated with higher QoL scores (23,24,33,34,41,44,51). Residing in a rural area was associated with poor QoL (18,23,34). There was a consensus that food security increased QoL scores (39,41,57). Also, malnutrition (24,33) and poor diet diversity (22) were associated with lower scores. Findings for the association between body mass index and QoL were inconsistent based on the three studies investigating this factor. Patients with abdominal obesity (21) or underweight (23) had poorer physical scores whereas being overweight increased mental scores (41). Knowledge of the partner's HIV status or disclosure of one's own status were associated with better QoL (18,21,32). Stigma negatively affected psychological and mental domains of QoL (33,34,57), and so did a high-risk sexual behavior (35,53) or having more than one sexual partner (27).

### **Clinical factors**

A higher CD4 count (54), more specifically, a count above 200 cells/mm<sup>3</sup> (32,42,46,50), or 350 cells/mm<sup>3</sup> (21) was associated with higher QoL scores. Mental health factors such as depressive disorders (29,40,52,54,57) psychological distress (28), mental disorder (37) or post-traumatic stress disorder (53) were associated with lower QoL scores. Patients with less severe WHO clinical staging scored higher in most QoL domains (25,32,42), but mainly in the physical domain (33,54). Poorer physical scores were measured in symptomatic patients (19,57). Tuberculosis (TB) co-infection was found to have a negative association with physical (23,32) and psychological (33) scores. Several studies reported the association of higher viral load with lower QoL (48,54). An increase in physical and mental health summary scores at follow-up was measured in patients who had lower baseline QoL scores (45,49).

### **Therapy-related factors**

The effect of treatment duration or follow up time on quality of life was extensively studied. All eleven studies measuring this association reported that longer treatment duration or follow up time was associated with higher QoL scores. Moreover, being on ART was associated with higher QoL scores (18,35,47), while treatment-related side effects or toxicity was negatively associated with both physical and mental domains of QoL (34,41,48,49). Unsurprisingly, four studies found that adherence to treatment was associated with improved QoL (27,34,36,46).

## Factors associated with QoL in studies of “good” quality

We stratified our results according to our assessment of the quality of individual studies (Supplementary Table 2). When evaluating factors associated with QoL in studies rated as “good”, we found that being on ART and being employed were most frequently reported. Age, gender and depression were also found to be main factors associated with overall or domains of QoL. A comparison of our findings in prospective cohorts with those in cross-sectional studies did not indicate any marked trends. However, more factors, especially sociodemographic, were investigated in cross-sectional studies. Reasons for this trend were unclear but it is possible that longitudinal studies focused on detecting changes or developments in specific variables of interest, which would make analyses of other factors less meaningful.

Table 5. Risk and protective factors associated with higher or lower quality of life.

Factors associated with higher QoL	Factors associated with lower QoL
Higher education	Older age
Being employed/higher SES	Being a woman
Being married/cohabiting	Residing in a rural area
Receiving social or family support	Food insecurity/malnutrition/poor diet diversity
Being treated in an NGO	Stigma
Knowing partner's HIV status/disclosing own status	High-risk sexual behavior/high number of partners
Higher CD4 count	Depression/psychological distress/mental disorder/PTSD
Lower WHO clinical stage	Tuberculosis
Higher baseline QoL scores	Higher viral load
Longer treatment duration or follow up time	Treatment-related side effects or toxicity
Receiving ART	
Adhering to ART	

*QoL: quality of life, NGO: non-governmental organization, ART: antiretroviral therapy, PTSD: post-traumatic stress disorder*

## Discussion

We conducted a systematic review to identify and compile the factors associated with QoL among ART-treated HIV patients in sub-Saharan Africa to address the lack of comprehensive overview on this issue. Our review uncovered multiple factors associated with QoL and we categorized them into three groups: sociodemographic factors, which included age, education, socioeconomic status, gender, marital status and social or family support; clinical factors, which included CD4 count and mental disorder; and treatment-related factors, which included treatment duration and ART treatment. Our findings were based on data from 41 studies carried out in 14 countries, including countries where the number of PLHIV is the highest in the region (i.e. South Africa, Nigeria, Kenya, and Tanzania). The populations included in our review came from various backgrounds and settings. We were able to gather evidence from primarily high-quality studies, and overall, the results presented in our review are reflective of the current literature on the topic.

Sociodemographic risk factors were found to influence QoL more frequently than clinical or treatment-related factors. This was unsurprising considering that it is simple and inexpensive to collect patients' characteristics and it does not require any special equipment or laboratory analyses. As a result, more sociodemographic risk factors were included in our analyses and this may explain why 12 sociodemographic factors were associated with QoL in three or more studies in our review, compared with nine studies for clinical factors and only four for treatment-related factors. Our findings are consistent with results from prior research, notably Degroote's (2014) review of the determinants of QoL among PLHIV in high-income countries (59). This review of the literature included 49 studies mainly conducted in the North America and European countries. The author reported that social and demographic determinants of QoL such

as gender, age, family situation, or employment similarly outnumbered clinical, psychological or behavioral determinants of QoL, even though the authors used more subcategories to summarize the determinants of QoL.

We found both similarities and differences between Degroote's findings in high-income countries and our own results in sub-Saharan Africa. Similarities were that several factors such as ART, depression, stigma or social support have been extensively studied in the literature and they were expected to influence QoL in low- and high-income settings alike. In fact, these factors directly or indirectly influence health outcomes, regardless of the population affected, as reported in Degroote (2014) and confirmed in our review.

The main difference between Degroote's review and ours was that certain determinants of QoL were only relevant in high-income countries, while others only had a significant impact in sub-Saharan Africa. For example, anxiety disorders were associated with lower physical and mental health in high-income countries, but this association was not investigated in any of the 43 studies in our review since screening for anxiety and certain mental health disorders are less common in low-income countries, and those disorders only account for a small fraction of the total burden of illness. Another example is healthy nutrition, which was a determinant of QoL in high-income countries, but not investigated in the studies in our review. In contrast, TB is a common comorbidity among PLHIV in sub-Saharan Africa and it was found to be negatively associated with QoL in three studies in our review. TB was not evaluated in any of the studies included in Degroote's review, as it is not a health priority in high-income countries, even in PLHIV.

Our results also complement findings from a previous systematic review assessing changes in QoL after treatment with antiretroviral drugs in cohort studies worldwide (60). In the

two studies conducted in sub-Saharan Africa in that review (South Africa and Uganda), ART increased PHS and MHS domains of QoL over 1 year, with the greatest increase occurring at 12 and 16 weeks, respectively. Of the 15 studies included in our review that found an association between ART or duration of ART and QoL, seven were prospective cohorts. In all cohort studies but one, treatment duration or follow up time (which is a proxy for treatment duration) were at least six months, and a statistically significant association was found between treatment/follow up duration and overall (22), physical (32,39,57) and mental (31) domains of QoL. This confirms that ART is one of the most significant factors affecting QoL over time and its immediate start after diagnosis remains one of the most reliable ways to improve patients' QoL.

Our systematic review had several strengths. First, our focus on the sub-Saharan experience provides essential data that have not been summarized before in this region despite the severity of the epidemic and the high prevalence and incidence rates. As shown in our review, numerous studies assessing the QoL of ART-treated HIV patients were conducted in sub-Saharan Africa in the last five years and a summary of their findings was overdue to inform stakeholders and provide relevant evidence to guide decision making. Second, we identified and reported risk factors associated with QoL that were not previously described. Specifically, characteristics pertinent to low-income countries such as food insecurity or TB emerged as factors influencing QoL.

Our review also had limitations. First, multiple instruments were used to measure QoL, and although all were standardized and previously validated, their diversity implies a certain heterogeneity when combining results across studies. Some measures provided by instruments such as MOS-HIV are summarized into physical and mental domains of QoL, while other instruments assess as many as nine different domains (e.g. Functional Assessment of HIV

Infection [FAHI] or SF-36). However, the impact of this heterogeneity is limited since this review did not specifically seek to assess how individual domains of QoL were influenced by various factors. Second, we included studies published from 2007 to 2019 and during this long timespan, access to ART considerably increased in sub-Saharan Africa. It is likely that the factors reported by PLHIV in the late 2000s vary from those reported in the late 2010s because of the difference in the availability of treatment during those two periods (61). Finally, sample sizes varied across studies and it is likely that chances of detecting statistically significant associations between certain factors and QoL were increased with larger sample sizes. Further exploration is warranted to assess how this issue affect our findings.

## **Conclusion**

The QoL of ART-treated PLHIV in sub-Saharan Africa is mainly driven by sociodemographic, clinical and treatment-related risk factors similar to those affecting the QoL of PLHIV in the rest of the world. Yet, risk factors still rampant in poor- and middle-income countries such as TB and food insecurity have a non-negligible impact and should be monitored closely.

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## Appendix

Supplementary Table 1. Search terms for Medline (May 7, 2019).

	Search Term	Number of Hits
1	HIV-1/ or HIV-2/ or HIV/ or HIV Seropositivity/	665
2	hiv infections/ or acquired immunodeficiency syndrome/	
3	(hiv or aids).ti,ab,kw.	
4	1 or 2 or 3	
5	"Quality of Life"/	
6	("Quality of Life" or QOL or HRQoL or "Health-related quality of life").ti,ab,kw.	
7	5 or 6	
8	africa/ or "africa south of the sahara"/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or south sudan/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/	
9	(Angola or benin or botswana or burkina faso or burundi or cameroon or cape verde or "central african republic" or chad or congo or "cote d'ivoire" or djibouti or eritrea or ethiopia or gabon or gambia or ghana or guinea or kenya or lesotho or liberia or malawi or mali or mauritania or mozambique or namibia or niger or nigeria or rwanda or senegal or "sierra leone" or somalia or saharan or sudan or swaziland or tanzania or togo or uganda or zambia or Zimbabwe).ti,ab,kw.	
10	8 or 9	
11	4 and 7 and 10	

Supplementary Table 2. Characteristics and key findings of 41 articles included in the narrative review.

Author, Year Country	Study Design, Follow-up time or dates, Sample Size	Age Gender	First Line Regimen, Treatment duration	Population Description	Setting	QoL Instrument	Factors associated with overall or domains of QoL
Risk of Bias Rating: “Good” – Prospective Cohort							
Sackey, 2018 Ghana	6 mos. follow up N=152	$\bar{x}$ 40 yrs. 84.1% women	ART >6 mos.	45.7% married. 82.2% employed.	Multicenter (six district hospitals in Accra)	EQ-5D*	<b>Food security, high diet diversity, longer follow up time</b> (higher)  PHS: Lower <b>education level</b> , probable <b>depression</b> and higher <b>WHO stage</b> (lower). MHS: Female <b>gender</b> (lower). <b>Study visit</b> (6 mos.) (higher) GPGI: <b>Alcohol consumption</b> , lower <b>education level</b> , probable <b>depression</b> (lower)
Mutabazi- Mwesigire, 2015 Uganda	6 mos. follow up N=586	$\geq$ 18 yrs. 66% women	ART Not Reported	60% married. 82% employed. 74% CD4 count 101–350 cells/ $\mu$ L.	Mulago National Referral Hospital.	MOS- HIV <sup>#</sup> , GPGI <sup>s</sup>	<b>Common mental disorder</b> (moderate to very high) (lower physical and mental QoL). No <b>source of income</b> (lower mental QoL)
Deribew, 2013 Ethiopia	6 mos. follow up N=455	$\bar{x}$ 33.4 yrs. 59.4% women	ART Not Reported	88.6% employed. $\bar{x}$ CD4 cell count 383.7 cells/ $\mu$ L.	Jimma, Nekemte and Adama hospitals	WHOQOL- HIV BREF** (Amharic version)	
Weiser, 2012 Uganda	median 2.1 yrs. follow up N=406	median 35 yrs. 72% women	ART median 13.9 mos.	43.6% married. 30.3% unemployed. Median CD4 cell count 197.5 cells/ $\mu$ L.	Uganda AIDS Rural Treatment Outcomes (UARTO). Regional Referral Hospital Immune Suppression Syndrome (ISS) Clinic	MOS-HIV	PHS: Severe <b>food insecurity</b> , increasing <b>age</b> , female <b>gender</b> , being <b>married</b> (lower). Increased <b>duration of ART</b> (higher)
Wouters, 2009 South Africa	24 mos. follow up N=268	$\bar{x}$ 37.9 yrs. 65.3% women	ART Treatment naive	100% CD4 < 200 cells/ $\mu$ L and/or WHO stage IV. 47.8% some secondary education.	Public-sector ART programme in the Free State Province	EQ-5D	After 12 mos. of ART: physical and emotional QoL: <b>CD4 count, viral load, treatment outcome</b> (higher). <b>Adverse effects</b> (lower). Physical QoL: <b>emotional QoL (higher)</b> . After 24 mos. of ART: physical and emotional QoL: <b>CD4 count, viral load, treatment outcome</b> (higher). Physical QoL: <b>emotional QoL</b> (higher)
Stangl, 2007 Uganda	12 mos. follow up N=947	$\bar{x}$ 38.7 yrs. 75% women	HAART Treatment naive	35.2% married or cohabiting. 53.5% primary education. $\bar{x}$ CD4 cell count	Home-based AIDS Care Project.	MOS-HIV	PHS: increased <b>time on HAART</b> , higher <b>CD4 cell count</b> , and <b>religion</b> (Protestant) (higher). <b>Source of income</b> (being dependent), higher

124.1 cells/μl

**depression** scores, **WHO stage** III-IV (lower).  
MHS: increased **time on HAART**, higher **CD4 cell count**, and **religion** (Protestant) (higher). **Source of income** (being dependent), higher **depression** scores and increased **plasma HIV-1 copies** (lower).

Risk of Bias Rating: “Good” – Cross-sectional							
Yaya, 2019 Togo	May-Aug 2016 N=880	$\bar{x}$ 39.6 yrs. 78.4% women	90.5% on ART Not Reported	51.7% living in couple. 17.6% no formal education. 71.7% CD4 count >350 cells/mm <sup>3</sup> .	Multicenter. Centrale and Kara regions	WHOQOL- HIV BREF	<b>Education level</b> (secondary and higher), <b>health region</b> (Kara), <b>ART</b> , <b>knowledge of partner's HIV status</b> (good global QoL).  PHS: regular source of <b>income</b> , zidovudine-based <b>regimen</b> (higher). Having <b>symptoms</b> , female <b>gender</b> , <b>age</b> above 40 y, inability to <b>cope</b> with HIV, lopinavir/ritonavir-based <b>regimen</b> (lower) MHS: Inability to <b>cope</b> with HIV, presence of any <b>symptom</b> , presence of <b>pain</b> , <b>types of ART regimen</b> (lower).
Etenyi, 2018 Kenya	Dec 2015-May 2016 N=501	range 36-45 yrs. 69.5% women	Tenofovir- based or Zidovudine- based >6 mos.	52.6% married. 46.7% secondary education level.	Kenyatta National Hospital Comprehensive Care Center	MOS-HIV	Elevated <b>depressive</b> scores (lower).  PHS: currently <b>married</b> (higher). <b>CD4 counts</b> <350 <b>cells/μL</b> , <b>abdominal obesity</b> , <b>physically inactive</b> or <b>hypertensive</b> (lower). MHS: currently <b>married</b> (higher). <b>Did not disclose HIV+ serostatus</b> , <b>abdominal obesity</b> , <b>tobacco users</b> (lower). In both genders: <b>education</b> (illiterate) (I, SR, E), <b>occupation</b> (unemployed) (P, PSY, SR, E), <b>undernutrition</b> (BMI < 18.5 kg/m <sup>2</sup> ) (male: P, I, E; female: P, PSY, I, E), <b>depression</b> (all domains), <b>tuberculosis</b> (male: all domains except E and SRPB; female: all domains except SRPB), <b>anemia</b> (male: P, PSY, E; female: P, PSY, I, E) and no <b>family support</b> (male: PSY, SR, SRPB; female: P, PSY, SR, SRPB) (lower). In females: <b>rural residence</b> (male: PSY, SR, SRPB; female: P, PSY, SR, SRPB) (lower).
Nyongesa, 2018 Kenya	Nov 2016-Mar 2017 N=84	$\bar{x}$ 40.1 yrs. 78.6% women	ART Not Reported	56% married. No more than primary level of education.	Comprehensive Care and Research Clinic	RAND SF- 36 <sup>##</sup>	
Biraguma, 2018 Rwanda	Nov 2014-June 2015 N=794	$\bar{x}$ 38 yrs. 64.6% women	87.9% on ART Not Reported	63.9% married. 59.9% primary education level. 67.4% lived in urban area.	Multicenter (Kigali City, Southern and Eastern provinces)	MOS-HIV	
Gebremichael, 2018 Ethiopia	Apr-May 2016 N=505	$\bar{x}$ 36.2 yrs. 50.3% women	ART Median 46 mos.	74.1% males / 62.2% females married. 92.0% males / 77.2% females employed.	Public health facilities in West shoa Zone	WHOQOL- HIV BREF	
Surur, 2017 Ethiopia	Apr-May 2014 N=400	60.8% ≥ 30 yrs.	HAART Not Reported	42.8% married. 35.5% secondary education. 44.5%	Gondar University	WHOQOL- HIV BREF	<b>Gender</b> (PSY, SRPB), <b>age</b> (PSY), <b>residence</b> (I), <b>educational status</b> (SR, E), <b>marital status</b> (E), and

		54.7% women		CD4 count $\geq 500$ cells/mm <sup>3</sup> .	Referral Hospital	(Amharic version)	<b>WHO stage</b> (all domains).  Older <b>age</b> (I, SR, E, SRPB), being <b>married</b> (P, SR), being <b>unemployed</b> (P, PSY, E, SRPB), <b>poor health status</b> (all domains), <b>coping with life</b> by contacting a person with ART (S), <b>no self-education on HIV</b> (all domains), <b>missing <math>\geq 1</math> appointment</b> (P, I, SR), <b>missing ART <math>\geq 1</math> time in the last 2 days</b> (PSY, E), <b>not understanding circumcision prevents HIV</b> (all domains except PSY), <b>not being aware of the multiple concurrent partnership program</b> (P, PSY, I), <b>having sex with <math>\geq 1</math> partner</b> (P, PSY, SRPB), <b>not discussing condom with the sex partner or not having a partner</b> (SR) (lower). <b>No coping experience</b> (I, SRPB) (higher).
Ndubuka, 2017 Botswana	Apr 2012-Not Reported N=456	$\bar{x}$ 43.9 yrs. 68% women	HAART >5 yrs.	17.5% married. 45% employed. 77.7% CD4 count $\geq 350$ cells/mm <sup>3</sup> . 98.2% full viral suppression.	Six ART clinics in southeastern Botswana	WHOQOL-HIV BREF	<b>Depression with pain comorbidity</b> (P, PSY, E) (lower).  Male <b>gender</b> (SR), secondary/or tertiary <b>education</b> (E), being <b>married or cohabiting</b> (SR), <b>a government health center facility</b> (SR), <b>social support</b> (SR, SRPB), <b>obtaining sufficient food with nutritional value</b> (all domains except SRPB), having the <b>opportunity to find or maintain a job</b> (all domains except SR), the <b>possibility to share common resources with other people</b> (PSY, E) (higher). Increased <b>age</b> (P, SR, I), <b>TB</b> (PSY), <b>being bed ridden</b> (P, SRPB, I), <b>WHO clinical stage IV</b> (P, SR), <b>depressive symptoms</b> (all domains), <b>stigma</b> (all domains except P), <b>worrying about the consequences of HIV disclosure</b> (SRPB), <b>worrying about taking care of family when passed away</b> (P, SRPB, I) (lower). No psychosocial <b>support outside family</b> (women: P, SR; men: P), <b>WHO stage I-III</b> (women: SRPB), <b>illiteracy</b> (women and men: P, SR), <b>rural residence</b> (women: PSY, I, E), no psychosocial <b>support from family/friends</b> (women: PSY, SR), high perceived
Mwesiga, 2015 Uganda	Sept-Dec 2013 N=345	median 35 yrs. 71.2% women	83.8% on HAART Not Reported	44.6% married. 40.6% secondary education level. CD4 count $\bar{x}$ 537 cells/mm <sup>3</sup> .	Mildmay Uganda care center	WHOQOL-BREF	
Mekuria, 2015 Ethiopia	Sept 2012-Apr 2013 N=664	$\bar{x}$ 37.6 yrs. 63.6% women	Nevirapine-based or Efavirenz-based Mean 26 mos.	52.1% married or cohabiting. 50.3% work full time. $\bar{x}$ CD4 count 150 cells/ $\mu$ L.	Ten healthcare facilities	WHOQOL-HIV BREF (Amharic version)	
Tesfay, 2015 Ethiopia	Feb-Apr 2012 N=494	women: $\bar{x}$ 35.5 yrs. men: $\bar{x}$ 39.8 yrs. 50.6% women	HAART Mean 44 mos.	32% women, 59% men married. 71.2% women, 95.1% men employed. Median CD4 cell counts: women: 366 cells/mm <sup>3</sup> ,	Five health institutions in Mekelle	WHOQOL-HIV BREF (Tigrigna version)	

men: 296 cells/mm<sup>3</sup>.

Mûnene, 2014 Kenya	Feb-Apr 2013 N=392	$\bar{x}$ 41.4 yrs. 68.9% women	HAART Median 4.5 yrs.	42.3% married. 50.3% paid employment.	Nyeri Provincial General Hospital	+SF-36	<b>stigma</b> (women: PSY; men: all domains except SR and E), younger <b>age</b> (women: SR), <b>family size</b> $\leq 2$ (women: SRPB; men: E), recent <b>side effect</b> (women: I), <b>non-adherence</b> (men: E, SRPB), being <b>unmarried</b> (men: SR) (lower). $\geq$ average <b>monthly income</b> (women: P, SR, E; men: I, SR), <b>&lt;36 mos. on ART</b> (women: P, SR), <b>&lt;36 mos. since diagnosis</b> (women: E), lower <b>WHO stage</b> (men: all domains except SR and SRPB) (higher) Aggregated PCS and MCS: <b>age, gender, religion, occupation, clinical symptoms, chronic illnesses, adherence, and duration on ART</b> .
Olisah, 2011 Nigeria	Sept-Dec 2006 N=310	$\bar{x}$ 35.5 yrs. 68.4% women	ART Mean 17.7 mos.	52.9% married. 38.7% unemployed. 14.2% depressive disorder.	Ahmadu Bello University Teaching Hospital	WHOQOL-BREF	<b>Depressive disorder</b> (all domains except E) (lower).
Boyer, 2012 Cameroon	Sept 2006-Mar 2007 N=1985	$\bar{x}$ 38.5 yrs. 70.7% women	ART >6 mos.	22.6% married. $\bar{x}$ CD4 count at ART initiation 137.7 cells/ml.	EVAL– French National Agency for Research on AIDS and Hepatitis (ANRS). 27 hospitals	MOS-SF-12	PCS: Increasing <b>age, financial difficulties</b> paying for HIV biological monitoring in the previous 3 mos., <b>living below the poverty line, BMI</b> $\leq 18.5$ kg/m <sup>2</sup> , <b>CD4 count</b> <100 cells/ $\mu$ l, <b>hospitalization</b> during the previous 6 mos., experience of <b>AIDS-defining events, side-effects</b> during the previous 4 weeks (lower). Female <b>gender</b> , university <b>educational level</b> (higher). MCS: Semi-urban <b>area of residence, financial difficulties</b> paying for HIV biological monitoring in the previous 3 mos., <b>living below the poverty line, side-effects</b> during the previous 4 weeks (lower). Increasing <b>age, being a homeowner</b> , always having at least <b>two meals per day, BMI</b> >25 kg/m <sup>2</sup> and strong <b>moral support</b> (higher).
Fan, 2011 Malawi	Sept 2005 N=267	$\bar{x}$ 37.8 yrs. 72.7% women	HAART Not Reported	48.3% married. 87.4% employed. 48% CD4 count <200 cells/mm <sup>3</sup> (AIDS).	Rainbow HIV Clinic	%MOS-SF-36	<b>WHO stage</b> III-IV (V, MH) (lower). AIDS ( <b>CD4 count</b> <200 cells/mm <sup>3</sup> ) (PF, BP, PCS) (lower).
Abera, 2010 Ethiopia	Aug-Oct 2007 N=422	$\bar{x}$ 32.3 yrs. 56.4% women	HAART >3 mos.	38.4% married. 41% employed.	Yirgalem, Hawassa and Shashemene hospitals	SF-36 (Amharic version)	<b>Duration of treatment</b> >12 mos. (RP, RE), <b>CD4 cell count</b> >200 cells/mm <sup>3</sup> (BP, VT, RE), <b>adherence to doses</b> of HAART (PHS), and <b>adherence to schedules</b> of HAART (all domains except VT) (higher).
Patel, 2009 Zimbabwe	June-Aug 2007 N=96	$\bar{x}$ 38.5 yrs. 100% women	ART Mean 14.8	35.4% married. 39.6% unemployed. $\bar{x}$ CD4 count	Chitungwiza Regional Hospital	MOS-HIV	<b>ART</b> (overall score, MHS) (higher).

Magafu, 2009 Tanzania	May 2007 N=329	mean 40.9 yrs. 66% women	mos. HAART >6 mos.	148.9 cells/mm <sup>3</sup> . 33.1% married. 7.3% unemployed.	Kagera regional hospital	SF-36 (Swahili version)	<b>Chronic diseases</b> comorbidity (MHS, PHS) (lower).
Bajunirwe, 2009 Uganda	Apr-Dec 2006 N=330	≥18 yrs. 67.2% women	ART >6 mos.	43.6% married. 20.3% CD4 cell count <200 cells/mm <sup>3</sup> .	Kitagata and Mbarara hospitals	MOS-HIV (Lunyankole version)	PHS: <b>CD4 count</b> ≥200 cells/mm <sup>3</sup> , informational <b>social support</b> (higher). MHS: past or recent <b>alcohol</b> use (lower).
Jong, 2016 Tanzania	Aug-Sept 2015 N=163	$\bar{x}$ 41 yrs. 76% women	91.4% on ART Not Reported	69.9% did not work for pay. $\bar{x}$ CD4 count 276.9 cells/mm <sup>3</sup> .	Six HIV clinics	MOS-SF-12	Gender ( <b>male</b> ), high <b>social capital</b> (higher).
Mweemba, 2008 Zambia	Not Reported N=160	$\bar{x}$ 36.5 yrs. 83.6% women	86.9% on ART Not Reported	40.6% married. 46.9% employed. $\bar{x}$ CD4 count 358 cells/μL.	Two rural and two urban antiretroviral clinics	WHOQOL-HIV	Younger <b>age</b> (SRPB), being <b>asymptomatic</b> (SRPB) (higher).
Risk of Bias Rating: "Fair" – Prospective Cohort							
Alemayehu, 2018 Ethiopia	6 mos. follow up N=439	$\bar{x}$ 36.4 yrs. 61.7% women	Efavirenz-based or Nevirapen-based or Other >6 mos.	14.1% unemployed. Median CD4 count 419 cells/μL.	Abdrafi Health center, Metema Hospital, Humera Hospital, University of Gondar Hospital	WHOQOL-HIV BREF (Amharic version)	No source of <b>income</b> (PSY, SR, I, E), no <b>social support</b> (all domains except SRPB), <b>severe acute malnutrition</b> (all domains except E) (lower).
Wubshet, 2014 Ethiopia	12 mos. follow up N=487	median 31 yrs. 57.7% women	ART Treatment naive	44% married. 41.5% employed. Median CD4 cell count 93 cells/μL.	University of Gondar Teaching Hospital, Gondar Health Center, Azezo Health Center	WHOQOL-HIV BREF (Amharic version)	<b>Follow up time</b> (PSY, P), <b>male</b> gender (P, overall), <b>disclosure of HIV status</b> (PSY, SR), <b>CD4 count</b> ≥200 cells/mm <sup>3</sup> (P, I, SR, E, overall), <b>WHO stage III-IV</b> (all domains except P and E), <b>good baseline QoL</b> (all domains) (higher). <b>Tuberculosis</b> co-infection (P, overall) (lower). PHS: Increased <b>age</b> , increased <b>symptom index</b> score, <b>depression</b> , <b>food insecurity</b> , internalized and enacted <b>stigma</b> (lower). Increased <b>follow up time</b> (higher).
Takada, 2012 Uganda	median 2.1 yrs. follow up N=422	$\bar{x}$ 34 yrs. 71% women	HAART Treatment naive	44% married. 85% primary education or more. CD4 count median 203 cells/mm <sup>3</sup> .	Mbarara Regional Referral Hospital	MOS-HIV	MHS: Increased <b>symptom index</b> score, <b>depression</b> , <b>unemployment</b> , <b>food insecurity</b> , internalized and enacted <b>stigma</b> (lower). Increased <b>follow up time</b> (higher).
Alibhai, 2010 Uganda	12 mos. follow up N=130	median 35 yrs. 62% women	Nevirapine-based or Efavirenz-based	42% married. 65% employed. Median CD4 cell count 144 cells/mm <sup>3</sup> .	Community-based antiretroviral treatment	MOS-HIV (Rutooro version)	PHS: Lower <b>baseline PHS scores</b> , younger <b>age</b> (higher). MHS: Lower <b>baseline MHS scores</b> , younger <b>age</b> (higher).

~12 mos.

(CBART)  
program.

## Risk of Bias Rating: “Fair” – Cross-sectional

Oladeji, 2017 Nigeria	March-Aug 2011 N=828	$\bar{x}$ 41.3 yrs. 71% women	90% on HAART Not Reported ART	57.4% married. 58.7% at least elementary school.	University College Hospital, Ibadan Starting ART Late (LSTART). Six secondary-level urban hospitals in Oromia State	WHOQOL-HIV BREF	<b>Suicidal behavior</b> (all domains) (lower)
Vo, 2016 Ethiopia	June 2012-Apr 2013 N=1180	median 34 yrs. 61% women	Male: median 33 mos. Female: median 160 mos.	65% men, 46% women married. 72% less than secondary education levels.		<sup>^</sup> HAT-QOL	<b>Psychological distress</b> (mild, high), <b>unemployment</b> , late <b>ART</b> initiation, being a man between the <b>ages of 30–39 yrs.</b> (vs. $\leq 29$ ), being a man reporting the last <b>sexual encounter</b> occurring in the previous 3 mos. to 1 year (vs. in the past 30 days) (lower).
Asangbeh, 2015 Cameroon	Sept-Nov 2013 N=202	$\geq 21$ yrs. NR	ART Not Reported		Mbengwi district hospital	WHOQOL-BREF	<b>Depressive symptoms</b> (lower).
McInerney, 2008 South Africa	Not Reported N=149	$\bar{x}$ 35.5 yrs. 64% women	ART Mean 4 mos.	34.3% married. 42% employed.	Clinics in Durban	MOS-SF-36 (English and isiZulu versions)	Physical function: Fewer <b>comorbid medical problems</b> , <b>social support</b> , a greater length of <b>time on ART</b> (higher).
Adewuya, 2008 Nigeria	Not Reported N=87	$\geq 18$ yrs. 56.3% women	ART Mean 29 mos.	23% married. 41.4% low socioeconomic status.	Living Hope Care center	WHOQOL-BREF	<b>Depressive disorder</b> (all domains except SR), <b>gender</b> (SR), and <b>presence of medical problems</b> (P, PSY) (lower). Highest <b>educational level</b> (all domains except SR), <b>perceived level of social support</b> (P, SR, overall), number of <b>dependent</b> (P), <b>age</b> (PSY, overall), <b>socioeconomic status</b> (E, overall) (higher)
Olley, 2008 Nigeria	Not Reported N=56	$\bar{x}$ 36.5 yrs. 53% women	HAART Not Reported	55% married. $\bar{x}$ 12 yrs. of education.	Nigerian Air Force Hospital	MOS-HIV-30	<b>PTSD</b> (PF, MF, RF, SF, HP), number of <b>negative life events</b> (PF, MF), <b>age</b> (PF), number of <b>symptoms</b> (PF), <b>risky sexual practices</b> (P)

## Risk of Bias Rating: “Poor” – Prospective Cohorts

Parcesepe, 2018 Ethiopia	Not Reported (Secondary Analysis) N=722	$\geq 18$ yrs. 100% women	ART Treatment naive	50.4% currently in relationship. 60.9% ever attended school.	LSTART. Six HIV clinics in the Oromia region	HAT-QoL	<b>Education</b> (never attended school) (overall function) (lower)
Tomita, 2014 South Africa	maximum 9 yrs. follow up N=51	$\bar{x}$ 25.9 yrs. 100% women	ART Treatment naive	75% married or stable partnership. 54.9% at least grades 11 or 12 of schooling. $\bar{x}$ CD4 count	CAPRISA 002 ART Cohort.	<sup>ss</sup> FAHI	<b>ART</b> (overall, PWB, EWB, SWB), <b>being married/having a stable partner</b> (overall, PWB, FGWB, CF) (higher). <b>Age 21–24y and 40–59y</b> (SWB), being <b>single</b>

				488 cells/mm <sup>3</sup> .			(overall, FGWB, CF), <b>high-risk peno-vaginal sex act</b> (SWB) (lower).
Bhargava, 2010 South Africa	6 mos. follow up N=102	$\bar{x}$ 38.5 yrs. 65.5% women	ART Mean 67.4 days Nevirapine-based or Efavirenz-based Treatment naive	$\bar{x}$ CD4 count 181.5 cells/mm <sup>3</sup> .	16 public clinics	EQ-5D	Increased yrs. of <b>education, emotional support</b> , increased <b>CD4 count</b> (higher).
Pitt, 2009 South Africa	48 weeks follow up N=295	$\bar{x}$ 34 yrs. 74% women		Median CD4 count 88 cells/mm <sup>3</sup> .	Hannan Crusaid Treatment Centre	MOS-SF-36	PHS: after 48 weeks, higher <b>pre-HAART scores</b> , baseline <b>viral load</b> $\leq 5.0$ log copies/ml, older <b>age</b> , <b>drug toxicity</b> (lower). MHS: after 48 weeks, higher <b>pre-HAART scores</b> (lower).
Risk of Bias Rating: "Poor" – Cross-sectional							
Ogbuji, 2010 Nigeria	2004-2007 N=514	mean 34.8 yrs. 65.5% women	ART Not Reported	54.1% married. 60.7% employed.	Three HIV care support centers	&QOLS	No statistically significant associations found

QoL = quality of life; HRQOL = health-related quality of life; NGO = non-governmental organization; PTSD = post-traumatic stress disorder

**\*\*WHOQOL-HIV** (Domains: Physical = P, Psychological = PSY, Level of Independence = I, Social Relationships = SR, Environment = E, Spirituality/Religion/Personal Beliefs = SRPB). **#MOS-HIV** = Medical Outcomes Study-HIV. **%MOS-SF-36** = Medical Outcomes Survey Short Form 36 (Physical functioning = PF, Role limitation due to physical problems = RP, Role limitation due to emotional problems = RE, Vitality = V, Mental health = MH, Social functioning = SF, Bodily pain = BP, General health = GH, Physical component summary = PCS, Mental component summary = MCS). **##RAND SF-36** = RAND 36-Item Short Form Survey. **\*EQ-5D** = EuroQol Five Dimensions Questionnaire. EQ-5D-3L = EuroQoL Five Dimensions Three-level. **^HAT-QOL** = HIV/AIDS-Targeted Quality of Life (Overall function = OF, life satisfaction = LS, health worries = HW, financial worries = FW, medication worries = MW, HIV mastery = HIVM, disclosure worries = DW, provider trust = PT, sexual function = SF). **\$GPGI** = Global Person Generated Index. **\$\$FAHI** = Functional Assessment of HIV Infection (Physical well-being = PWB, emotional well-being = EWB, functional/global well-being = FGWB, social well-being = SWB, cognitive functioning = CF). **+SF-36** = 36-Item Short-Form Health Survey (Bodily pain = BP, general health = GH, mental health = MH, physical function = PF, limitation in role due to emotions = RE, limitation in role due to physical health = RP, social function = SF, vitality = VT, physical health summary = PHS, mental health summary = MHS). **&QOLS** = Quality of Life Scale

## **JOURNAL ARTICLE 2**

**Drivers of Quality of Life Among HIV Patients Treated with Antiretroviral Therapy at a Community Health Clinic in Togo: A Cross-Sectional Survey.**

**Journal of the International AIDS Society**

## **Abstract**

**Introduction:** Few studies have investigated the factors associated with the physical and mental domains of quality of life (QoL) among HIV patients in western and central Africa, and none in Lomé, Togo. The objective of this study was to assess the QoL of adult HIV patients of a community health clinic with a strong social support component in Lomé and identify factors associated with QoL in this population.

**Methods:** A cross-sectional study was conducted at Espoir Vie Togo in July and August 2019 with 147 consecutive adult HIV patients receiving long-term antiretroviral therapy. QoL was assessed using the medical outcome study-HIV health survey (MOS-HIV). We identified risk and protective factors associated with physical health summary (PHS) and mental health summary (MHS) scores using multiple linear regression analyses with stepwise model selection.

**Results:** Mean (SD) PHS and MHS scores were 80.7 (13.9) and 66.7 (11.1), respectively. Younger age, male gender, food security, the absence of treatment-related side effects, and self-evaluated “excellent or very good” health status were significantly associated with higher PHS scores. Male gender, a higher education level, food security, family or social support and self-evaluated “excellent or very good” and “good” health status were significantly associated with higher MHS scores.

**Conclusions:** Patients treated at the clinic had an overall high QoL, which was associated with socio-demographics risk factors also found in other studies in western and central Africa. Our findings suggest that community health clinics with a strong social component positively impact the QoL of people living with HIV in western and central Africa.

## Introduction

The life expectancy of HIV patients who initiate antiretroviral therapy (ART) early and adhere to treatment has increased substantially in the last decade [1,2]. AIDS-related mortality decreased by 42% from 2004 to 2017 in eastern and southern Africa, and by 24% in western and central Africa [3]. As a result, HIV prevalence in the WHO Africa region is now steadily increasing [4]. In 2018, an estimated 110,000 people were living with HIV in Togo, of which 72,745 (66.1%) were registered in healthcare facilities, and 64,842 (59%) were receiving life-saving ART [5]. Because of the shift of HIV from a fatal disease to a chronic condition, quality of life (QoL) has emerged as a significant medical outcome in HIV management. Retaining HIV patients in long-term care so they achieve viral suppression is one of the key steps of UNAIDS' 90-90-90 treatment target, yet it remains a major challenge in sub-Saharan Africa [6]. One important way to overcome this challenge is to ensure patients maintain a high QoL as they cope with their disease. Optimizing treatment and care based on the risk factors affecting QoL may lead to an improvement in the overall management of people living with HIV (PLHIV) and ensure they effectively stay in care, remain asymptomatic and no longer transmit the disease.

Few studies investigating the determinants of QoL were conducted in western and central Africa. In Ghana, a prospective cohort of 152 PLHIV showed that food security and high diet diversity were associated with improvements in QoL scores over time [7]. In Nigeria, a cross-sectional study found that depressive disorder, lower socioeconomic status and education level and poor social support were associated with lower QoL scores [8]. Another cross-sectional study in Nigeria reported the association of suicidal behavior with

lower QoL scores [9]. More recently, a study conducted in inland regions of Togo suggested that patients on ART or those with at least a secondary education, or who had disclosed their HIV status or lived in the rural region of Kara in northern Togo, had a significantly higher overall QoL [10]. However, no research has been conducted in Lomé, the Togolese capital and a dynamic, growing urban area. Moreover, no research has been conducted in a community healthcare setting, where patients receive social support such as financial assistance or sponsored meals in addition to long-term care, and are more likely to adhere to treatment because of the clinic's patient-centered approach [11]. The current study was undertaken to assess the QoL of adult ART-treated HIV patients in such a clinic in Lomé, Togo, and identify the risk and protective factors associated with QoL.

## **Methods**

### ***Study Setting and Population***

We conducted a cross-sectional survey at Espoir Vie Togo (EVT) in July and August 2019. EVT is a community health clinic and a non-governmental organization whose mission is to provide treatment and social support to PLHIV in Togo [12]. It currently manages approximately 3,500 patients and has clinics in Lomé, the capital, and in Aného and Sokodé. Study participants were consecutive men and women PLHIV 18 years or older who visited the clinic in July and August 2019. Eligibility criteria were:  $\geq 18$  years, a confirmed HIV diagnosis and currently taking ART. Pregnant women were excluded. Patients were treated with an ART regimen consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) (usually lamivudine [3TC] and tenofovir disoproxil fumarate [TDF]), and one non-

nucleoside reverse transcriptase inhibitor (NNRTI) (usually efavirenz [EFV]) or one protease inhibitor (usually atazanavir or atazanavir/ritonavir).

### **Sample size**

We estimated the sample size based on a fixed model and R-squared increase for linear multiple regression. We assumed a medium population effect size, a power of 80%, a significance level of 5%, and 15 predictors. Using G\*Power software Version 3.1.9.4, a sample size of 140 was generated [13].

### **Data Collection**

The principal investigator (HS), a clinical psychologist (JMAE), and a youth outreach coordinator (EH) interviewed the participants in French using the medical outcome study-HIV health survey (MOS-HIV) before or after the doctor visit. Each survey lasted 10 to 15 minutes. Approximately ten participants were interviewed daily, one at a time, in a private consultation room. Participants were given a 500 CFA (~ US \$0.85) token as reimbursement for travel expenses. Prior to administering the survey, the following characteristics were collected from the medical records: gender, age, CD4 count, viral load, health status, serostatus (symptomatic or asymptomatic), treatment duration, ART regimen, line of treatment, treatment adherence and treatment-related side effects. Participants reported data on their education, employment, marital status, HIV status disclosure, social or family support, and alcohol use. Food insecurity was measured with Kleinman's validated one-item screening question [14]. Body mass index (BMI) was calculated from height and weight measurements taken prior to the interview. Adherence was defined as not missing two

consecutive doctor's appointments and taking all pills in the week preceding an appointment. All data were collected on a password-protected tablet computer.

### **Quality of Life Measure**

The MOS-HIV was used to assess QoL in our study population [15]. The French version of the survey was obtained from Mapi Research Trust (Lyon, France). The MOS-HIV is a disease-specific instrument that has been previously validated in various settings in sub-Saharan Africa [16,17]. It includes 35 items investigating health transition (HT) and 10 dimensions of QoL: general health perceptions (GH), pain (P), physical functioning (PF), role functioning (RF), social functioning (SF), energy/fatigue (EF), mental health (MH), health distress (HD), cognitive functioning (CF), quality of life (QL). Raw scores are computed then transformed to a 0 to 100 scale, with higher scores indicating better QoL.

### **Ethical Approval**

Ethical approval to conduct this study was obtained from the Comité de Bioéthique pour la Recherche en Santé (031/2019/CBRS) in Togo and from the Committee for the Protection of Human Subjects of the University of Texas Health Science Center at Houston (HSC-SPH-19-0357) in the United States. EVT granted their permission and provided logistics support for this study. All participants provided oral informed consent prior to study inclusion.

### **Statistical Analysis**

Descriptive statistics were presented as proportions for categorical variables, and means and standard deviations (SD) for continuous variables. For each participant, a physical health

summary score (PHS) and a mental health summary score (MHS) were generated from the dimensions of QoL. A factor analysis with oblique rotation was performed to obtain factor score coefficients, which were used to compute the PHS and MHS scores [18]. The scores were standardized to a scale with a mean of 50 and standard deviation of 10. These standardized PHS and MHS scores were used as the dependent variables in two separate regression analyses. Cronbach's alpha coefficients were calculated for dimensions with more than one item to measure the internal consistency of the questionnaire. An alpha greater than 0.70 was selected to demonstrate adequate reliability and was considered satisfactory for comparisons.

Two multiple linear regression analyses were fitted to determine the factors associated with QoL, one with PHS as the dependent variable, and the other with MHS as the dependent variable. All other measured variables were evaluated as candidate independent variables. Correlations among them were examined for multicollinearity. For each summary score (PHS and MHS), stepwise model selection was performed to determine the subset of variables best defining the relationship between the independent variables and the specific summary score under investigation. The variables included at the start of model selection were the ones found to have a p-value greater than 0.1 upon univariate analysis. The most parsimonious model for each summary score was selected and validated using a training and validation set.  $P < 0.05$  was set as the level of statistical significance. SAS software, Version 9.4 was used for all data analyses [19].

Table 6. Baseline characteristics of 147 HIV patients at Espoir Vie Togo.

Characteristic	N (%) or Mean (SD)
Gender	
Female	108 (73.5)
Male	39 (26.5)
Age (years)	43.2 (11.6)
Education	
None	25 (17)
Primary	48 (32.7)
Secondary	69 (46.9)
University	5 (3.4)
Employment	
Unemployed or retired	32 (21.8)
Employed part time	38 (25.8)
Employed full time	77 (52.4)
Marital status	
Single	26 (17.7)
Married/cohabiting	59 (40.1)
Divorced/separated/widowed	62 (42.2)
BMI (kg/m <sup>2</sup> )	23.8 (5.5)
HIV status disclosure	126 (87.5)
Social/family support	111 (75.5)
Alcohol use	
Never	88 (59.9)
<1/month	39 (26.5)
2-4/month	13 (8.8)
>2-3/week	7 (4.8)
Food insecurity	91 (61.9)
HIV serostatus (n=146)	
Symptomatic	15 (10.3)
Asymptomatic	131 (89.7)
CD4 count (cells/ $\mu$ l)	513.5 (350.2)
Viral load (n=89)	
Undetectable	60 (67.4)
$\leq 40$ copies/ml	6 (6.7)
>40 copies/ml	23 (25.9)
Treatment duration (months) (n=144)	94.3 (60.3)
Art regimen (n=140)	
3TC + TDF + EFV	88 (62.9)
3TC + TDF + ATV or ATVr	37 (26.4)
Other	15 (10.7)
Line of treatment	
1 <sup>st</sup>	34 (24.8)
1 <sup>st</sup> substituted	55 (40.2)
2 <sup>nd</sup>	48 (35)
Adherence	135 (93.8)
Side effects	33 (22.5)
Self-evaluated health status	
Excellent/very good	52 (35.4)
Good	83 (56.5)
Poor/mediocre	12 (8.2)

3TC=lamivudine, TDF=tenofovir, EFV=efavirenz, ATV=atazanavir, ATVr=atazanavir/ritonavir

## Results

Of the 157 patients who were approached for study participation, 147 agreed to participate, yielding a participation rate of 94%. 108 (73.5%) participants were female (Table 1). The mean age (SD) was 43.2 (11.6) years and the mean (SD) duration of treatment was 94.3 (60.3) months. Most patients had disclosed their HIV status to their partner or family (n=126; 87.5%), had family or social support (111; 75.5%), and suffered from food insecurity (91; 61.9%).

Table 7. MOS-HIV dimensions of quality of life for 147 HIV patients at Espoir Vie Togo.

Dimension	Mean (SD) [range]	Cronbach Alpha*
General health	58 (22.6) [10-95]	0.78
Pain	70.3 (23.3) [0-88.9]	0.77
Physical functioning	90.8 (15.1) [25-100]	0.77
Role functioning	88.1 (28.3) [0-100]	0.78
Social functioning	93.2 (16.6) [20-100]	-
Energy/fatigue	61 (14.5) [10-95]	0.77
Mental health	69 (13.9) [20-100]	0.76
Health distress	83.2 (16.9) [30-100]	0.78
Cognitive functioning	80 (15.3) [30-100]	0.79
Quality of life	49 (21.9) [0-100]	-
Health transition	57.7 (22.6) [0-100]	-
PHS	80.7 (13.9) [28.3-96.8]	
MHS	66.7 (11.1) [30.7-87]	

\*Cronbach's alpha coefficients were calculated for dimensions with more than one item.

Raw scores were transformed to a 0 to 100 scale.

PHS: physical health summary score; MHS: mental health summary score.

### *Quality of Life Scores*

The mean (SD) PHS and MHS scores were 80.7 (13.9) and 66.7 (11.1), respectively. The scores were relatively high on a 0-100 scale, and indicated an overall good QoL in the patient population. Table 2 shows the mean, SD and range for all the dimensions of the

MOS-HIV survey. The internal consistency of the survey was high. The Cronbach's alphas of the multi-item scales were adequate: GH (0.78), P (0.77), PF (0.77), RF (0.78), EF (0.77), MH (0.76), HD (0.78), CF (0.79).

### ***Factors Associated with Quality of Life***

For PHS, age, gender, food insecurity, ART adherence, side effects and self-evaluated health status were retained in the final model (Table 3). This subset of predictors explained 21% of the variance in PHS ( $R^2 = 0.21$ ). More specifically, lower PHS scores were associated with increasing age ( $p=0.01$ ) and female gender ( $p=0.02$ ), whereas higher PHS scores were associated with food security ( $p=0.045$ ), not experiencing treatment-related side effects ( $p=0.03$ ), and having an “excellent or very good” health status ( $p=0.003$ ). For MHS, gender, education, food insecurity, ART adherence, family or social support and self-evaluated health status were retained in the final model, which explained 30% of the variance in MHS ( $R^2 = 0.30$ ). Lower MHS scores were associated with female gender ( $p=0.02$ ), having a primary level of education ( $p=0.05$ ) and not having family or social support ( $p=0.006$ ). On the other hand, higher MHS scores were associated with food security ( $p<0.0001$ ), having an “excellent or very good” health status ( $p=0.001$ ), or a “good” health status ( $p=0.04$ ).

Table 8. Model selection of factors associated with quality of life in 147 HIV patients at Espoir Vie Togo

Variable	PHS	P value	MHS	P value
	$\rho$ (95% CI) ( $\times 10^3$ ) R <sup>2</sup> =0.21		$\rho$ (95% CI) ( $\times 10^3$ ) R <sup>2</sup> =0.30	
Intercept	140.26 (60.17, 220.35)	<0.001	3.36 (2.04, 4.69)	<0.001
Age (years)	-1.01 (-1.82, -0.21)	0.014		
Gender (female)	-25.33 (-46.40, -4.26)	0.019	-0.41 (-0.75, -0.074)	0.018
Food security	19.68 (0.42, 38.94)	0.045	0.61 (0.32, 0.91)	<0.001
Adherence	-25.31 (-63.23, 12.61)	0.189	-0.43 (-1.02, 0.16)	0.156
Side effects (absent)	26.87, 3.29, 50.44)	0.026		
Health status (ref. Poor or mediocre)				
Excellent or very good	58.51 (20.28, 96.73)	0.003	0.95 (0.37, 1.53)	0.001
Good	33.19 (-2.19, 68.56)	0.066	0.58 (0.028, 1.12)	0.040
Education (ref. University)				
None			-0.48 (-1.33, 0.36)	0.260
Primary			-0.80 (-1.59, -0.0005)	0.049
Secondary			-0.41 (-1.18, 0.37)	0.300
Social/family support			-0.46 (-0.78, -0.14)	0.006

PHS: physical health summary score, MHS: mental health summary score,  $\rho$ : regression coefficient, ref.: reference group

## Discussion

This cross-sectional study investigated the QoL of 147 ART-treated adult PLHIV in a community health clinic in Lomé, Togo. We measured relatively high PHS and MHS scores among patients treated at the clinic. Significant associations between physical and mental health summary scores and age, gender, education, food security, treatment-related side effects and self-evaluated health status were found.

Physical and mental domains of QoL measured in the EVT population were relatively higher than those observed in previous comparable studies (i.e. studies conducted in sub-Saharan Africa and using the MOS-HIV survey). Etenyi (2018) investigated a Kenyan outpatient population and reported PHS and MHS scores ranges between 60.14 (tenofovir regimen) and 61.9 (zidovudine regimen) and 51.3 and 51.83, respectively [20]. Biraguma

(2018) measured PHS scores of 63.96 and MHS scores of 53.43 in a Rwandan patient population treated at public health centers [21]. It is likely that QoL scores in our population were higher because EVT is a medical center that supports its patients socially in addition to providing treatment in the long term. In fact, many patients receive clinic-sponsored meals the day of their doctor visit, while others receive financial assistance for their education or to pursue training opportunities. In addition, patients participate in a “causerie” (French for “informal talk”) prior to seeing the doctor and collecting their prescriptions. The “causerie” is a social worker-animated informal group talk providing patients with general disease information and coping mechanisms to help maintain their overall well-being in good state. All these patient-oriented elements lead to higher quality of care and better patient-provider relationship, which ultimately contribute to better patient outcomes and higher QoL, as suggested by a previous cross-sectional study [11].

As expected, several socio-demographic factors influenced the QoL of EVT patients. Age and gender, two well-known determinants of health, [22,23] were associated with PHS (age), and both PHS and MHS (gender). This confirms findings from previous research in western and central Africa [24,25]. Among HIV patients across 27 hospitals in Cameroon, Boyer (2012) reported lower physical component scores (PCS) but higher mental component scores (MCS) with increasing age, after adjusting for other socio-demographic and treatment-related covariates. Thus, age was established as a major driver of QoL, as anticipated. The association was positive for MCS, most likely because of the more significant role social support plays in adolescents’ and young adults’ lives. However, the association was negative for PCS, possibly because of physical senescence. When examining research in eastern

Africa, similar trends were observed [26-28]. In a Ugandan prospective cohort study, Mutabazi-Mwesigire (2015) reported that female gender was associated with lower MHS scores after adjustment [26]. In a cohort study also conducted in Uganda, Weiser (2012) reported lower PHS score in women treated at a regional referral hospital [27]. Although no specific explanation for these negative associations was reported in both studies, previous research has suggested that lower QoL measured in women may be attributable to gender differences in the reporting of psychological illnesses and somatic complaints [29,30].

Unsurprisingly, food insecurity was negatively associated with mental and physical health. This is predictable in sub-Saharan Africa, where it continues to be a daily concern for millions of people. One of the reasons explaining this association is the exacerbation of side effects caused by the lack of food to accompany ART [31]. This directly impacts the health outcomes and QoL of HIV patients who skip meals to afford their medication or do not adhere to treatment because of the lack of food. Our findings are similar to results from previous research in Ghana, Ethiopia and Uganda, where decreased QoL scores were measured in patients reporting food insecurity [32-34]. In a cross-sectional study of 664 HIV patients in Ethiopia, Mekuria (2015) specifically found that being able to obtain food with sufficient nutritional value was key to increasing physical, psychological, social, independence and environmental domains of QoL scores [33].

Our study had several strengths. We investigated QoL in a region not well studied before and we provided insight on the QoL of adult PLHIV receiving ART in a patient-oriented community clinic in Lomé. Moreover, we included a wide range of independent variables in our analysis and assessed pertinent factors such as food insecurity and treatment-

related side effects. Also, using a linear regression with model selection allowed us to control for confounding variables and select the variables best explaining the relationship between physical and mental domains of QoL and several risk or protective factors. This study also had limitations. The cross-sectional design limited our ability to establish a temporal relationship between the dependent and independent variables. Additionally, although the use of trained investigators instead of a self-administration approach to administer the MOS-HIV questionnaire was necessary due the lack of reading ability for several patients, it may have caused patients to inflate the positivity of their responses. As a result, QoL scores may have been overestimated due to social desirability bias. Also, our study was conducted in one community clinic in Lomé therefore our findings may not be generalizable to different settings.

Overall, the social support provided by the clinic in addition to treatment is likely to positively impact patients' QoL and overall wellbeing [11]. Future research should be extended to pediatric populations and potentially focus on comparing treatment satisfaction in patients treated in public hospitals and those treated in community health clinics.

## **Conclusion**

This study suggests that PLHIV treated at a patient-oriented community health clinic in Lomé, Togo, had high physical health summary scores and moderately high mental health summary scores, as assessed by the MOS-HIV health survey. Age, gender, education, food security, treatment-related side effects and self-evaluated health status were significantly associated with physical and mental health summary scores in this population. Sustained care

in a community health clinic, where the factors influencing QoL are also addressed during patient management, is key to ensure long-term viral suppression in PLHIV in Togo.

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### **JOURNAL ARTICLE 3**

**Impact of Long-Term Care on the Quality of Life of HIV Patients in a Community Health Clinic in Togo: A Qualitative Study.**

**AIDS and Behavior**

## **Abstract**

Qualitative assessments of the quality of life (QoL) of HIV patients treated with antiretroviral therapy (ART) in western and central Africa are few in comparison to those in other parts of sub-Saharan Africa, Europe, and North America. Yet, valuable information can be discovered from patients' individual experiences that can identify new variables not included in typical surveys. We interviewed 12 HIV patients receiving long-term ART at Espoir Vie Togo, a community health clinic providing social support, during July and August 2019. All interviews were recorded, transcribed, and analyzed using a thematic analysis. Participants described good QoL as being in good health and being physically and mentally functional. Family, social and community support, the presence of a supporting individual, being on ART and food security were the main factors influencing QoL. In this cohort, participants experienced difficulties accepting their positive status, and often experienced perceived and enacted stigma. Ultimately, the positive effects of long-term care led participants to become more "responsible" and better cope with their disease.

## **Introduction**

The prevalence of people living with HIV (PLHIV) in sub-Saharan Africa has risen steadily in the last decade because of the increased access to life-saving antiretroviral therapy (ART) (1). Although the HIV/AIDS epidemic has declined since its peak in 2005, HIV prevalence in sub-Saharan Africa is still the highest in the world, with an estimated 25.6 million PLHIV at the end of 2018 (2). In Togo, a small West African nation with a population of 7.9 million as of 2018, approximately 65,000 people received ART out of an estimated 110,000 PLHIV (3). The country made considerable progress towards limiting the spread of the epidemic, as shown by key indicators: in 2018, approximately 66% PLHIV knew their status, 89% of them received ART and 79% of the 21,000 PLHIV under ART who were able to have their viral load measured had viral suppression (4,5,6). These rates place Togo among the countries closest to reaching the 90-90-90 targets in sub-Saharan Africa, notably because of its small size, and because the epidemic has historically been moderate compared to more affected countries such as South Africa or Uganda. Nevertheless, the country-wide measures taken by health authorities to control the epidemic have been relatively successful so far (3,4). At the patient level, these milestones mean that HIV infection is no longer a death sentence and it is possible for newly infected individuals who initiate ART early and adhere to treatment to live a long and productive life (7). In fact, HIV has shifted from a fatal infection to a chronic disease when antiretrovirals became widely available in Togo after the “3 by 5” initiative was launched in 2003 to provide 3 million doses of ART to people living with HIV (PLHIV) in low- and middle-income countries by the end of 2005 (8). One of the challenges in HIV management today despite the

increased access to ART is to ensure patients are sufficiently empowered to adequately cope with their disease. Ideally, HIV patients should be able to maintain high rates of adherence to be virally suppressed over time and no longer transmit the disease (9). To this end, quality of life (QoL) has emerged as a significant follow-up outcome aiming at mitigating the challenges associated with lifelong treatment such as sustained adherence and economic difficulties (10).

Several studies have investigated QoL among PLHIV across sub-Saharan Africa to determine the factors associated with QoL and to capture individual life experiences (11,12,13). Specifically, several public health studies in western and central Africa have taken a qualitative approach and given voice to HIV patients to deeply understand their experience (14-17). In Cameroon, Alomepe (2016) interviewed women living with HIV and described the challenges they faced. The emerging themes included the trauma of discovering one's status, the difficulties of living with HIV, the lack of resource and support, and stigma (14). In addition to their illness, these issues affected their ability to perform their central role in their family. In a qualitative study conducted in Ethiopia, Alemayehu (2017) described the main aspects affecting QoL in visceral leishmaniasis and HIV coinfecting males: liveability of the environment, utility of life, life ability of a person and appreciation of life (16). The study highlighted the multidimensional nature of QoL and the importance of starting specific programs to address these issues. In another qualitative study of newly infected patients conducted in Nigeria, Ogbuji (2010) found that psychological factors such as sadness, hopelessness, anxiety and fear were widely reported by PLHIV as negative

factors influencing QoL, although certain life adjustments and psychological support allowed to better cope with the disease (17).

Among factors affecting the QoL of PLHIV, stigma is frequently cited as one of the most enduring, despite general knowledge of the positive effects of ART on curbing the HIV epidemic (18). Several types of stigma have been described, including enacted and perceived stigma, both strongly acting as barriers to coping with the disease. Enacted stigma includes acts of discrimination and negative treatment from external sources towards PLHIV. Perceived stigma is the awareness and fear of being perceived negatively in society because of one's HIV status, causing the avoidance of social experiences and opportunities (18). Previous research has indicated that perceived stigma has a negative impact on overall QoL, but it may vary according individual contexts and different settings (19).

The World Health Organization describes QoL as an “individual perception”, and individual experiences vary according to social, cultural and religious contexts. Receiving sustained treatment also strongly influence individual experiences because of its strong and durable positive effects on the mental and physical health of HIV patients (20,21). There is more to learn about subjective factors associated with QoL shaped by personal, cultural or social experiences that are unique to each patient, especially in the context of a community health clinic, where patients are long-term ART recipients and experience strong social support in addition to receiving treatment (22). In such a population, certain underlying factors other than traditional socio-demographic and treatment-related factors significantly influence patients' QoL and general wellbeing. Therefore, the objective of this study was to understand patients' definitions of QoL, identify and gain additional knowledge on

underlying and undiscovered indicators of quality of life, and better understand the life experiences of HIV patients receiving long-term ART in a community health clinic in Togo.

## **Methods**

### ***Study Setting and Population***

We conducted 12 semi-structured interviews of six female and six male patients receiving long-term ART in July and August 2019 at Espoir Vie Togo (EVT), a community health clinic and non-governmental organization treating and providing social support to HIV patients in Togo. EVT currently manages approximately 3,500 patients and has clinics in Lomé, the capital, and in Aného and Sokodé (22). Consecutive patients of the outpatient clinic in Lomé were asked to participate in the study prior to their doctor visit and participants received a 500 CFA (~ US \$0.85) token as reimbursement for travel expenses. Eligibility criteria to participate in the study were being 18 years or older, having a confirmed HIV diagnosis and currently receiving ART for more than six months.

### ***Data Collection***

Face-to-face individual interviews were designed to give participants the opportunity to discuss their perceptions of QoL and factors influencing their QoL. The primary investigator (HS), assisted by a clinical psychologist with qualitative interview experience (JMAA), conducted the interviews, which took place in a private consultation room. All interviews were held in French, the official language and first language of most participants, and lasted approximately 15 minutes. The interviews were recorded on a digital audio

recorder. Written notes were also taken by the study investigator during the discussion. All participants agreed to be recorded.

Prior to starting the interview, the following characteristics were collected from the patient's medical record: age, CD4 count, treatment duration, line of treatment, and adherence. Gender, education level, employment, marital status, HIV status disclosure, food insecurity and social or family support were self-reported. Adherence was defined as not missing two consecutive doctor's appointments and taking all of one's pills in the week preceding an appointment. Food insecurity was measured with Kleinman's validated one-item screening question (23).

Based on an interview guide developed specifically for this study, the study investigator used a series of open-ended questions to encourage participants to share their experience and describe how their lives were affected by HIV (interview guide available from HS). The questions prompted participants to share their definition of QoL and describe their perceived determinants of QoL. The discussion was kept relatively informal to let participants engage in a conversation rather than in a question-answer session. This approach also encouraged participants to give honest answers.

### ***Data Analysis***

All interviews were transcribed and translated from French to English. We used pseudonyms throughout the study when quoting participants to maintain anonymity. Data analysis was performed using OpenCode version 4.0 (24). Data were analyzed following a thematic analysis. English transcripts were read multiple times to become familiar with the

content. The primary investigator (HS) used an open coding approach to capture the participants' perception of QoL. After coding several transcripts, a set of codes was defined and subsequently used for similar recurring concepts. Additional codes were incorporated into the analytical framework as they were identified in subsequent transcripts. Several themes emerged and were examined at the latent level: the investigator sought to detect underlying ideas and concepts by analyzing patients' words beyond what was said verbatim during the interviews. All themes were reviewed by an experience researcher who did not take part in the interviews (SM).

### ***Ethical Approval***

Ethical approval for this study was obtained from the Comité de Bioéthique pour la Recherche en Santé (031/2019/CBRS) in Togo, and from the University of Texas Health Science Center at Houston's Committee for the Protection of Human Subjects (HSC-SPH-19-0357) in the United States. Prior to study inclusion, all participants were read a script describing the study before providing oral informed consent.

### **Results**

Twelve participants (6 women, 6 men) were enrolled in the study. All patients who were approached for study participation agreed to participate. The mean age was 32.6 years, and the majority had at least a secondary level of education and were single (Table 1). The mean duration of treatment was 96 months, and six participants were on their second line of treatment. All participants were adhering to treatment according to the study definition.

### ***Definition of a good quality of life***

Most participants described QoL as a combination of intertwined factors that resulted in a good QoL when all were functioning well. David told us: “To have a good quality of life is to be able to do any activity that would be expected of you. In other words, having the power to go about your business as usual without any constraints” (interview 1, David, 23 years old). When specific features were discussed, “being in good health” was repeatedly mentioned as the main, if not the sole definition. Good QoL was also defined as overall wellbeing and being functional at the physical and mental levels. Justine mentioned that a good QoL was conditional on taking ART, thus acknowledging the importance of the role played by medications in improving symptoms and overall wellbeing (interview 3, Justine, 18 years old). Kossi shared a different perspective on the definition of QoL that was outside of the usual scales: in his opinion, good QoL was about being free of problems, which negatively affected his mental health and prevented him from focusing on the important things in his life (interview 10, Kossi, 19 years old).

Table 9. Baseline Characteristics of 12 HIV Patients at Espoir Vie Togo.

Characteristic	N (%) or Mean (SD)
Gender	
Female	6 (50)
Male	6 (50)
Age (years)	32.6 (14.8)
Education	
Primary	1 (8.3)
Secondary	9 (75)
University	2 (16.7)
Employment	
Unemployed	7 (58.3)
Employed	5 (41.7)
Marital Status	
Single	8 (66.7)
Married/Cohabiting	2 (16.7)
Divorced/Separated	2 (16.7)
HIV Status Disclosure	11 (91.7)
Food Insecurity	8 (66.7)
Line of Treatment	
First	3 (30)
First Substituted	1 (10)
Second	6 (60)
Adherence	12 (100)
Family or Social Support	9 (75)
Treatment Duration (months) (n=11)	96 (84.1)
CD4 (cells/ $\mu$ L) (n=11)	613.9 (347.9)

### ***Determinants of QoL***

Living with HIV is challenging and imposes many constraints but for patients receiving long-term ART, general health improvements related to medication intake allow patients to focus more on their quality of life, and less on their health. At EVT, patients receive free treatment and are followed by psychologists, and this relieves part of the concerns related to being able to afford the therapy. Patients described the factors that improved or deteriorated their quality of life. For example, the support received by family

and friends helped several patients cope with their disease. David described the positive influence he received from some members of his family after discovering he was HIV positive: “In my family, only my brothers and my sister knew my status. They were always watching after me, they always gave me advice. When I tried to break certain rules, they helped me get back on track.” Additionally, the medical and social support provided by EVT and its community played an important part in successfully managing the disease, as Grace stated: “I pray every day for EVT to continue their work because they work so well. They give us advice, they give us food” (interview 2, Grace, 44 years old).

Sometimes, it was a specific person who played a key role in a patient’s ability to successfully cope with the disease. Friends and family members are often cited as supporting groups, but it could be a single individual who made a difference in this patient’s life. Leila said: “I have a friend (not a boyfriend), who knew my illness from the beginning. He is the first person I told. He really supported me. When he talks to me, I forget that I am sick” (interview 5, Leila, 40 years old).

The benefits of taking ART was mentioned during several interviews. Because our population was long-term ART recipients, patients were maintained on stable regimens and they have had the opportunity to discuss and address potential side effects with the doctor. Kossi said: “Before taking ART, I got sick very often, but now, I only get sick once or twice in a three-month period.” Referring to his height, he added: “I even grew taller.” (interview 10, Kossi, 19 years old).

Food insecurity and the toxicity associated with taking ART without a meal were significant problems for low income patients and young adults. Many patients were aware of the

possible consequences on treatment adherence. Linda reported: “I know that taking the treatment keeps me in good health. But taking the treatment means I must eat too, and if I don’t, there will be side effects. So sometimes, if I know I won’t eat, I won’t take my medications because of the side effects” (interview 4, Linda, 23 years old).

Participants mainly described factors that contributed to improve their QoL such as family or social support and being under life-saving treatment. Because patients were receiving treatment for over 6 months and were on good health, they did not spontaneously think of negative factors, however, risk factors negatively associated with QoL were also discussed. Stigma is an enduring concern for PLHIV and it was brought up often enough during the interviews to emerge as a theme.

### ***Experiencing enacted and perceived stigma***

Study participants from both genders clearly understood the negative toll HIV had on their lives and they were able to easily communicate on their experiences. Several participants stated that they were negatively affected by the lack of awareness in the general population and they complained they were systematically judged and stigmatized although they were receiving ART and their disease was perfectly under control. Enacted stigma refers to acts of discrimination and negative treatment from external sources towards PLHIV. It was usually experienced outside of the close circle of friends or family knowing the participant’s HIV status. Perceived stigma originated within participants and they felt it when misinformation about HIV was circulated and they feared they would be treated negatively if their status was disclosed. Ousmane said: “Here’s the difference between you and an HIV

negative person: sometimes, you cannot even stay among your friends because you may not feel well and be afraid people discover you have HIV” (interview 12, Ousmane, 50 years old).

Like Ousmane, several participants indicated they had to hide their status to avoid stigma, discriminations or insults. Moreover, some participants said they were ashamed of their disease. Participants acknowledged it was harder to make platonic or romantic connections because of their status and perceived stigma, and their fear of rejection and enacted stigma. For example, Joel revealed: “I’m afraid sometimes to have romantic relationships, while an HIV negative person can live his life fully as he wants.” (interview 11, Joel, 18 years old). The lack of sexual partner was also brought up by Grace, who knew her status deteriorated her intimacy: “since I’ve had HIV, I do not make love anymore and it bothers me. When I find a partner, he tells me he does not want to use a condom so I have to refuse because I do not want that” (interview 2, Grace, 44 years old).

Despite being under long-term treatment and having their disease under control, many participants are paralyzed by perceived stigma and fear the upsetting effects of enacted stigma. Some participants admitted they had lost friends or family because perceived and enacted stigma led them to avoid situations in which they could be shamed, some chose to stay away from people and preferred to be solitary. The desire to avoid stigma was so strong it led some to being abstinent, which some also described as being more “responsible” as we see in the next theme.

### ***Becoming more “responsible”***

Being infected with HIV unexpectedly uncovered optimistic reactions and feelings of responsibility among several patients over time. In fact, some participants mentioned that they developed an increase in responsibility because of their disease, while others experienced a positive change in their behavior after being diagnosed and starting ART.

Edem reflected on his past life and offered a powerful statement:

Before my diagnosis, I lived a life not quite as one wishes, I had unprotected sex, I had multiple partners, I drank a lot of alcohol, and I smoked too. After the diagnosis, I stopped having unprotected sex and being with multiple partners. I no longer smoke or drink. I would tell a newly infected person to get tested, to follow the advice of doctors, to take the medication every day and at the times indicated, to eat well, and to protect himself during each intercourse.” (interview 9, Edem, 59 years old).

This radical change in behavior was not infrequent in our population. At many occasions, being responsible vis-à-vis taking medications, and being responsible by adopting a healthier behavior was how participants chose to deal with their disease after several months under treatment. Speaking about the disease, Ousmane said: “You have to live with it. Live your life! Follow the advice of doctors, take your medicine in time, and you'll be happy like any other man. There are people damaging their own health because they tell themselves “I'm a sick person” (interview 12, Ousmane, 50 years old). It is likely that the patients in our study who become responsible and adopted positive attitudes were only able to do so because their disease were well-controlled and no longer represented the main concern in their daily lives.

### ***Grief and difficulties of status acceptance***

Although maintaining good physical health was no longer a barrier for performing daily activities for participants in our sample of long-term care receivers, we collected a few testimonials that reflected persistent emotional distress and a feeling of grief for a way of living that was lost. In fact, Ousmane confessed that the hardest thing for him was the quest he pursued after discovering his positive status. He absolutely wanted to know how he became infected and after several months of unsuccessful attempts to discover what happened, he found peace only when he decided to let go and move on:

At first, I tried to find out where it came from, but I could not find the answer.

People warned me it could drive me crazy to absolutely want to know how it happened. Later, I understood it was true. I was devastated for a while, but I knew I had to give up to move forward, so this is my spirit now. (interview 12, Ousmane, 50 years old).

This feeling of grief was similar to what other patients experienced, as they struggled to accept and live with their newly discovered positive status. Kossi believed that one's own perception of the disease determined their QoL, whether it was good or bad, so it was preferable to accept one's condition and look forward: "often we, HIV patients, demean ourselves, and society does nothing but repeat the way we treat ourselves" (interview 10, Kossi, 19 years old). Marie also experienced difficulties when she discovered her status and saw her life change abruptly. She recalled: "I did not go out anymore. I was afraid to be sick so I stayed at home. I was crying and I did not have any friends anymore" (interview 6,

Marie, 48 years old). These experiences show the emotional difficulties of discovering one's positive status, and they suggest many participants have personal struggles before finding much needed support, sometimes through family and loyal friends, but often in community clinics like EVT.

## **Discussion**

We investigated the life experiences and perceptions of QoL of twelve HIV patients receiving long-term ART in a community health clinic in Lomé, Togo. Participants defined good QoL as being in good health and being functional at a physical and mental level. The main factors influencing QoL were family, social and community support, the presence of a supporting individual, being on ART and food insecurity. The positive effects of long-term care often transformed patients and allowed some of them to become responsible vis-à-vis their disease. However, prior to developing positive attitudes over time, participants first experienced personal difficulties related to their newly discovered positive status, and they continue to face stigma, even after overcoming their personal struggles.

Overall, our findings diverged from Ogbuji's (2010), who reported predominantly negative feelings and experiences in a qualitative study of newly diagnosed HIV patients in Nigeria (17). In Ogbuji's study, many participants reported that HIV was a punishment for their previous careless lifestyle, others were overwhelmed by discrimination, stigmatization and feelings of embarrassment. A few patients went as far as contemplating suicide. We note that Ogbuji's research involved newly diagnosed patients while our study population included long-term ART recipients. Although it is difficult to make meaningful comparisons,

our findings suggest that life experiences and QoL are likely to improve over time because of the positive effects of sustained antiretroviral treatment. Hence, Ogbuji's population illustrated patients' overall health impairment at the early stage of the disease whereas our population exemplified a possible positive evolution after several months of treatment. The better health outcomes and positive transformation of patients over time in our sample can also be attributed to the overall positive impact of EVT's disease management strategy during patient follow up. In fact, the clinic has a very strong social component and its team of psychologists support patients in their daily needs (22).

Our study confirms previous research suggesting experiences of enacted and perceived stigma are main concerns for patients and negatively affect QoL and overall wellbeing among PLHIV. In a mixed sample of patients, health personnel and care providers, Adedimeji (2010) reported that perceived stigma contributed to the non-disclosure of one's status (15). Patients preferred limiting the disclosure of status to their close friends and family, and they sought treatment in places where they could remain anonymous. Women were disproportionally affected, as described by Alomepe (2016). They faced enacted stigma from their communities and even their families, because of the false perception that women with HIV engaged in immoral activities (14). In addition, they felt powerless as they lost their preponderant role as a pillar of society, as it is often the case for women in the sub-Saharan African culture. Similar experiences with perceived stigma were described in our study because regardless of the setting, HIV patients felt powerless in front of an issue coming from external sources and driven by negative perception of the disease. Adedimeji's study was conducted 10 years ago, when ART was not as generalized in sub-Saharan Africa

as it is today. In the early 2010s, the general population still negatively perceived people living with HIV due to the lack of awareness, and it seems this trend is perduring today although it is unclear to what extent.

Our findings are in accordance with those reported in Uganda by Mutabazi-Mwesigire (2014), who conducted in-depth interviews at three and six months follow up with patients in an urban clinic as part of a prospective cohort study (25). The author reported that happiness was a strong indicator of good QoL and it was supported by good social networks and family. Happiness, and more generally, appreciation of life, reflected the positive attitude HIV patients can adopt to face their condition and improve their QoL, especially when they have been treated with ART for a long period of time. Although happiness was not specifically named in our study, many factors mentioned by our interviewees were proxies, specifically mental wellbeing.

Several determinants of QoL described in this study were seldom investigated in previous research. Feelings of responsibility and the lack of sexual intercourse or the lack of sexual partner are often overlooked when considering HIV patients' overall wellbeing, yet, those features were found to hinder several participants' ability to feel whole. Additionally, family and social support are often cited as significant factors positively affecting QoL, but we noted that only one person can sometimes make a difference in a patient's life and provide sufficient support when needed, especially if the patient and the confident were close prior to the disease, or if the person in need prefers to not disclose their status to other people and remain discreet.

It was not surprising that food insecurity was discussed by interviewees in our study, considering that it continues to be a major issue in developing countries. In Togo, an estimated 69% of households were living below the poverty line in 2015 (26). Food insecurity is thought to exacerbate ART-related side effects, and its effects on decreasing adherence to treatment in resource-limited settings have been previously demonstrated (27,28). Musumari (2013) reported on the negative impact of food insecurity on adherence among patients on ART, on ART-retreatment and those ultimately lost to follow-up. This issue was significant enough for UNAIDS to recommend stakeholders to associate food assistance programs to ART programs (29).

Our study had several strengths. All participants who were approached for study participation agreed to participate, limiting selection bias. Also, because all participants agreed to be recorded, the content of the interviews was accurately transcribed, and it allowed the analysis to be based on complete and detailed material, supported by written notes. This study also had limitations. We interviewed patients who were followed up in a community health clinic providing social support, and we anticipated their overall wellbeing and QoL to be better than patients cared for in public hospitals. Also, the mean treatment duration of 96 months in our population indicates that our results are not applicable to newly-diagnosed HIV patients. Finally, our sessions lasted approximately 15 minutes, which was relatively brief to conduct in-depth interviews.

## **Conclusion**

This study assessed HIV patients receiving long-term care at a community health clinic with a strong social support component in Lomé, Togo, to better understand patients' definitions of QoL, how HIV impacted their lives, and define the factors influencing QoL from their perspective. Despite the early difficulties and enacted and perceived stigma experienced by HIV patients, ART and other sociodemographic factors can improve their overall wellbeing and QoL over time.

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## CONCLUSION

We carried out this dissertation to synthesize current knowledge on the factors associated with QoL among ART-treated HIV patients in sub-Saharan Africa, and identify novel factors associated with QoL to provide foundations for the optimization of HIV care, based on the sociodemographic, clinical, behavioral, and psychological determinants of QoL. Our long-term goal was to provide robust evidence to help improve the overall management of people living with HIV.

This dissertation confirmed the significant impact of certain factors associated with QoL such as ART, age, education level, gender, CD4 count, and mental health, but also encountered pertinent factors such as food insecurity, tuberculosis, and the lack of sexual partner. We highlighted several themes patients experience when coping with their disease such as experiencing enacted and perceived stigma, becoming more “responsible”, and facing difficulties accepting HIV status.

One of the strengths of this dissertation was the focus on the sub-Saharan African experience, a severely affected region, where essential summary data on the factors associated with QoL was lacking. We chose to support our research with robust evidence collected from a systematic review and direct our efforts towards discovering new information collected in real-world settings. On the other hand, this dissertation was limited by its lack of generalizability. In fact, Togolese HIV patients treated at a community health clinic are not representative of PLHIV in sub-Saharan Africa. This dissertation was also

limited by the small number of patients' testimonies in our interviews which limited our ability to gain further insight on the life experience of HIV patients in this setting.

Nevertheless, we are confident that this dissertation addressed current gaps in knowledge and opened the door to future research. We reported that the QoL scores of HIV patients treated at a community health clinic in Togo were relatively higher compared to equivalent studies in Kenya and Rwanda. Future research may be conducted to attempt a comparative analysis evaluating the QoL and treatment satisfaction of patients treated at Espoir Vie Togo, or other non-governmental organizations, versus patients treated at a public healthcare facility, which lack the social support component provided at Espoir Vie Togo and similar facilities. Furthermore, additional research may be conducted on certain factors influencing QoL reported in our interviews to assess whether they are quantitatively associated.

## APPENDICES

### Appendix A: Ovid Medline Search Strategy

1. HIV-2/ or HIV/ or HIV Seropositivity/ or HIV-1/
2. hiv infections/ or acquired immunodeficiency syndrome/
3. (hiv or aids).ti,ab,kw.
4. 1 or 2 or 3
5. "Quality of Life"/
6. ("Quality of Life" or QOL or HRQoL or "Health-related quality of life").ti,ab,kw."
7. 5 or 6
8. africa/ or "africa south of the sahara"/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or south sudan/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
9. (Angola or benin or botswana or burkina faso or burundi or cameroon or cape verde or "central african republic" or chad or congo or "cote d'ivoire" or djibouti or eritrea or ethiopia or gabon or gambia or ghana or guinea or kenya or lesotho or liberia or malawi or mali or mauritania or mozambique or namibia or niger or nigeria or rwanda or senegal or "sierra leone" or somalia or saharan or sudan or swaziland or tanzania or togo or uganda or zambia or Zimbabwe).ti,ab,kw.
10. 8 or 9
11. 4 and 7 and 10

## Appendix B: PubMed Search Strategy

1. (HIV-2[mesh] or HIV[mesh] or HIV Seropositivity[mesh] or HIV-1[mesh]) OR (hiv infections[mesh] or acquired immunodeficiency syndrome[mesh]) OR (hiv[tiab] or aids[tiab])
2. ("Quality of Life"[mesh]) OR ("Quality of Life"[tiab] or QOL[tiab] or HRQoL[tiab] or "Health-related quality of life"[tiab])
3. (africa[mesh] or "africa south of the sahara"[mesh] or africa, central[mesh] or cameroon[mesh] or central african republic[mesh] or chad[mesh] or congo[mesh] or "democratic republic of the congo"[mesh] or equatorial guinea[mesh] or gabon[mesh] or africa, eastern[mesh] or burundi[mesh] or djibouti[mesh] or eritrea[mesh] or ethiopia[mesh] or kenya[mesh] or rwanda[mesh] or somalia[mesh] or south sudan[mesh] or sudan[mesh] or tanzania[mesh] or uganda[mesh] or africa, southern[mesh] or angola[mesh] or botswana[mesh] or lesotho[mesh] or malawi[mesh] or mozambique[mesh] or namibia[mesh] or south africa[mesh] or swaziland[mesh] or zambia[mesh] or zimbabwe[mesh] or africa, western[mesh] or benin[mesh] or burkina faso[mesh] or cape verde[mesh] or cote d'ivoire[mesh] or gambia[mesh] or ghana[mesh] or guinea[mesh] or guinea-bissau[mesh] or liberia[mesh] or mali[mesh] or mauritania[mesh] or niger[mesh] or nigeria[mesh] or senegal[mesh] or sierra leone[mesh] or togo[mesh]) OR (Angola[tiab] or benin[tiab] or botswana[tiab] or burkina faso[tiab] or burundi[tiab] or cameroon[tiab] or "cape verde"[tiab] or "central african republic"[tiab] or chad[tiab] or congo[tiab] or "cote d'ivoire"[tiab] or djibouti[tiab] or eritrea[tiab] or ethiopia[tiab] or gabon[tiab] or gambia[tiab] or ghana[tiab] or guinea[tiab] or kenya[tiab] or lesotho[tiab] or liberia[tiab] or malawi[tiab] or mali[tiab] or mauritania[tiab] or mozambique[tiab] or namibia[tiab] or niger[tiab] or nigeria[tiab] or rwanda[tiab] or senegal[tiab] or "sierra leone"[tiab] or somalia[tiab] or saharan[tiab] or sudan[tiab] or swaziland[tiab] or tanzania[tiab] or togo[tiab] or uganda[tiab] or zambia[tiab] or Zimbabwe[tiab])

## Appendix C: Embase Search Strategy

1. (HIV-2 or HIV or HIV Seropositivity or HIV-1) OR (hiv infections or acquired immunodeficiency syndrome) OR hiv.ab,kf,ti. OR aids.ab,kf,ti.
2. Quality of Life.ab,kf,ti. OR QOL or HRQoL OR health-related quality of life
3. 'sub-saharan africa' or 'africa south of the sahara' or africa, central or cameroon or 'central african republic' or chad or congo or 'democratic republic of the congo' or 'equatorial guinea' or gabon or 'africa, eastern' or burundi or djibouti or eritrea or ethiopia or kenya or rwanda or somalia or south sudan or sudan or tanzania or uganda or 'africa, southern' or angola or botswana or lesotho or malawi or mozambique or namibia or south africa or swaziland or zambia or zimbabwe or 'africa, western' or benin or burkina faso or cape verde or cote d ivoire or gambia or ghana or guinea or guinea-bissau or liberia or mali or mauritania or niger or nigeria or senegal or 'sierra leone' or togo

## Appendix D: PsycINFO Search Strategy

1. HIV-2/ or HIV/ or HIV Seropositivity/ or HIV-1/
2. hiv infections/ or acquired immunodeficiency syndrome/
3. (hiv or aids).ti,ab
4. 1 or 2 or 3
5. "Quality of Life"/
6. ("Quality of Life" or QOL or HRQoL or "Health-related quality of life").ti,ab
7. 5 or 6
8. africa/ or "africa south of the sahara"/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or south sudan/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/
9. (Angola or benin or botswana or "burkina faso" or burundi or cameroon or cape verde or "central african republic" or chad or congo or "cote d'ivoire" or djibouti or eritrea or ethiopia or gabon or gambia or ghana or guinea or kenya or lesotho or liberia or malawi or mali or mauritania or mozambique or namibia or niger or nigeria or rwanda or senegal or "sierra leone" or somalia or saharan or sudan or swaziland or tanzania or togo or uganda or zambia or zimbabwe).ti,ab
10. 8 or 9
11. 4 and 7 and 10

## Appendix E: French Version of the Verbal Consent Script



### SCRIPT VERBAL INVITATION À PARTICIPER À LA RECHERCHE

**Titre de l'étude :** Détermination des facteurs déterminants de la qualité de vie des patients séropositifs sous traitement antirétroviral

**Chercheur principal :** Oubote Sangbana, Doctorant, UT Health, School of Public Health

**Numéro IRB:** HSC-SPH-19-0357

Je m'appelle Hassan Sangbana et je suis doctorant en épidémiologie au Health Science Center de l'Université du Texas à Houston (UTHealth).

Nous menons une étude pour identifier les principaux facteurs influençant la qualité de vie des patients séropositifs sous traitement antirétroviral.

Je vous invite à participer parce que vous êtes un patient atteint du VIH. Si vous acceptez de participer à cette étude, il vous sera demandé de répondre aux questions du questionnaire MOS-HIV, ce qui devrait prendre environ 20 minutes. Aucune réponse que vous fournissez ne peut être utilisée pour vous identifier.

Les risques liés à la participation à cette étude incluent les violations de la confidentialité et la perte de la vie privée. Nous ne regarderons que votre carte de visite devant vous et aucune information d'identification personnelle ne sera collectée.

Nous apprécions votre participation à l'étude. La participation est volontaire et vous pouvez sauter les questions auxquelles vous ne souhaitez pas répondre. Vous pouvez également arrêter de participer à tout moment. Votre décision de participer n'aura aucun impact sur vos soins de santé à Espoir Vie Togo.

Si vous avez des plaintes, des suggestions ou des questions concernant vos droits en tant que volontaire de recherche, vous pouvez contacter le Comité pour la protection des sujets humains (CPHS) au +1 (713) -500-7943. Si vous avez des questions concernant l'étude, vous pouvez me contacter au 98 15 15 03 ou par courrier électronique à l'adresse suivante : [hassan.o.sangbana@uth.tmc.edu](mailto:hassan.o.sangbana@uth.tmc.edu).

Avez-vous des questions pour moi ?  
Voulez-vous participer à cette étude ?

## Appendix F: Espoir Vie Togo's Patient Routine Visit Card (Page 1 [Left] and 2 [Right])

**Visite n° :** \_\_\_\_\_ **Date:** \_\_\_\_/\_\_\_\_/\_\_\_\_  
 Température: \_\_\_\_\_ Pouls: \_\_\_\_\_ Tension artérielle: \_\_\_\_\_  
 Poids : \_\_\_\_\_ Taille Si Enfant: \_\_\_\_\_ Age: \_\_\_\_\_  
 Etat : Valide ☐ Mobile ☐ Alité ☐  
 Grossesse: Oui : \_\_\_\_\_ Non: \_\_\_\_\_  
 Si oui âge de la grossesse: \_\_\_\_\_  
 Bilan de suivi biologique réalisé: oui ☐ Si Oui Date [\_\_\_\_/\_\_\_\_/\_\_\_\_] Non ☐  
 CD4: \_\_\_\_\_ Date de réalisation: \_\_\_\_\_  
 Charge virale : \_\_\_\_\_ Lymphocytes (%) : \_\_\_\_\_  
**Décision thérapeutique (TARV) :**  
 Début: ☐ Poursuite ☐ Modification: ☐ Arrêt: ☐  
 Motif de substitution de TARV: \_\_\_\_\_  
 Motif de passage au TARV de 2<sup>nd</sup>e ligne: \_\_\_\_\_  
 Motif de l'arrêt: \_\_\_\_\_  
**Traitement ARV:**  
 Ligne: 1<sup>ère</sup> Ligne originale ☐ 1<sup>ère</sup> Ligne substituée ☐ 2<sup>nd</sup>e Ligne ☐  
 Combinaison thérapeutique: \_\_\_\_\_  
 Durée de traitement: \_\_\_\_\_  
**Autres Traitements:**  
 Traitement d'une IO: oui ☐ non ☐  
 Prophylaxie cotrimoxazole: oui ☐ non ☐  
 Prochain rendez-vous \_\_\_\_/\_\_\_\_/\_\_\_\_

Motif de substitution de TARV	Motif d'arrêt
1. Toxicité / effets secondaires 2. Grossesse 3. Suspicion de grossesse 4. TB rechute 5. Nouveau médicament disponible 6. Rupture de stock de médicaments 7. Autre (spécifier) _____ <b>Motif de passage au TARV de 2<sup>nd</sup>e ligne :</b> 1. Echec du traitement clinique 2. Echec immunologique 3. Echec virologique	1. Echec thérapeutique 2. Non observance 3. Toxicité, complications 4. Maladie hospitalisation 5. Le patient manque de ressources 6. Autres décisions du patient 7. Interruption planifiée 8. Rupture de stock 9. Autres

**Infections opportunistes** (types et traitements prescrits) \_\_\_\_\_  
**Effets indésirables** (préciser si ARV ou IO) \_\_\_\_\_  
**Co infection TB/VIH** (chez tous les patients, chercher la tuberculose à chaque contact/consultation pour identifier les suspects)  
 (chez les suspects de la tuberculose, faire la démarche diagnostique de la tuberculose)  
 \*Tuberculose suspectée = présence d'au moins un des signes suivants: Fièvre, toux, amaigrissement, sueur nocturne...  
**examen paraclinique demandé:** \_\_\_\_\_  
**Tuberculose suspectée:** oui ☐ non ☐  
**Tuberculose confirmée:** oui ☐ non ☐  
 • Si oui, précisez la date de diagnostic: \_\_\_\_/\_\_\_\_/\_\_\_\_  
 • Traitement antituberculeux: \_\_\_\_\_  
 • Autres pathologies associées : (HTA ; Diabète; Hépatite; drépanocytose...) \_\_\_\_\_  
**Observance ARV:**  
 Respect des rendez-vous : oui ☐ non ☐  
 Nombre de dose oubliée ou non prise au cours de la dernière semaine: \_\_\_\_  
 Si diagnostic d'inobservance référer pour éducation thérapeutique et évaluer le patient.

ANALYSES	RESULTATS	DATE	ANALYSES	RESULTATS	DATE
TAUX D'HEMOGLOBINE			AMYLASEMIE		
ALAT ou SGPT			LIPASEMIE		
CREATINEMIE			CPK		
GLYCEMIE			AUTRES (à préciser)		
TRIGLYCERIDES					
CHOLESTEROLEMIE					

## Appendix G: English Version of the MOS-HIV

### MOS-HIV 35-ITEM INSTRUMENT

**INSTRUCTIONS TO PATIENT:** Please answer the following questions by placing a "x" in the appropriate box.

1. In general, would you say that your health is:

(check one)

Excellent..... 1 ☐

Very Good ..... 2 ☐

Good ..... 3 ☐

Fair ..... 4 ☐

Poor..... 5 ☐

2. How much **bodily** pain have you generally had during the **past 4 weeks**?

(check one)

None..... 1 ☐

Very Mild ..... 2 ☐

Mild..... 3 ☐

Moderate ..... 4 ☐

Severe..... 5 ☐

Very Severe ..... 6 ☐

3. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

(check one)

Not at all ..... 1 ☐

A little bit..... 2 ☐

Moderately ..... 3 ☐

Quite a bit..... 4 ☐

Extremely ..... 5 ☐

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(English (United States) MOS-HIV Questionnaire Version 2.1)

MOS-HIV\_V2.1- United States/English - Mapi Research Institute.  
ID5988 / MOS-HIV\_AU2.1\_eng-USort.doc

4. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	(check one box on each line)		
	YES, Limited A Lot	YES, Limited A Little	NO, Not Limited At All
	1	2	3
a. The kinds or amounts of <b>vigorous</b> activities you can do, like lifting heavy objects, running or participating in strenuous sports.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. The kinds or amounts of <b>moderate</b> activities you can do, like moving a table, carrying groceries or bowling.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Walking uphill or climbing a few flights of stairs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Bending, lifting or stooping.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Walking one block.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Eating, dressing, bathing, or using the toilet.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. Does your health **keep** you from working at a job, doing work around the house or going to school?

(check one)

Yes ..... 1 ☐

No ..... 2 ☐

6. Have you been unable to do **certain kinds or amounts** of work, housework, or schoolwork because of your health?

(check one)

Yes ..... 1 ☐

No ..... 2 ☐

For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

	(mark one box on each line)					
	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
	1	2	3	4	5	6
7. How much of the time, during the past 4 weeks, has your <b>health limited your social activities</b> (like visiting with friends or close relatives)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. How much of the time, during the past 4 weeks:						
a. Have you been a very nervous person?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Have you felt calm and peaceful?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Have you felt downhearted and blue?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Have you been a happy person?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Have you felt so down in the dumps that nothing could cheer you up?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(check one box on each line)

	All Of the Time	Most of the time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
	1	2	3	4	5	6
9. How often during the <b>past four weeks</b> :						
a. Did you feel full of pep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Did you feel worn out?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Did you feel tired?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Did you have enough energy to do the things you wanted to do?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Did you feel weighed down by your health problems?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Were you discouraged by your health problems?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Did you feel despair over your health problems?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Were you afraid because of your health?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	(check one box on each line)						
	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time	
	1	2	3	4	5	6	
10. How much of the time, during the <b>past 4 weeks</b> :							
a.	Did you have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b.	Did you forget things that happened recently, for example, where you put things and when you had appointments?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c.	Did you have trouble keeping your attention on any activity for long?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d.	Did you have difficulty doing activities involving concentration and thinking?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	(check one box on each line)					
	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False	
	1	2	3	4	5	
11. Please check the box that describes whether each of the following statements is true or false for you.						
a.	I am somewhat ill.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b.	I am as healthy as anybody I know.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c.	My health is excellent.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d.	I have been feeling bad lately.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

12. How has the quality of your life been during the **past 4 weeks**? That is, how have things been going for you?

(check one)

Very well; could hardly be better ..... 1 ☐

Pretty good ..... 2 ☐

Good and bad parts about equal ..... 3 ☐

Pretty bad ..... 4 ☐

Very bad; could hardly be worse ..... 5 ☐

13. How would you rate your physical health and emotional condition now compared to **4 weeks ago**?

(check one)

Much better ..... 1 ☐

A little better ..... 2 ☐

About the same ..... 3 ☐

A little worse ..... 4 ☐

Much worse ..... 5 ☐

**THANK YOU VERY MUCH**

## Appendix H: French Version of the MOS-HIV

### QUESTIONNAIRE MOS-HIV 35 ITEMS

**INSTRUCTIONS:** Répondez aux questions suivantes en mettant une croix dans la case qui correspond le mieux à votre cas.

1. En général, diriez-vous que votre santé est:

(cochez une seule case)

- Excellente..... 1 ☐
- Très bonne..... 2 ☐
- Bonne..... 3 ☐
- Médiocre..... 4 ☐
- Mauvaise..... 5 ☐

2. Quelle a été l'intensité des douleurs **physiques** dont vous avez éventuellement souffert au cours des **4 dernières semaines**?

(cochez une seule case)

- Aucune douleur..... 1 ☐
- Douleurs très légère..... 2 ☐
- Douleurs légère..... 3 ☐
- Douleurs modérée..... 4 ☐
- Douleurs intense..... 5 ☐
- Douleurs très intense..... 6 ☐

3. Au cours des **4 dernières semaines**, dans quelle mesure **les douleurs** vous ont-elles gêné(e) dans votre travail habituel (professionnel et domestique)?

(cochez une seule case)

- Pas du tout..... 1 ☐
- Un petit peu..... 2 ☐
- Modérément..... 3 ☐
- Beaucoup..... 4 ☐

Enormément .....5 ☐

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(French (France) MOS-HIV Questionnaire Version 2.1)  
MOS-HIV\_AU2.1\_fra-FR\_nonMapi

4. Les questions suivantes concernent les activités que vous êtes éventuellement amené(e) à faire durant une journée normale. Est-ce que  votre santé vous limite actuellement  dans ces activités?

	(Cochez une case par ligne)		
	Oui, beaucoup	Oui, un peu	Non, pas du tout
	1	2	3
a. Des <b>activités intenses</b> , telles que la course, soulever des objets lourds ou pratiquer un sport éprouvant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Des <b>activités modérées</b> , telles que déplacer une table, porter un sac de provisions ou jouer aux boules	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Monter à pied une côte ou quelques étages	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Se pencher, soulever un objet ou se baisser	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Faire une centaine de mètres à pied	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Manger, s'habiller, prendre un bain ou aller aux toilettes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. Votre état de santé vous **empêche-t-il** d'exercer une activité professionnelle, de vous occuper de votre maison (ménage, bricolage), d'aller au lycée (à l'université)?

(cochez une seule case)

Oui..... 1 ☐

Non..... 2 ☐

6. Avez-vous été gêné(e) pour accomplir **certaines tâches** professionnelles, domestiques (ménage, bricolage) ou scolaires / universitaires, du fait de votre état de santé?

(cochez une seule case)

Oui..... 1 ☐

Non..... 2 ☐

Pour chacune des questions suivantes, répondez en cochant la case qui se rapproche le plus de ce que vous avez ressenti au cours de ces 4 dernières semaines.

	(Cochez une case par ligne)					
	Tout le temps	La majorité du temps	Une grande partie du temps	De temps en temps	Peu de temps	Jamais
	1	2	3	4	5	6
7. Pendant combien de temps, au cours des 4 dernières semaines, <b>votre état de santé a-t-il limité votre vie sociale</b> (comme de rendre visite à des amis, à de la famille proche)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Pendant combien de temps, au cours des 4 dernières semaines:						
a. Avez-vous été quelqu'un de nerveux?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Vous êtes-vous senti(e) calme et paisible?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Vous êtes-vous senti(e) triste et déprimé(e)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Avez-vous été quelqu'un d'heureux?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Vous êtes-vous senti(e) si cafardeux(se) que rien ne pouvait vous réjouir?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(Cochez une case par ligne)

	Tout le temps	La majorité du temps	Une grande partie du temps	De temps en temps	Peu de temps	Jamais
	1	2	3	4	5	6
9. Pendant combien de temps au cours des <b>4 dernières semaines</b> ?						
a. Vous êtes-vous senti(e) plein(e) d'entrain et de vitalité?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Vous êtes-vous senti(e) épuisé(e)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Vous êtes-vous senti(e) fatigué(e)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Avez-vous eu suffisamment d'énergie pour faire ce que vous vouliez faire?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Vos problèmes de santé vous ont-ils pesé?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Vos problèmes de santé vous ont-ils démoralisé(e)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Vos problèmes de santé vous ont-ils désespéré(e)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Votre état de santé vous a-t-il fait peur?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(Cochez une case par ligne)

	Tout le temps	La majorité du temps	Une grande partie du temps	De temps en temps	Peu de temps	Jamais
	1	2	3	4	5	6
10. Pendant combien de temps, au cours des 4 dernières semaines:						
a. Avez-vous eu des difficultés pour raisonner et résoudre des problèmes, par exemple, faire des projets, prendre des décisions, apprendre quelque chose de nouveau?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Avez-vous oublié, par exemple, des choses qui sont arrivées dernièrement, des rendez-vous, où vous aviez mis vos affaires?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Avez-vous eu des difficultés à rester attentif(ve) longtemps, quelque soit votre activité?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Avez-vous eu des difficultés à avoir des activités demandant concentration et réflexion?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

(Cochez une case par ligne)

	Totalement vrai	Plutôt vrai	Je ne sais pas	Plutôt faux	Totalement faux
	1	2	3	4	5
11. Précisez dans quelle mesure chacune des affirmations suivantes est "vraie" ou "fausse" pour vous.					
a. Je suis un peu malade	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Je suis en aussi bonne santé que n'importe qui	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Ma santé est excellente	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Je me sens plutôt mal ces derniers temps	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

12. Quelle a été la qualité de votre vie durant les **4 dernières semaines**? (Comment les choses ont-elles été pour vous?)

(cochez une seule case)

Très bonne; aurait difficilement pu être meilleure..... 1 ☐

Assez bonne ..... 2 ☐

Parfois bonne, parfois mauvaise..... 3 ☐

Assez mauvaise ..... 4 ☐

Très mauvaise, aurait difficilement pu être pire ..... 5 ☐

13. Comment évaluez-vous votre état physique et affectif actuel en le comparant à **ce qu'il était il y a 4 semaines**?

(cochez une seule case)

Bien meilleur ..... 1 ☐

Un peu meilleur ..... 2 ☐

A peu près le même ..... 3 ☐

Un peu moins bon ..... 4 ☐

Bien moins bon ..... 5 ☐

**MERCI POUR LE TEMPS QUE VOUS AVEZ  
CONSACRE A CE QUESTIONNAIRE**

## Appendix I: Espoir Vie Togo Support Letter



# ESPOIR VIE-TOGO

Cel : 00 228- 90 06 15 08 Tél. 00 228 22 51 46 56 E-mail : espoirvietogo@gmail.com  
N° compte bancaire Ecobank 7010181400566001 Web: www.espoirvietogo.org

N°Réf : 055/2019/EVT/DE

Lomé le,

April 15, 2019

Committee for the Protection of Human Subjects  
UTHealth School of Public Health  
6410 Fannin, Suite 1100  
Houston, Texas 77030

To Whom It May Concern:

I am writing to express my support for Oubote Sangbana's research study, "Determining the Drivers of Quality of Life in HIV Patients Treated with Antiretroviral Therapy" to be conducted by Oubote and a few members of Espoir Vie Togo in the Spring of 2019 in Lomé (Togo) at Espoir Vie Togo, Centre Medico-Social LUCIA.

Espoir Vie Togo is very supportive of research efforts dedicated to improving the condition of HIV patients not only in sub Saharan Africa, but all around the world.

To that end, Espoir Vie Togo, Atsou-Alley and Nina Dapam, MD, will collaborate to conduct the research aforementioned. Espoir Vie Togo will make necessary arrangements (including making patient charts available upon procurement of informed consent) to facilitate Oubote's research.

During the period of the research (approximately one month), Oubote will be permitted to abstract data regarding risk factors influencing patients' quality of life and administer the WHOQOL-HIV BREF questionnaire to approximately 103 patients. No identifiable patient information is to be abstracted. We expect Oubote to follow all standard research practices to maintain patient privacy.

We look forward to learning the results of Oubote's research.

With kind regards,

Dr Ephrem MENSAH  
Executive Director of Espoir Vie Togo



ONG reconnue d'utilité publique N°468/MCDAT/2008 du 10 septembre 2008; 7 BP : 14543 Lomé 7  
Direction Nationale: Djidjole Aflao-Gakli, Rue Agbetra, face maison n°442, non loin de l'Ecole " La Sagesse"; Lomé-Togo

## Appendix J: Outcome Letter from the Comité de Bioéthique pour la Recherche en Santé

MINISTRE DE LA SANTE ET DE  
L'HYGIENE PUBLIQUE

REPUBLIQUE TOGOLAISE

*Travail – Liberté – Patrie*



### **EXAMEN DE PROTOCOLE DE RECHERCHE**

**TITRE DU PROJET** : « Identification des déterminants de la qualité de vie des patients séropositifs traités par antirétroviraux »

**Thèse de doctorat**

**Promoteur** : Université de Texas, (Texas School of Public Health, department of epidemiology), USA

**Investigateur Etudiant** :

- M. Hassan Oubote SANGBANA, MPH

**Comité de thèse** :

- Dr Charles Drkoh, directeur de thèse
- Dr Stacia DeSantis, chaire de biostatistique
- Dr Sheryl McCurdy, chaire santé globale
- Dr Patricia Dolan Mullen, chaire revue systématique
- Dr Christine Markham, reviseur externe.

**Co-investigateurs** :

- Dr Nina Dapam, EVT TOGO Lomé
- Jean Marie ATSOU-ALLEY, psychologue clinicien, EVT TOGO, Lomé
- Maurice ADJARI, Sociologue, PNLS, Lomé.

**Lieu d'intervention** : CMS de l'ONG Espoir Vie Togo (EVT) à Lomé - Togo.

**AVIS N° 034/2019/CBRS du 31 juillet 2019 (En 2<sup>ème</sup> lecture)**

Le Comité de Bioéthique pour la Recherche en Santé (CBRS) s'est réuni le 31 juillet 2019 pour évaluer, en 2<sup>ème</sup> lecture, le protocole de recherche relatif à l'étude suivante : « Identification des déterminants de la qualité de vie des patients séropositifs traités par antirétroviraux ».

A l'issue de la mise en commun des rapports d'étude présentés par des personnes ressources, le CBRS s'est prononcé sur :



### 1- La présentation du dossier

- Documents du protocole d'étude : les documents sont bien présentés. Les observations du CBRS ont été prises en compte.

### 2. La validité scientifique du dossier

**Conception scientifique :** Le protocole est bien conçu. En effet, avec l'expansion des programmes d'accès aux médicaments ARV en Afrique, l'espérance de vie des PVVIH a considérablement augmenté. Mais compte tenu de la morbidité de cette affection chronique, il y a un impact sur la qualité de vie des malades. Il est important d'identifier les facteurs associés à la qualité de vie des PVVIH afin de les prendre en compte dans la prise en charge des patients.

**Hypothèse :** Le problème est bien identifié : il y a une altération de la qualité de vie des PVVIH sous ARV souvent associés à des facteurs non pris en compte au quotidien.

**Méthodologie :** C'est une étude transversale déclarative. Détermination de la zone d'étude : Centre médico-social Lucia de l'ONG EVT.  
Détermination de l'échantillon de départ et description de techniques de collecte de données bien faites.

**Faisabilité :** Il s'agit d'une étude réalisable. Il s'agit d'une enquête simple à réaliser auprès des PVVIH sous ARV sans aucune méthode invasive. Il n'y a pas d'impact négatif pour les patients.

**Objectifs :** Les objectifs sont bien définis.

#### **Intérêt de l'étude :**

L'intérêt de l'étude est indéniable.

**Références scientifiques :** Les références sont assez fournies.

### 3. L'acceptabilité éthique

Le formulaire de consentement est disponible ; une notice d'information est jointe.

Les recommandations du CBRS relatives à la publication et à la collaboration avec des co-investigateurs du Togo (EVT et PNLS) sont prises en compte.

MINISTRE DE LA SANTE ET DE  
L'HYGIENE PUBLIQUE

REPUBLIQUE TOGOLAISE

*Travail – Liberté – Patrie*



**4. La conclusion**

Le CBRS à l'unanimité de ses membres présents, a émis un **AVIS FAVORABLE** pour l'exécution au Togo de l'étude relative à l'« **Identification des déterminants de la qualité de vie des patients séropositifs traités par antirétroviraux** ».

NB : Le promoteur devra déposer à la fin de l'étude au secrétariat du CBRS, copie du rapport final en cinq (5) exemplaires.

Fait à Lomé, le 31 juillet 2019

Le Rapporteur :



ALEZA Mazabalo

La Présidente



Professeur  
Mireille DAVID

## Appendix K: Outcome Letter from UTHealth's Committee for the Protection of Human Subjects (CPHS)



### Committee for the Protection of Human Subjects

6410 Fannin Street, Suite 1100  
Houston, Texas 77030

Oubote Sangbana  
School of Public Health

May 08, 2019

HSC-SPH-19-0357 - *Determining the Drivers of Quality of Life in HIV Patients Treated with Antiretroviral Therapy*

The above named project is determined to qualify for exempt status according to 45 CFR 46.101(b)

**CATEGORY #2:** *Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:*

- a. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; AND ,*
- b. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.*

*(NOTE: The exemption under Category 2 DOES NOT APPLY to research involving survey or interview procedures or observation of public behavior when individuals under the age of 18 are subjects of the activity except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.)*

**CHANGES:** Should you choose to make any changes to the protocol that would involve the inclusion of human subjects or identified data from humans, please submit the change via iRIS to the Committee for the Protection of Human Subjects for review.

#### **INFORMED CONSENT DETERMINATION:**

Waiver of Documentation of Informed Consent (verbal consent)

**INFORMED CONSENT:** When Informed consent is required, it must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process.

**HEALTH INSURANCE PORTABILITY and ACCOUNTABILITY ACT (HIPAA): Exempt from HIPAA**

**STUDY CLOSURES:** Upon completion of your project, submission of a study closure report is required. The study closure report should be submitted once all data has been collected and analyzed.

Should you have any questions, please contact the Office of Research Support Committees at 713-500-7943.

## Appendix L: Outcome Letter from UTHealth's CPHS – Protocol Change – Travel

### Reimbursement



#### Committee for the Protection of Human Subjects

6410 Fannin Street, Suite 1100  
Houston, Texas 77030

#### **NOTICE OF APPROVAL TO IMPLEMENT REQUESTED CHANGES**

July 01, 2019

**HSC-SPH-19-0357** - Determining the Drivers of Quality of Life in HIV Patients Treated with Antiretroviral Therapy  
PI: Dr. Oubote Sangbana

Reference Number: 189681

**PROVISIONS:** Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: By Expedited Review and Approval

CHANGE APPROVED: Addition of travel compensation

REVIEW DATE: July 1, 2019

APPROVAL DATE: July 1, 2019

CHAIRPERSON: L. Maximilian Buja, MD

A handwritten signature in black ink that reads "L. Maximilian Buja".

Upon receipt of this letter, and subject to any provisions noted above, you may now implement the changes approved.

**CHANGES:** The principal investigator (PI) must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. **ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.**

**INFORMED CONSENT:** Informed consent must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. **Please note that if revisions to the informed consent form were made and approved, then old blank copies of the ICF MUST be destroyed. Only copies of the appropriately dated, stamped approved informed consent form can be used when obtaining consent.**

**UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS:** The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious

harm to subjects, and of any adverse drug reactions.

**RECORDS:** The PI will maintain adequate records, including signed consent documents if required, in a manner that ensures subject confidentiality.

## Appendix M: Outcome Letter UTHHealth's CPHS – Protocol Change – Sample Size Increase



### Committee for the Protection of Human Subjects

6410 Fannin Street, Suite 1100  
Houston, Texas 77030

### NOTICE OF APPROVAL TO IMPLEMENT REQUESTED CHANGES

July 13, 2019

**HSC-SPH-19-0357** - Determining the Drivers of Quality of Life in HIV Patients Treated with Antiretroviral Therapy  
PI: Dr. Oubote Sangbana

Reference Number: 190404

**PROVISIONS:** Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: By Expedited Review and Approval

CHANGE APPROVED: Increase sample size to 140 subjects

REVIEW DATE: July 13, 2019

APPROVAL DATE: July 13, 2019

CHAIRPERSON: L. Maximilian Buja, MD

A handwritten signature in black ink that reads "L. Maximilian Buja".

Upon receipt of this letter, and subject to any provisions noted above, you may now implement the changes approved.

**CHANGES:** The principal investigator (PI) must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. **ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.**

**INFORMED CONSENT:** Informed consent must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. **Please note that if revisions to the informed consent form were made and approved, then old blank copies of the ICF MUST be destroyed. Only copies of the appropriately dated, stamped approved informed consent form can be used when obtaining consent.**

**UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS:** The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious

harm to subjects, and of any adverse drug reactions.

**RECORDS:** The PI will maintain adequate records, including signed consent documents if required, in a manner that ensures subject confidentiality.

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