UNSUPPRESSED VIRAL LOAD AMONG HIV-POSITIVE CHILDREN AND ADOLESCENTS ON ANTIRETROVIRAL THERAPY IN LUBUMBASHI, DEMOCRATIC REPUBLIC OF THE CONGO: MAGNITUDE, DETERMINANTS, BARRIERS, AND FACILITATORS.

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223152330

A thesis submitted to the School of Applied Human Sciences, College of Humanities, University of KwaZulu-Natal, Westville College, in fulfilment of the requirements for the degree of Doctor of Philosophy in Health Promotion

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A thesis by Manuscripts submitted to the School of Applied Human Sciences, College of Humanities, University of KwaZulu-Natal in fulfilment of the academic requirements for the degree of Doctor of Philosophy in Health Promotion (PhD).

This is to attest that contents outlined in this thesis are the original research work done and reported by the author (Olivier K. Mukuku). The research work detailed in this thesis has not been previously submitted to any tertiary institution for award of a degree or diploma. The use of other researchers/scientists' work in the text has been acknowledge accordingly.

As the candidate's supervisors, we have approved this thesis for submission

Supervisor

Name: Prof. Kaymarlin Govender **Signed:** [redacted] **Date:** August 10th, 2025

Format of dissertation

This thesis was presented as a manuscript format, which included submitted and prepared journal articles that have emanated from the research project in this field.

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DECLARATION 1: PLAGIARISM

I *Olivier Kabiriko Mukuku* declare that;

The research reported in this dissertation, except where otherwise indicated, and is my original work.

This dissertation has not been submitted for any degree or examination at any other institution or university.

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Date: August 10th, 2025

DECLARATION 2: PUBLICATIONS AND MANUSCRITPS

Journal articles

Article 1

Mukuku O, Govender K, Wembonyama SO, Kiakuvue YN. Magnitude and characteristics of unsuppressed HIV viral load in children and adolescents on antiretroviral therapy in sub-Saharan Africa: a systematic review and meta-analysis. **The Lancet HIV 2025**; 12(7):e506-e521. https://doi.org/10.1016/S2352-3018(25)00039-6

Contributions: *O.M. developed the protocol and participated in the study design, study selection, data extraction, statistical analysis, and drafting the initial versions of the manuscript. Y.N.K. and S.O.W. involved in study selection, data extraction, and quality assessment. S.O.W., and K.G. collaborated, as study supervisors, in designing the study, preparing and revising the subsequent manuscript drafts, as well as the final draft of the manuscript. All authors read and approved the final version of the manuscript.*

Article 2

Mukuku O, Govender K, Wembonyama SO. Barriers and facilitators to HIV viral load suppression among adolescents living with HIV in Lubumbashi, Democratic Republic of the Congo: A qualitative study. **Plos ONE 2025**; 20(3): e0320417. https://doi.org/10.1371/journal.pone.0320417

Contributions: *O.M. and K.G conceptualized the study, designed the methodology, and conducted the validation. O.M. performed formal analysis and collected the data; O.M., K.G., and S.O.W. prepared the original draft of the manuscript and contributed to the review and editing; K.G. and S.O.W. provided supervision. All authors critically reviewed and approved the final version of the manuscript for publication.*

Article 3

Mukuku O, Govender K, Wembonyama SO. Prevalence and determinants of unsuppressed HIV viral loads among children and adolescents living with HIV on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: a retrospective cross-sectional study. **BMJ Open. 2025**; 15(7):e094657. https://doi.org/10.1136/bmjopen-2024-094657

Contributions: *O.M. and K.G conceptualized the study, designed the methodology, and conducted the validation. O.M. performed formal analysis and collected the data; O.M., K.G., and S.O.W. prepared the original draft of the manuscript and contributed to the review and editing; K.G. and S.O.W. provided supervision. All authors critically reviewed and approved the final version of the manuscript for publication.*

Research topic

Mukuku O, Govender K, Kulohoma B, Wembonyama SO. Challenges in reaching the UNAIDS 95-95-95 targets in Sub-Saharan Africa: Status, innovations, and pathways forward. **Frontiers in Public Health** 2025; Volume 13. https://www.frontiersin.org/research-topics/66743/challenges-in-reaching-the-unaids-95-95-95-targets-in-sub-saharan-africa-status-innovations-and-pathways-forward

DEDICATION

This work is dedicated to my parents, Laurent Mukuku and Marie-Styve Mukazi, who always believed in me and taught me never to settle for less.

I would also like to thank my wife, Martiale Madeleine Sininemera, who continually challenges all gender preconceptions and manages our demanding domestic life to support my long working hours. I salute you.

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I dedicate also this work to the children and adolescents living with HIV who courageously shared their experiences with us during the course of this study, the research team for their dedication and hard work, and my family for their unwavering support and sacrifices throughout this journey.

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ABSTRACT

Background.

Despite the proven effectiveness of antiretroviral therapy, achieving and maintaining viral load suppression among children and adolescents living with HIV remains a significant challenge, particularly in resource-limited settings such as Lubumbashi, Democratic Republic of the Congo. Barriers to optimal adherence to antiretroviral therapy contribute to unsuppressed viral load, increasing the risk of disease progression and HIV transmission. Understanding the magnitude, determinants, barriers, and facilitators of viral load suppression is crucial for designing effective interventions.

Objectives.

This study aimed to determine the prevalence of unsuppressed viral load among children and adolescents living with HIV on antiretroviral therapy in Lubumbashi and to identify the factors associated with unsuppressed viral load. Additionally, it explored the barriers and facilitators influencing adherence to antiretroviral therapy and achieving viral load suppression from the perspectives of children and adolescents living with HIV, their caregivers, and healthcare workers.

Methods.

A convergent mixed-methods study was conducted from June to September 2024 in HIV care clinics in Lubumbashi. The quantitative component consisted of a multicenter cross-sectional study including 847 children and adolescents living with HIV aged 0 to 19 years on antiretroviral therapy for at least six months with available viral load results. Data were collected using an observational checklist and analyzed using STATA version 16. Bivariable and multivariable logistic regression models were used to identify factors associated with unsuppressed viral load.

The qualitative component involved in-depth interviews with 39 adolescents living with HIV aged 13 to 19 years, 14 caregivers, and focus group discussions with 16 healthcare workers. Participants were purposively selected based on their roles in HIV care and treatment. Data were thematically analyzed using NVivo 14, guided by the socioecological model, to explore barriers and facilitators to adherence to antiretroviral therapy and to achieve viral load suppression.

Results.

The prevalence of unsuppressed viral load among children and adolescents living with HIV was 24.7% (209/847). Factors significantly associated with unsuppressed viral load included having married caregivers (AOR= 2.4; 95% CI: 1.2 to 5.0), non-perinatal HIV transmission (AOR=2.3; 95% CI: 1.2–4.5), advanced WHO clinical stages (AOR= 3.5; 95% CI: 1.0 to 13.7), poor/fair adherence to antiretroviral therapy (AOR= 107.8; 95% CI: 50.3 to 231.1), and antiretroviral therapy-induced side effects (AOR= 3.8; 95% CI: 1.9 to 7.9).

The qualitative analysis identified barriers to antiretroviral therapy adherence and viral load suppression based on the socio-ecological model. Individual-level obstacles included economic constraints, forgetfulness, misconceptions about treatment necessity, and lack of food. Family-level barriers included insufficient support and stigma. Interpersonal stigma and discrimination also played a role. Facilitators, however, included strong social support, counseling, reminder tools, and positive healthcare worker-patient relationships, all of which helped improve adherence and viral load suppression.

Conclusion.

Reducing unsuppressed viral load among children and adolescents living with HIV in Lubumbashi requires a multifaceted approach, integrating family and community support,

simplified antiretroviral therapy regimens, and enhanced healthcare worker capacity to provide comprehensive care. Targeted policy interventions and cross-sectoral collaboration are essential to improving adherence to antiretroviral therapy and achieving sustained viral load suppression in this vulnerable population.

Keywords: HIV, children, adolescents, viral load suppression, antiretroviral therapy, adherence, Lubumbashi, DRC.

ABREVIATIONS

95 % CI	95 % confidence interval
AIDS	Acquired Immunodeficiency Syndrome
ALHIV	adolescents living with HIV
aOR	adjusted odds ratios
ART	antiretroviral therapy
AUC	area under the curve
CALHIV	children and adolescents living with HIV
cOR	crude odds ratio
DRC	Democratic Republic of the Congo
EID	early infant diagnosis
FGD	focus group discussions
GHSA	Global Health Security Agenda
GRH	General Referral Hospital
HC	Health Center
HCW	healthcare workers
HIV	human immunodeficiency virus
HZ	Health Zone
IDI	in-depth interviews
JBI	Joanna Briggs Institute
NPV	Negative predictive value
OI	opportunistic infection
OR	odds ratio
ROC	receiver operating characteristic
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PLHIV	people living with HIV
PMTCT	prevention of mother-to-child transmission
PNLS	National HIV/AIDS Programme (Programme National de Lutte contre le Sida et les IST [in french])
PPV	Positive predictive value
PrEP	pre-exposure prophylaxis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RR	relative risk

SDGs	Sustainable Development Goals
SRH	sexual and reproductive health
SSA	Sub-Saharan Africa
STI	sexually transmitted infection
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TB	tuberculosis
UHC	Universal Health Coverage
UNAIDS	United Nations Programme on HIV and AIDS
USVL	unsuppressed viral loads
VL	viral load
VLS	viral load suppression
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION AND RATIONALE FOR THE RESEARCH

The global effort to 'end HIV transmission' is guided by the United Nations Programme on HIV and AIDS (UNAIDS) strategic objectives (UNAIDS, 2014; UNAIDS, 2020). These objectives are aimed at achieving by 2030: 95 % of all HIV-positive people should be aware of their status, 95 % of those who know their status should be on antiretroviral therapy (ART), and 95 % of those receiving ART should have a suppressed viral load (VL). With regard to this third objective, VL monitoring is widely used as an indicator of treatment efficacy at both individual and program levels (Calmy et al., 2007).

The proposed study investigated a concern amongst HIV clinicians about the progress of many national ART programmes toward achieving these objectives. The concern is that while many ART programmes in Sub-Saharan Africa (SSA) are recording substantive progress generally, there is less progress in the case of children and adolescents living with HIV (CALHIV) compared to adults living with HIV, particularly with regard to viral load suppression (VLS). A recent study by Han et al. (2021) on viral load suppression (VLS) revealed that while adult populations were nearing the UNAIDS 95% target, progress among children and adolescents remained significantly slower and fell well short of global benchmarks. This disparity was also evident in the Democratic Republic of the Congo (DRC), where a 2021 review of the national HIV/AIDS program reported that only 11% of children living with HIV on antiretroviral therapy (ART) had achieved viral suppression (PNLS, 2021). This alarmingly low figure highlights the persistent challenges in pediatric HIV care, including limited access to routine viral load monitoring, shortages of age-

appropriate ART formulations, and insufficient adherence support tailored to younger populations.

The proposed study focused on three research main questions:

1° What are the prevalence and factors associated with USVL among CALHIV on ART in Lubumbashi, in the DRC?

2° What are barriers and facilitators to ART adherence and VLS among adolescents living with HIV (ALHIV) in Lubumbashi, in the DRC?

The proposed study aims to provide empirical evidence on the state of the HIV programme for CALHIV in the DRC, in order to assess the validity of the concern raised about the slow progress towards achieving VLS targets.

1.1. Background to the study

1.1.1. The Global Health Security Agenda

The Sustainable Development Goals (SDGs), adopted by the United Nations in September 2015, outline global targets to be achieved by 2030, with a specific emphasis on SDG 3. This goal not only aims to end the epidemics of HIV, tuberculosis, malaria, and other communicable diseases, but also emphasizes the importance of Universal Health Coverage (UHC). UHC ensures that everyone, regardless of their socioeconomic status, has access to essential, high-quality healthcare services (UN, 2015; Acharya et al., 2018). SDG 3 calls for a comprehensive public health approach, focusing on both prevention and treatment, while addressing the root causes of diseases through improvements in health systems worldwide (UN, 2015). In addition to eradicating these epidemics, SDG 3 seeks to reduce the global disease burden, promote mental health, and ensure that vulnerable populations, particularly people living with HIV (PLHIV), receive timely and effective care to improve

their health outcomes and quality of life (WHO, 2020a). Achieving UHC is central to this goal, as it guarantees equitable access to high-quality healthcare, irrespective of financial constraints. The goal of UHC within SDG 3 stresses not only the availability of services but also the quality of care provided, which is especially important for marginalized groups (UN, 2015). To achieve SDG 3, it is essential to integrate mental health services into primary healthcare, expand access to essential medicines, and address the social determinants of health that disproportionately affect vulnerable populations, including PLHIV (Global Fund, 2021). Strengthening health systems, enhancing workforce training, and fostering community-based solutions are crucial to ensuring services are responsive to the needs of high-risk groups such as women, adolescents, and people living in rural areas (WHO, 2020a). Furthermore, SDG 3 aims to reduce the social inequalities that hinder access to healthcare, as stigma and discrimination are significant barriers to care for PLHIV. Policies that address these health inequities are crucial in ensuring that marginalized populations can access the services they need (UNAIDS, 2024). Achieving SDG 3 requires global cooperation. Governments, international organizations, donors, and communities must collaborate to strengthen health systems, implement evidence-based policies, and scale up programs focusing on prevention, treatment, and care. Through these collective efforts, countries can reduce HIV-related morbidity and mortality and significantly improve health outcomes for those affected (Global Fund, 2021).

In recent years, the world has faced numerous public health challenges, from infectious diseases to chronic conditions, exacerbating existing inequalities and exposing the vulnerabilities of healthcare systems. The COVID-19 pandemic has served as a stark reminder of the importance of a unified global health agenda. With the world becoming more interconnected, it is crucial that we work together to address health-related issues and prioritize equitable access to healthcare services (Solar et al., 2022; Jensen et al., 2021).

This collaboration, involving governments, international organizations, and communities, is pivotal to reducing health disparities and improving health outcomes, ensuring that no one is left behind, especially in times of crisis like the pandemic.

The Global Health Security Agenda (GHSA) represents a shared commitment among nations, organizations, and individuals to tackle the most pressing health challenges facing the world today. Recognizing health as a fundamental human right, this collective effort aims to improve the well-being of people across the globe. From addressing infectious diseases to promoting universal healthcare, the GHSA plays a crucial role in fostering a healthier and more equitable world (GHSA, 2018). The GHSA was officially launched in February 2014 as a multilateral and multisectoral initiative, in response to the growing global threats posed by emerging infectious diseases, antimicrobial resistance, and weaknesses in health systems (Katz et al., 2014). It is not a United Nations (UN) initiative but works in close coordination with key international bodies such as the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organisation for Animal Health (WOAH/OIE). Unlike traditional UN agencies, the GHSA does not have a fixed physical office; instead, it operates as a collaborative platform guided by a rotating chairmanship and supported by steering groups composed of member countries. Countries such as the United States, Finland, and Indonesia have previously held leadership roles within the GHSA framework. The agenda aligns with the International Health Regulations (IHR 2005) and emphasizes practical tools like the Joint External Evaluation (JEE) to assess and improve national health security capacities. The third phase of the GHSA, covering the period from January 1, 2024, to December 31, 2028, reflects a renewed commitment by member countries to strengthening global preparedness and response capacities. This phase emphasizes measurable progress in health security through sustained investment in public health systems, support for evidence-based and

collaborative policymaking at both national and international levels, and enhanced multisectoral and technical collaboration. Building on the successes of the previous phases, GHSA continues to play a critical role in the global health security architecture (GHSA, 2024). The GHSA sets forth a collective vision for addressing pressing health issues that affect countries worldwide. By promoting collaboration and resource allocation, this agenda seeks to mitigate the adverse effects of health disparities and improve overall well-being. The GHSA's key components include Disease prevention and control, Health system strengthening, Health equity, and Multisectoral collaboration (Wolicki et al., 2016; Katz et al., 2014; GHSA, 2018).

Access to quality healthcare is a cornerstone of the GHSA, which aims to ensure that everyone, regardless of their socio-economic background, has access to essential health services without experiencing financial hardship. The World Health Organization (WHO) advocates for UHC, promoting strong health systems, adequate health financing, and equitable distribution of healthcare resources. By prioritizing primary healthcare and strengthening health systems, UHC aims to improve health outcomes for all, although progress remains uneven across countries (WHO & WB, 2021). The GHSA recognizes the importance of strong and resilient health systems. Adequate infrastructure, skilled healthcare workers, reliable supply chains, and robust data management systems are essential to effectively respond to health challenges. Capacity-building programmes, investment in healthcare workforce education, and the implementation of digital health technologies contribute to building sustainable health systems that can deliver quality care to all (GHSA, 2018).

Addressing inequalities in child and adolescent health is a critical component of the GHSA. This involves improving access to and the quality of healthcare for children and adolescents, addressing social determinants of health, and promoting equity in health

outcomes. Global initiatives such as the SDGs reflect this by including targets related to reducing child mortality, improving maternal health, and ensuring universal access to quality healthcare services. These efforts aim to improve the health and well-being of children and adolescents, leading to healthier communities and future generations (Acharya et al., 2018; WHO & WB, 2021).

1.1.2. UNAID's 95 – 95 – 95 targets

The 95%-95%-95% UNAIDS strategic objective is an ambitious target aimed at ending the HIV/AIDS epidemic by 2030. It builds on the earlier 90-90-90 targets launched in 2014 (UNAIDS, 2014) and was introduced in 2021 to accelerate progress and close remaining gaps in HIV diagnosis, treatment, and viral suppression (UNAIDS, 2021). The objective, known as "95 – 95 – 95", aims to ensure that 95 % of people living with HIV (PLHIV) know their status, 95 % of those who know their status are on antiretroviral therapy (ART), and 95 % of those on ART have suppressed viral loads (VLs). This objective is critical because it addresses the three key stages of the HIV/AIDS epidemic: diagnosis, treatment, and VLS. UNAIDS continues to work towards this objective, recognizing its importance in ending the epidemic (UNAIDS, 2020). This framework is also aligned with the commitments of the SDGs, particularly SDG 3, which aims to end the epidemics of AIDS, tuberculosis, malaria, and other communicable diseases by 2030, while ensuring UHC. These global objectives reinforce the importance of achieving universal health coverage and improving the quality of care, including for PLHIV (Acharya et al., 2018; UN, 2015).

To achieve the 95 – 95 – 95 objectives, the first step is to increase the number of people who know their HIV status. This can be done through various methods, including testing campaigns, community outreach programmes, and self-testing kits. After diagnosis, the next step is to ensure immediate access to ART, which can suppress the virus and prevent

morbidity and mortality. By putting 95 % of those who know their status on ART, new HIV transmissions can be significantly reduced. Lastly, it is crucial to ensure that those on ART achieve viral load suppression (VLS), meaning the amount of virus in their blood is reduced to very low levels. In many cases, this level is so low that it becomes undetectable with standard tests. However, definitions of VLS can vary depending on the threshold used—for example, WHO defines suppression as a VL of fewer than 1000 copies/mL, while other programs may use <200 or <50 copies/mL (WHO, 2016). This three-pronged approach can be an effective way of stopping the spread of HIV/AIDS (WHO, 2016; 2020b; 2021).

The 95–95–95 objective is achievable, as evidenced by several countries that have made significant progress towards achieving these targets. For instance, in Botswana in 2021, 95.1 % of PLHIV knew their status, 98.0% of those who knew their status were on ART, and 97.9 % of those on ART had suppressed VLs (Mine et al., 2022). Similarly, in Eswatini (formerly Swaziland) in the same year, 93% of PLHIV knew their status, 91% of those who knew their status were on ART, and 89 % of those on ART had suppressed VLs (UNAIDS, 2021b). However, there is still much work to be done, especially in SSA, where access to testing and linkage to treatment services is limited. Stigma and discrimination also remain significant challenges in HIV/AIDS prevention and treatment efforts (Frescura et al.? 2022; Chipanta et al., 2022).

In addition to the 95–95–95 objectives, UNAIDS has set several other ambitious targets aimed at ending the HIV/AIDS epidemic. These targets include reducing new HIV transmissions to fewer than 370,000 in 2025, reducing AIDS-related deaths to fewer than 250,000 in 2025, and eliminating HIV-related stigma and discrimination (UNAIDS, 2021c).

Achieving these targets will require sustained and coordinated efforts from governments, organizations, and individuals worldwide. However, with the right investments, policies, and programmes, the HIV/AIDS epidemic can be eradicated. This involves investing in testing and treatment services, expanding access to ART, and reducing stigma and discrimination. Additionally, it involves involving communities and empowering individuals to take charge of their health.

1.1.3. The focus on children and adolescents as vulnerable populations, in often 'high risk' populations with regard to HIV and other sexual and reproductive health issues

Children and adolescents are among the most vulnerable populations when it comes to sexual and reproductive health (SRH) issues, including HIV. Despite significant progress in the prevention and treatment of HIV, children and adolescents are disproportionately affected by the epidemic. According to UNICEF (UNICEF, 2023), 2.58 million of 39.0 million PLHIV worldwide in 2022 were children aged 0-19 years. Each day in 2022, approximately 740 children acquired HIV and approximately 274 children died from AIDS-related causes, mostly due to inadequate access to HIV prevention, care, and treatment services. Children and adolescents living with HIV also face unique challenges, including the need for lifelong treatment and the risk of stigma and discrimination (Govender et al. 2023; Jimu et al., 2021). In addition to HIV, children and adolescents are also vulnerable to a range of other SRH issues, including unintended pregnancies, sexually transmitted infections (STIs), and sexual violence (Maharaj, 2022). These issues can have significant physical, emotional, and social consequences and can impact the health and well-being of children and adolescents well into adulthood (Cowden et al., 2020).

Several factors contribute to the vulnerability of children and adolescents to HIV and other SRH issues. Biological factors, such as incomplete physical development and the

immaturity of the immune system, can increase the risk of infection and disease progression (Govender et al., 2023). Social and economic factors, such as poverty, limited access to education, and gender inequality, can also contribute to vulnerability by limiting access to information and resources (Maharaj, 2022). Cultural factors, such as traditional gender roles and norms around sexuality, can also influence behavior and attitudes toward SRH (Cowden et al., 2020; De Meyer et al., 2014). Despite the clear need for SRH services among children and adolescents, many face significant barriers to accessing these services. Stigma and discrimination can deter young people from seeking care, while legal barriers, such as age restrictions on accessing contraception, can limit their options (Nmadu et al., 2020). Lack of confidentiality and privacy can also be a concern, particularly in settings where SRH is stigmatized or taboo (Kamruzzaman et al., 2022; Nmadu et al., 2020). In addition, children and adolescents may face additional challenges in accessing SRH services due to their age and developmental stage. For example, younger children may not have the language or cognitive skills to understand HIV and SRH information, while adolescents may face unique challenges related to their evolving identities and relationships.

It is crucial to consider the unique needs and concerns of children and adolescents when designing and implementing SRH programs. These programs should be tailored, age-appropriate, and effective in addressing the underlying social and cultural factors that contribute to their vulnerability. Engaging young people directly in the development of programmes can be helpful, and services such as counseling, testing, and treatment for STIs and HIV should be made accessible and welcoming to them. HIV testing and treatment services, including pre-exposure prophylaxis (PrEP) and ART, can play a critical role in preventing new infections and improving outcomes for those living with HIV (Gill et al., 2020; Embleton et al., 2023). Starting ART as soon as children and adolescents are

diagnosed and following the treatment plan can help them live nearly normal lifestyles (WHO, 2016). Adolescents with HIV who are not consistently virally suppressed are at a higher risk of acquiring medication resistance and spreading the virus to others, which is particularly concerning given that adolescence is often the time when HIV risk behavior is highest (Dahourou et al., 2017).

1.1.4. Challenges and limitations facing pediatric and adolescent ART programmes

Globally, in 2022, there were an estimated 39.0 million [33.0 million – 45.7 million] PLHIV, of whom 2.58 million [1.91 million – 3.47 million] were under 19 years of age, and over 90 % of them lived in SSA (UNICEF, 2023). HIV is a significant threat to children and adolescents as they account for 15 % of AIDS-related mortality (UNICEF, 2021). Failure to achieve the UNAID's 95 – 95 – 95 targets for children and adolescents in SSA, where 90% of the children living with HIV reside, means that new infections will continue to rise, and HIV-related mortality will persist for decades to come (Govender and Bekker, 2021).

Pediatric and adolescent ART programmes have undergone significant developments over the years, but they still face challenges and limitations. These programmes have come a long way since their inception. One of the most significant developments has been the introduction of combination ART, which has greatly improved treatment outcomes. The WHO recommends combination ART for all children and adolescents living with HIV, regardless of their CD4 count or clinical stage (WHO, 2021). Another notable development has been the expansion of access to ART. In 2021, 52% of children under 15 years of age were receiving ART globally, which represents an increase from 43% in 2016. This has been made possible through various initiatives, such as the Global Plan towards the elimination of new HIV transmissions among children by 2015 and keeping their mothers

alive (UNAIDS, 2011). In addition, early infant diagnosis (EID) and the prevention of mother-to-child transmission (PMTCT) have been increasingly focused on. EID enables early identification of HIV-positive children, which allows for early initiation of ART and improves treatment outcomes. PMTCT interventions have also been successful in reducing the number of new HIV transmissions among children. UNICEF's global HIV response is designed to eliminate new HIV transmissions in children through expanded PMTCT programmes, testing, treatment and retention for children, adolescents and mothers to reduce HIV–related mortality, and scaling up targeted combination HIV prevention for adolescents, with strategies and targets adapted to each region and country (UNICEF, 2018).

Despite these developments, pediatric and adolescent ART programmes still face significant challenges. One of the biggest challenges is the lack of access to testing and treatment services. In SSA, many CALHIV are often diagnosed very late in the progression of the disease, and when antiretroviral treatment is started late, their immune systems may already be seriously compromised. Early pediatric screening for HIV is often not carried out because some caregivers (parents or guardians) rely solely on their child's apparent good health, and others believe that children infected during the perinatal period do not survive until the end of their childhood (Mukuku et al., 2019; Ngwej et al., 2017). Another challenge is the lack of age-appropriate formulations of ART. However, limited availability of child-friendly formulations and challenges in determining appropriate dosages based on age and weight can impact treatment options and complicate medication administration. Many CALHIV have difficulty taking adult formulations of ART, which can lead to poor adherence and suboptimal treatment outcomes. While progress has been made in developing pediatric-friendly formulations—such as granules, dispersible tablets, and fixed-dose combinations—there remains a need for wider availability and accessibility of

these age-appropriate options, especially in resource-limited settings (WHO, 2022; Schlatter et al., 2016). In addition, adherence to ART regimens is crucial for achieving VLS and preventing the development of drug resistance. However, children and adolescents may face unique adherence challenges including stigma, forgetfulness, lack of family support, or difficulty understanding the importance of long-term medication adherence. Psychologically, CALHIV may face various psychosocial challenges, including stigma, disclosure concerns, mental health issues, and adherence-related stress (Oladunni et al., 2021). It is crucial to provide adequate psychosocial support, including counseling, peer support, and interventions addressing mental health needs. However, such support may be limited in resource-constrained settings. Additionally, ALHIV undergo a transition from pediatric to adult care, which can be critical and challenging. This period is characterized by significant biological, psychological, and social changes. Transition-related challenges may include gaps in care, loss to follow-up, lack of age-appropriate services, and difficulties in adapting to a new healthcare setting (Cowden et al., 2020).

In addition, it is important to consider that, similar to adults, pediatric and adolescent populations are at risk of developing viral resistance to ART. This can lead to treatment failure and limited treatment options. To address this challenge, monitoring treatment response, conducting timely VL testing, and ensuring sustained access and adherence to existing ART regimens are crucial (Yan et al., 2022; Cissé et al., 2019; Rubio-Garrido et al., 2021).

Resource constraints, and limited healthcare resources, including diagnostic tools, medications, laboratory infrastructure, and trained healthcare workers (HCWs), can pose significant challenges to the implementation and sustainability of pediatric and adolescent ART programmes, particularly in low-resource settings (WHO, 2021).

1.1.5. Progress and challenges in HIV prevention and treatment in the Democratic Republic of the Congo

Despite progress in recent years, HIV remains a significant public health challenge in the DRC. The country faces numerous obstacles in implementing effective prevention and treatment programmes, including limited funding, weak healthcare infrastructure, and social stigma surrounding HIV. HIV prevalence rates in the DRC vary widely depending on the province and population group. According to UNAIDS (2021b), the national prevalence rate among adults aged 15 to 49 was 0.7 % in 2021. Compared to other countries in SSA, the DRC's HIV prevalence rate is relatively low. However, due to its large population and high burden of disease, the absolute number of PLHIV in the country is estimated to be 540,000 adults and children living with HIV [440,000 – 650,000] (UNAIDS, 2021b).

The DRC faces numerous challenges in implementing effective HIV prevention and treatment programmes. One major obstacle is limited funding, both from domestic sources and international donors. This has led to shortages of essential medicines and supplies, as well as a lack of trained healthcare workers. Additionally, weak healthcare infrastructure and logistical barriers such as poor transportation networks make it difficult to provide services to remote and underserved areas. Another challenge is the social stigma surrounding HIV, which can prevent people from seeking testing and treatment services (PNLS, 2021). A further challenge is a war, which has a significant impact on the DRC's HIV programme. It disrupts health services, limits access to medicines, increases vulnerability to HIV, weakens health infrastructures and leads to internal displacement or cross-border migration, exacerbating the stigma and discrimination faced by PLHIV.

Despite the significant challenges, the DRC has made progress in recent years in responding to the HIV epidemic. Collaboration between government, non-governmental organizations, and international partners has been established to support PLHIV's well-being. The government has developed a comprehensive national strategic plan, which includes focusing on key populations and increasing access to testing and treatment services (PNLS, 2020; Lillie et al., 2019).

In addition, there have been successful pilot programmes using innovative approaches such as community-based testing and self-testing kits. These programmes have helped increase testing rates and identify more PLHIV who can then be linked to care (Tonen-Wolyec et al., 2019; 2021; Izizag et al., 2018; Ingala et al., 2023; EGPAF, 2018).

One of the significant achievements of the DRC's HIV programme is the remarkable increase in access to ART. As of 2021, 82% of PLHIV in the country were receiving ART, up from just 8% in 2010. This increase in access to treatment has led to a significant reduction in AIDS-related deaths, with mortality rates falling from 0.56‰ in 2010 to 0.12‰ in 2019. Furthermore, the DRC has made considerable progress in PMTCT of HIV. In 2021, 61 % of pregnant women living with HIV received ART to prevent transmission to their babies, up from 6 % in 2010. This has resulted in a substantial decline in the number of new HIV transmissions among children, with the number of new infections dropping from 13,000 in 2010 to 6,500 in 2021 (AIDSinfo, 2021).

According to a 2022 report by Médecins Sans Frontières (MSF), the Democratic Republic of the Congo (DRC) has made progress in addressing HIV/AIDS, but significant challenges persist. MSF opened the country's first outpatient treatment center providing free care to people living with HIV (PLHIV) in Kinshasa in May 2002. At that time, the situation was critical: over one million Congolese men, women, and children were living

with HIV, but antiretroviral therapy (ART) was both scarce and unaffordable (MSF, 2022). UNAIDS estimated that, in the early 2000s, AIDS-related deaths ranged from 50,000 to 200,000 annually (UNAIDS, 2002).

Since then, ART coverage has improved, and AIDS-related mortality has declined. In 2021, an estimated 540,000 people were living with HIV in the DRC, of whom approximately 82% knew their status, and 82% of those were receiving ART (UNAIDS, 2021b). However, around one-fifth of PLHIV still lacked access to treatment, and 14,000 AIDS-related deaths were reported that year. Despite progress, VLS data remain limited, particularly among children.

National data reveal striking disparities in ART coverage by age group. While 88% of adults aged 15 and older living with HIV were receiving ART, only 38% of children under 15 had access to treatment (PNLS, 2021). A study by Shah et al. (2021) analyzing data from 241 CDC-funded HIV/AIDS clinics in Kinshasa and Haut-Katanga provinces found that children under 15 years of age had significantly higher mean VLs compared to those aged 15 and older ($p < 0.001$).

By the end of 2021, approximately 63,000 children in the DRC were living with HIV, yet only 38% were receiving ART. This low coverage resulted in an estimated 6,500 new pediatric infections and 4,300 AIDS-related deaths in children under 15 (UNAIDS, 2021b). Viral load suppression among children remains alarmingly low. According to the PNLS (2021), only 11% of children on ART showed evidence of VLS. This was the first nationally reported VLS rate since the WHO recommended routine VL monitoring in 2016.

1.1.6. Financing HIV programs in the Democratic Republic of the Congo: donor role and impact on health systems strengthening

For more than two decades, the Democratic Republic of the Congo has made significant progress in the fight against HIV, thanks to the commitment of international donors. Among the key players in this fight, the Global Fund to fight AIDS, Tuberculosis and Malaria, as well as the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), play a crucial role. These two institutions have enabled the DRC to strengthen its health systems, improve access to care, and reduce the HIV epidemic, although challenges persist in some regions and for certain vulnerable populations.

The DRC, a country with a population of over 90 million, has a high burden of HIV, with an estimated 540,000 PLHIV (range: 440,000 – 650,000) (UNAIDS, 2021b). Despite strides in controlling the epidemic, significant challenges persist in the prevention, treatment, and care of PLHIV. The HIV pandemic profoundly impacts public health and local economies, exacerbated by factors like poverty, population mobility, armed conflict, and limited access to care in remote areas. International donors, notably PEPFAR and the Global Fund to fight AIDS, Tuberculosis and Malaria, have played a crucial role in supporting the DRC's endeavors in this realm. Their funding has facilitated the expansion of access to ART, promotion of prevention strategies, and enhancement of health systems through innovative initiatives (PEPFAR, 2022; Global Fund, 2022).

The Global Fund, which funds programmes to fight HIV, tuberculosis and malaria, plays a leading role in the fight against HIV in the DRC. Since the country joined this initiative in 2003, the DRC has been able to benefit from considerable funding to strengthen its health infrastructure, improve access to treatment and expand the coverage of prevention programmes. One of the major successes of this support is the increase in antiretroviral

treatment coverage. In 2010, only 8% of PLHIV had access to these treatments, a percentage that has increased significantly to 75% in 2020 (Global Fund, 2022). Global Fund to fight AIDS, Tuberculosis and Malaria funding has also helped improve drug stockpile management, develop training programs for health workers, and increase coverage of HIV testing services. These efforts have contributed to a significant reduction in the number of new HIV infections and deaths. Between 2010 and 2020, the number of AIDS-related deaths fell by 60%, and new infections fell by 66%, representing remarkable progress in controlling the epidemic (Global Fund, 2022). However, despite these advances, the Global Fund to fight AIDS, Tuberculosis and Malaria emphasizes the need to strengthen care for the most vulnerable groups, such as children, adolescents and key populations such as sex workers and men who have sex with men. Reducing stigma and discrimination, as well as improving services for these groups, remain priorities in the fight against HIV in the DRC (Global Fund, 2022).

The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) is a significant contributor to the HIV response in the Democratic Republic of the Congo (DRC). Since its inception in 2007 in the DRC, PEPFAR has allocated over $900 million towards HIV prevention, treatment, and care programs. This support has enabled more than 5 million Congolese individuals to access HIV testing services and assisted over 200,000 PLHIV in initiating ART (PEPFAR, 2022). These initiatives have resulted in a notable decrease in HIV-related mortality and have propelled progress towards achieving the UNAIDS target of 95-95-95 by 2030. In its ongoing commitment, PEPFAR actively engages with the National AIDS Control Program (PNLS) and implements strategic programs focused on attaining epidemic control in key provinces like Haut–Katanga, Lualaba, and selected health zones in Kinshasa, which collectively account for approximately 50% of all PLHIV in the DRC. The PEPFAR Country Operational Plan (COP) strategy for the period

spanning October 1, 2022, to September 30, 2023 (COP 2022), upholds the programmatic priorities established in COP 2021, with a particular emphasis on expanding and reinforcing people-centric interventions to hasten epidemic control in these provinces. The positive trajectory observed in Haut-Katanga and Lualaba underlines progress towards epidemic control, prompting additional allocation of resources and efforts in these regions during COP22 (PEPFAR, 2022). Concurrently, PEPFAR/DRC continues to advance towards the 95-95-95 target in Haut-Katanga and Lualaba, while enhancing services and optimizing case identification in Kinshasa. Special attention is directed towards identifying men, adolescent girls, young women, and children living with HIV. Overall, PEPFAR is implementing saturation efforts across 57 health zones and multiple military sites, encompassing over 600 health facilities. The estimated total number of PLHIV in PEPFAR-supported health zones stands at 374,371 (PEPFAR, 2022). Through collaborative efforts with the Congolese government and civil society, ambitious yet attainable objectives were established for COP22, resulting in an additional 78,872 individuals initiating antiretroviral treatment by September 2023. Aligned with global priorities, including the Global Fund's strategy to combat HIV, Tuberculosis, and Malaria, PEPFAR, through its Vision 2025 strategy, aims to reduce new infections with a specific focus on vulnerable populations like girls and women. It also enhances prevention of mother-to-child transmission programs and services for children living with HIV (PEPFAR, 2022). Additionally, PEPFAR's strategy in the DRC centers on fortifying health systems by enhancing data collection, improving care quality, and promoting community-led solutions. By prioritizing sustained care for PLHIV and addressing obstacles related to social and economic disparities—such as stigma, discrimination, and gender inequality—PEPFAR actively contributes to a more inclusive and efficient HIV response in the DRC (PEPFAR, 2022; Kim, 2022).

Funding from the Global Fund to fight AIDS, Tuberculosis, and Malaria and PEPFAR makes it possible to ensure free prevention, screening, treatment and follow-up services for PLHIV in the DRC. This free access is essential to remove economic barriers and promote adherence to ART, thus contributing to the achievement of the UNAIDS 95-95-95 targets by 2030 (PEPFAR, 2022; Global Fund, 2022). Targeted testing, indexed, and community testing campaigns have enabled millions of Congolese to know their HIV status. With this funding, PLHIV have free access to ART, thereby reducing HIV-related morbidity and mortality. These efforts are reinforced by regular viral load monitoring and the adoption of differentiated models of care, such as multi-month dispensing of ART and treatment self-management, thus improving patient adherence and management (PEPFAR, 2022; Global Fund, 2022).

However, recent funding cuts to PEPFAR by the U.S. government have raised serious concerns about the sustainability of HIV program achievements in the DRC. The reduction in financial support could significantly undermine essential interventions, including ART provision, viral load monitoring, and community-based initiatives targeting vulnerable populations. As a pillar of the national HIV response, PEPFAR's budgetary constraints risk reversing progress toward epidemic control, particularly in high-burden provinces such as Kinshasa, Haut-Katanga, and Lualaba. Additionally, these funding uncertainties threaten the expansion of differentiated service delivery models, which have played a crucial role in enhancing ART adherence. To address these challenges, the Congolese government and its partners must explore alternative funding mechanisms and intensify advocacy efforts to sustain critical HIV services and safeguard the progress made over the past two decades.

1.1.7. Democratic Republic of the Congo's HIV programme for children and adolescents

The state of the DRC's HIV programme, especially for children and adolescents, has been challenging, but efforts have been made to address the epidemic. While progress has been made in some areas, the DRC still faces significant barriers compared to the accomplishments of other SSA countries. In the country, many children living with HIV are not diagnosed until they are already very sick, making it more difficult to provide effective treatment (Mukuku et al., 2019; Ngwej et al., 2017). Due to limited access to comprehensive sexual education and a lack of awareness among young people, prevention programmes targeting CALHIV in the DRC have faced obstacles. The prevalence of child marriage and early sexual initiation contributes to the vulnerability of adolescents to HIV acquisition. Limited access to prevention tools such as PrEP further hampers the prevention efforts for this population. Several African countries, including Tanzania (Kidman et al., 2020), South Africa (Gill et al., 2020; George et al. 2022), and Kenya (Embleton et al., 2023), have implemented successful prevention programmes targeting young people, leading to a decline in HIV incidence in this population. A recent study showed that South African adolescent girls and young women aged 15 to 24 years who accessed three or more DREAMS (Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe)-like interventions were more likely to have undergone HIV testing (Adjusted odds ratio = 2.39; 95% CI: 2.11 – 2.71) and to have used condoms consistently in the previous 12 months (Adjusted odds ratio = 1.68; 95% CI: 1.33 – 2.12) than those who were not exposed to any interventions (Govender et al., 2022).

Efforts should be made to increase awareness and education to reduce HIV stigma and discrimination among CALHIV, and promote testing and treatment (Ngwej et al., 2017). However, accessing HIV services is challenging, especially for those living in remote areas,

due to inadequate healthcare facilities and limited availability of testing and treatment centers. Pediatric HIV testing and treatment services are not as widely available as needed, resulting in many undiagnosed and untreated cases among CALHIV. Attrition is a significant challenge for HIV-positive children and adolescents in ART programmes, and low pediatric treatment coverage exacerbates the HIV/AIDS situation among them (Ditekemena et al., 2014). Stigma and discrimination against PLHIV, including children and adolescents, create additional barriers to accessing testing and treatment services (Ngwej et al., 2017). Many SSA countries have scaled up access to pediatric HIV testing and treatment services, ensuring that a higher proportion of CALHIV receive the necessary care. Countries like Malawi (MacKenzie et al., 2017), Cameroon, and Zambia (Dougherty et al., 2021; van Dijk et al., 2014; Sutcliffe et al., 2023) have made significant progress in providing ART to children, resulting in improved health outcomes. Similarly, the age of introducing disclosure of HIV status to the child is 12 years in the DRC, 7 years and over in Zambia, 8 to 10 years in Tanzania, 10 years in Lesotho, 11 years in Malawi and Rwanda (EGPAF, 2018a).

Integrating HIV services with other healthcare services has been challenging due to weak health systems and health services fragmentation (Whembolua et al., 2019; Shah et al., 2021; Bulstra et al., 2021). Coordinated efforts to address the unique needs of children and adolescents, including psychosocial support, reproductive health, and mental health services, are essential but often lacking. However, some African countries have implemented successful community-led initiatives to address the unique needs of PLHIV, reducing stigma and improving access to services. For example, community-based organizations and support groups in countries like Mozambique (Pfeiffer et al., 2010), Kenya (Odeny et al., 2013), and Rwanda (Price et al. 2009) play a vital role in providing psychosocial support, education, and advocacy for CALHIV.

1.1.8. Conceptual framework on determinants of HIV viral suppression in children and adolescents

Over the past few decades, HIV/AIDS has emerged as one of the most severe global health challenges, particularly impacting SSA, where the disease burden is the greatest (WHO, 2023). The widespread introduction of ART has dramatically shifted the outlook, transforming HIV from a fatal illness into a manageable chronic condition (Kumah et al., 2023). The main objective of ART is to achieve VLS to undetectable levels, a step that not only improves the health and longevity of PLHIV but also eliminates the risk of viral transmission to others, as demonstrated by the Partner Study (Rodger et al., 2019). However, despite substantial progress in expanding ART access, ensuring consistent VLS remains a challenge, particularly among CALHIV in SSA (UNAIDS, 2014; 2023). Current data indicate that a large majority of PLHIV achieve VLS within six months of starting ART, provided that they adhere strictly to their ART regimen (Hoenigl et al., 2016; Dorward et al., 2020). In cases where VLS is not achieved within the first six months of ART, seven out of ten PLHIV are able to achieve VLS later on with enhanced support for ART adherence (Beja et al., 2022; Bonner et al., 2013). CALHIV experience lower rates of VLS due to various obstacles in adhering to treatment (Khamadi et al., 2023; Quaker et al., 2024). In SSA, where about 85 % of all CALHIV live, the inability to meet the 95 – 95 – 95 goals will likely result in continued HIV-related deaths and new infections for many years (Govender and Bekker, 2021).

USVL among CALHIV in SSA present a significant public health concern. In 2022, around 100,000 children and adolescents succumbed to AIDS-related causes, primarily affecting those under 10 due to inadequate access to HIV prevention, care, and treatment services (UNAIDS, 2023). Attaining VLS in CALHIV is crucial not only for individual

health outcomes but also for curbing HIV transmission and advancing towards the UNAIDS targets. The WHO has emphasized the necessity of providing comprehensive counseling on adherence to ART for individuals with USVL, highlighting the ongoing need for adherence support (UNAIDS, 2023).

Data on VLS among CALHIV are scarce in the DRC. Moreover, studies in SSA have shown varying rates of VLS among ALHIV across countries, ranging from 15.89% in Tanzania (Khamadi et al., 2023) to 51.28% in Nigeria (Isaac et al., 2020). Studies indicate that CALHIV face higher rates of virological failure and poorer treatment outcomes compared to adults, largely due to developmental changes, stigma, and discrimination (Han et al., 2021). Several studies conducted among CALHIV receiving ART have identified various factors that predict USVLs. In SSA, factors such as the burden of daily pill-taking, fear of stigma, lack of psychosocial support, and systemic barriers like limited access to healthcare services intensify these challenges (Madiba et al., 2019; Biadgilign et al., 2009). For example, research from Tanzania has shown that perceived stigma and fear of unintentional disclosure of HIV status significantly hinder achieving suppressed VL among CALHIV (Ally et al., 2023; Bitwale et al., 2021). Other factors, including sociodemographic factors such as younger age, male gender, educational level, orphan status, and rural residence; clinical factors such as poor nutritional status, low CD4+ T-cell count, advanced WHO staging, presence of opportunistic infections, history of tuberculosis, and poor adherence to treatment; ART regimen factors such as side effects, dosing frequency, nevirapine-based treatment, drug substitution, and treatment duration; health service factors such as access to ART services, availability of medication, relationship with health care providers, and quality of services delivery; and behavioral and socioeconomic factors such as poverty, social support, stigma, discrimination, religion, traditional health-seeking behavior, non-disclosure of HIV status, retention in care, and

adherence to ART (Bitwale et al., 2021; Davey et al., 2018; Desta et al., 2020; Gordon et al., 2022; Mchomvu et al., 2022; Mukumbang et al., 2017; Nglazi et al., 2012; Van Wyk et al., 2020; Shumetie et al., 2021; Okonji et al., 2021; Quaker et al., 2024; Somi et al., 2021; van Liere et al., 2021).

In Lubumbashi, DRC, achieving VLS among CALHIV remains a significant public health challenge. This issue is not unique to the DRC but is prevalent even in many low- and middle-income countries, including urban settings like Lubumbashi. Here, CALHIV face multiple barriers to effective HIV care, such as limited access to well-equipped health facilities, inadequate treatment adherence support, and pervasive stigma and discrimination within both healthcare settings and the broader community (Mukuku et al., 2024; Ngwej et al., 2017). These factors collectively hinder their ability to achieve and sustain viral suppression.

HIV viral suppression is influenced by multiple factors as depicted in the conceptual framework in Figure 1.1. These factors vary according to demographic characteristics, geographical setting, and health system dynamics, and therefore, it is necessary to investigate the factors influencing VLS among CALHIV in different contexts.

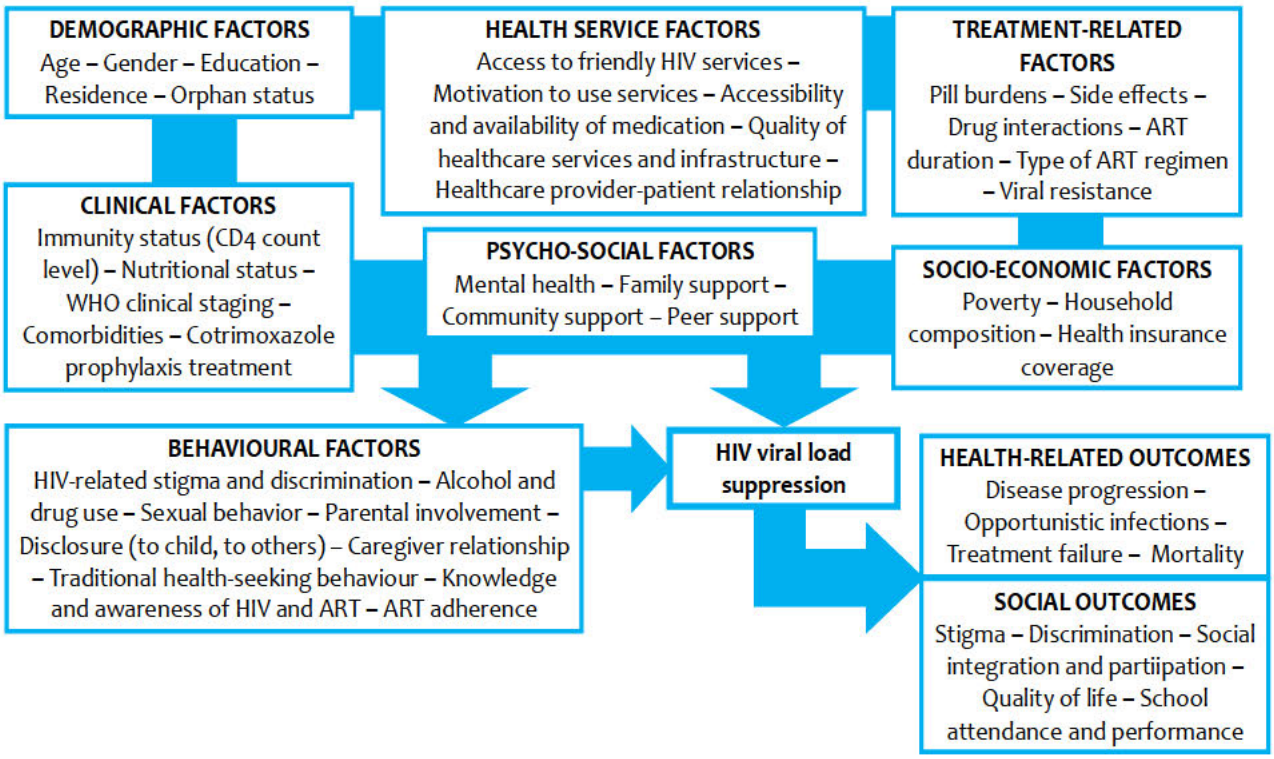

Figure 1.1 Conceptual framework on factors associated with HIV viral load suppression in children and adolescents

1.2. Statement of the problem

VLS is a key therapeutic goal and biological marker of ART effectiveness, directly linked to reduced HIV-related morbidity, mortality, and transmission. While countries across SSA face challenges in achieving VLS among CALHIV, recent data suggest that the DRC may face more acute and unique challenges. Notably, only 11% of HIV-positive children on ART in the DRC show evidence of viral suppression, according to the DRC's National HIV/AIDS Programme (PNLS, 2021). This rate is significantly lower than those observed in many other SSA countries and may reflect systemic issues within the national ART program for CALHIV.

Understanding why the DRC lags so far behind in this regard may offer a clearer window into the structural and contextual barriers to achieving VLS—barriers that may be less

visible in countries where overall ART program performance is stronger. Yet, despite this troubling gap, there is limited published research on ART outcomes among CALHIV in the DRC. The few available studies focus primarily on PMTCT interventions, HIV disclosure, adherence, or HIV-TB coinfection, but not specifically on VLS or its determinants.

Given this gap, it is critical to explore both the extent of USVL and the factors influencing it among CALHIV in Lubumbashi. This city provides a strategic setting for investigating broader ART program failures, and the study will also help assess the validity and reliability of PNLS-reported data. While there are similarities between the challenges observed in Lubumbashi and those documented elsewhere in SSA—such as adherence difficulties and health system limitations—the extreme disparities in VLS suggest a potentially more fragile health infrastructure and unmet needs in the DRC. This study aims to investigate these issues and identify actionable determinants, barriers, and facilitators that can guide more tailored and effective ART interventions for CALHIV.

1.3. Research questions

As part of this research project, we aim to investigate the determinants, barriers, and facilitators of VLS in CALHIV, which remains a critical challenge in achieving the third 95% target of the UNAIDS 95-95-95 goals, particularly in SSA and the DRC.

The specific research questions are:

- What is the prevalence of USVL among CALHIV on ART in Lubumbashi, DRC?
- What are the specific factors associated with USVL among CALHIV on ART in Lubumbashi, DRC?

- What are the primary barriers experienced by ALHIV in achieving VLS in Lubumbashi, DRC?
- What factors facilitate VLS among ALHIV in Lubumbashi, DRC?

1.4. Hypotheses

The following are the hypotheses of the study:

- The prevalence of USVL among CALHIV on ART in Lubumbashi, DRC, is comparable to or even exceeds that observed in other SSA settings, reflecting both shared and context-specific challenges, contributing to the failure to achieving the third 95% target of the UNAIDS 95-95-95 goals.
- Key risk factors such as poor ART adherence, advanced HIV clinical stages, caregiver characteristics, and socio-economic factors significantly increase the risk of USVL among CALHIV in Lubumbashi, DRC.
- Barriers such as stigma, limited psychosocial support, and inadequate healthcare access hinder VLS, while facilitators including adherence counseling and strong social support promote successful VLS among ALHIV in Lubumbashi, DRC.

1.5. Study aims and objectives

The primary aim of this study is to investigate the prevalence and determinants of USVL among CALHIV in Lubumbashi, DRC, and to identify the barriers and facilitators that influence VLS in this population.

The objectives of this study were:

- To determine the prevalence of USVL among CALHIV on ART in Lubumbashi, DRC.

- To identify the specific factors associated with USVL among CALHIV in Lubumbashi, DRC.
- To explore the primary barriers that prevent ALHIV from ART-adherence and achieving VLS in Lubumbashi, DRC.
- To identify the factors that facilitate ART-adherence and achieving VLS among ALHIV in Lubumbashi, DRC.

1.6. Organization of the thesis

This thesis is divided into six chapters.

Chapter one provides an introduction giving an overview of the Global Health Security Agenda, the UNAIDS 95-95-95 targets, the vulnerability of CALHIV, the challenges of HIV programmes for CALHIV, and the current status of HIV programmes in the DRC. This chapter also outlines the research questions, the purpose and specific objectives of this study.

Chapter two presents a systematic review and meta-analysis on the magnitude and factors associated with VLS among CALHIV globally, in the SSA countries.

Chapter three provides a description of the study's methodology which will outline the design, site, and population study, and sampling method used, the collection method and analysis of data. This section will also explain the strategies that were implemented in the study to improve the validity and reliability of the results. The ethical considerations will be presented in the last section of this chapter.

Chapter four presents the findings from our fieldwork and is divided into two main sections. The first section covers the quantitative analysis of VL testing and VLS, establishing baseline estimates of VLS among CALHIV (aged 0 to 19 years) on ART in

Lubumbashi. The second section focuses on the qualitative study, exploring the perceived facilitators and barriers to achieving VLS and maintaining ART adherence among ALHIV (aged 13 to 19 years) on ART in Lubumbashi.

Chapter five focuses on the discussion of the study findings, comparing these findings to the results of other related and similar studies in the literature and using this existing body of knowledge to help explain the findings. The study limitations are presented in the last section of this chapter.

Chapter six presents the study's conclusions and recommendations drawn from the research findings.

CHAPTER TWO

MAGNITUDE AND CHARACTERISTICS OF UNSUPPRESSED HIV VIRAL LOAD IN CHILDREN AND ADOLESCENTS ON ANTIRETROVIRAL THERAPY IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

2.1. Introduction

The scourge of HIV/AIDS has been one of the most daunting health challenges of the past few decades (WHO, 2024). Despite the grim outlook in the early years of the epidemic, the introduction and subsequent widespread availability of ART has been a game-changer, transforming HIV from a death sentence into a chronic condition that can be managed effectively with the right treatment and care. This medical breakthrough has extended the lifespans and improved the quality of life for millions of people across the globe (Kumah et al., 2023). However, the struggle against HIV/AIDS is far from over, particularly in SSA, which bears the heaviest burden of the disease. The region is home to approximately two-thirds of the world's HIV-positive population, highlighting the critical importance of effective ART management in these countries (UNAIDS, 2024).

In 2023, of the 39.9 million PLHIV globally, 1.4 million [1.1–1.7 million] were children under 15 years old. SSA accounted for approximately 66% of all HIV cases and 85% of CALHIV worldwide. Around 590,000 [430,000–920,000] children aged 0–14 years living with HIV did not have access to ART in 2023 (UNAIDS, 2024). ART coverage among adults aged 15 years and older was 77% [62–90%], but only 57% [41–75%] among children, with even lower viral load suppression (VLS) rates: 48% [39–60%] for children compared

to 73% [66–81%] for adults. The persistent gaps in early diagnosis and access to effective treatment led to approximately 76,000 [53,000–110,000] child deaths in 2023, with 73% of these occurring in children under 10 years old. Despite representing just 3% of PLHIV, children accounted for 12% of all HIV-related deaths (UNAIDS, 2024).

The 95%-95%-95% UNAIDS strategic objective, aimed at ending the HIV transmission by 2030, seeks to ensure that 95% of PLHIV know their status, 95% of those who know their status are on ART, and 95% of those on ART have suppressed VLs (UNAIDS, 2014). The rapid expansion of ART availability in SSA is a commendable achievement, yet its potential impact is undermined when patients fail to achieve or maintain VLS (Nash et al., 2018; Teasdale et al., 2020). VLS is the primary goal of ART, as it not only improves the health outcomes for the individual but also reduces the risk of HIV transmission to others. Despite these benefits, USVLs remain a significant problem, particularly among CALHIV on ART in SSA (Gordon et al., 2022; Djiyou et al., 2023; Nabukeera et al., 2021; Mageda et al., 2023). This public health issue not only threatens the lives of the individuals affected but also poses a risk to the broader goal of controlling and eventually eradicating HIV/AIDS. Failure to achieve the UNAID's 95-95-95 targets for CALHIV in SSA, where 85% of the children living with HIV reside, means that new infections will continue to rise, and HIV-related mortality will persist for decades to come (Govender and Bekker, 2021). Understanding the prevalence of USVL and identifying contributing factors are vital for shaping healthcare policy, improving clinical management, and designing public health interventions. Our systematic review synthesizes existing evidence on these determinants, addressing a crucial knowledge gap. This is particularly important for children and adolescents, who face unique challenges with lifelong ART, including stigma and discrimination (Govender et al., 2023; Jimu et al. 2021).

Therefore, this review aimed at, first, determining the meta-analyzed prevalence of USVL among CALHIV on ART in SSA, and second, examining the factors contributing to this magnitude of USVL at a regional level. The expected benefits of this systematic review are numerous.

2.2. Methods

2.2.1. Steps followed and Protocol registration

The nine steps outlined by Higgins *et al.* (2022) were followed for this systematic review (Figure 2.1). These include: (1) formulating review questions, (2) defining inclusion and exclusion criteria, (3) preparing the protocol, (4) locating studies and developing search strategies, (5) selecting studies to include, (6) assessing risk of bias or study quality, (7) collecting data, (8) analyzing and presenting results, and (9) interpreting results.

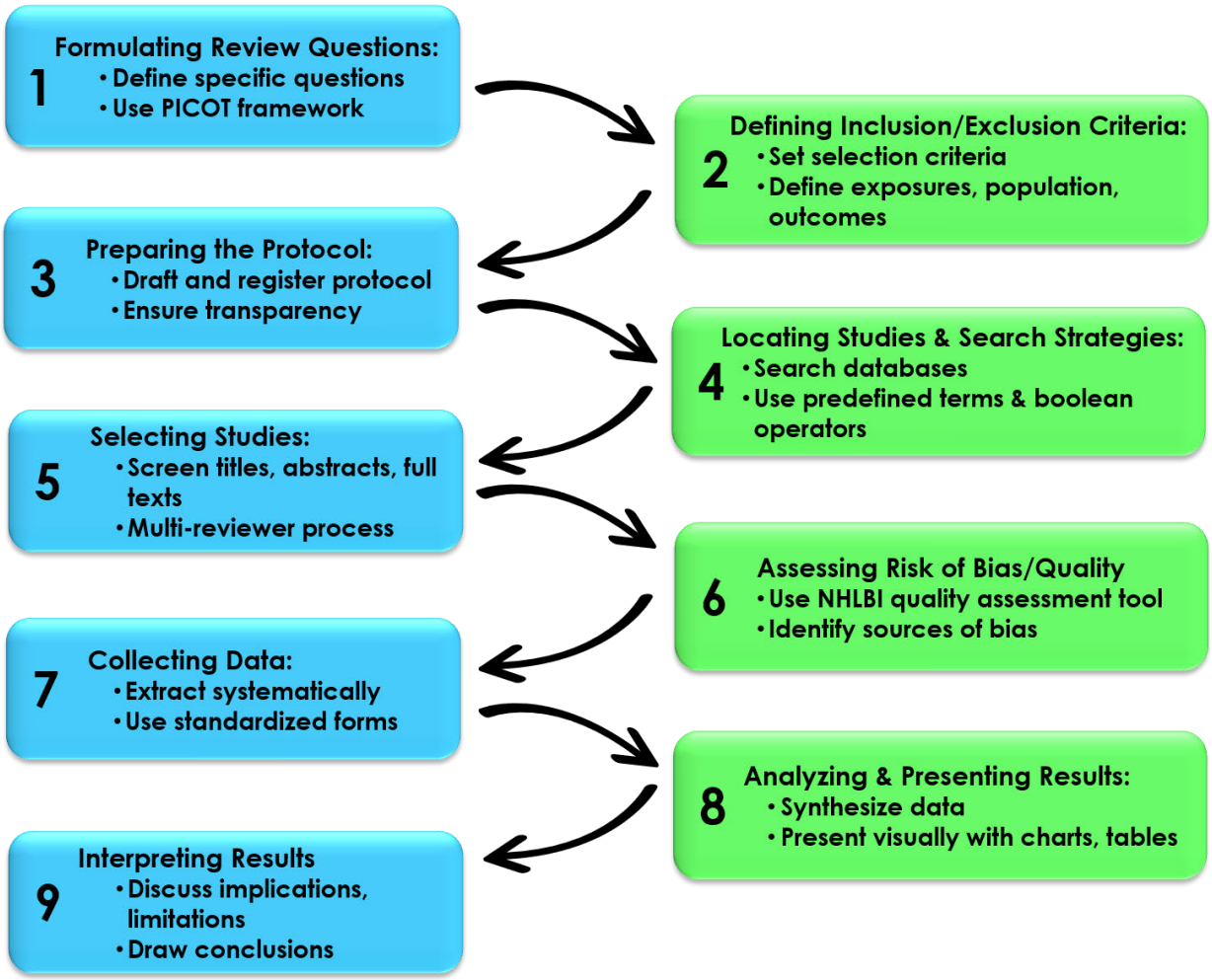

Figure 2.1 Systematic review process flowchart with key steps.

The study protocol is registered on the Prospero website (CRD42023451212, see APPENDIX F) prior to data extraction, and the review complies with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Page et al., 2021).

2.2.2. Eligibility criteria and information sources

The literature search followed these criteria: (1) Published studies in peer-reviewed journals and grey literature; (2) Study population included HIV-positive children and adolescents (< 20 years) on ART; (3) Reported associations between risk factors and VLS, using the WHO-defined threshold of < 1,000 copies/mL (WHO, 2023), with VL measurements

assessed at least six months after the initiation of ART to ensure that the evaluation of viral suppression reflects the effects of long-term treatment adherence and efficacy; (4) All studies from SSA (2010 – 2024).

The exclusion criteria included studies focused solely on adults, publications before 2010, reviews, case reports, editorials, letters, and conference abstracts. Additionally, studies that used viral load (VL) thresholds inconsistent with the WHO definition of viral load suppression (VLS), i.e., <1,000 copies/mL, were excluded. This included studies defining unsuppressed viral load (USVL) using alternative cutoffs such as ≥80, ≥400, ≥500, or ≥5,000 copies/mL (Puga et al., 2016; Dow et al., 2014; Van Dijk et al., 2011; Nsanzimana et al., 2019). Studies combining data for adults and children were also excluded. Discrepancies between reviewers were resolved through full-text evaluation. In cases of missing data, two email attempts were made to contact corresponding authors before excluding the study.

2.2.3. Search strategy

This systematic review identifies relevant studies on VLS. The search was conducted across multiple electronic bibliographic databases, including Web of Science, Google Scholar, Scopus, PsycINFO, Embase, PubMed/ MEDLINE, EBSCOhost Research Databases, and Wiley Online Library. Grey literature and manual searches were also conducted to find unindexed/ not published/ researched articles on the topic. All publications that report on VLS in HIV-positive children and/or adolescents were considered.

All studies meeting the defined inclusion criteria and published between January 2010 and April 2024 were searched in the designated databases. The search procedure was tested and refined by conducting a database search using the search syntax, which was then replicated and modified as required for the other database searches. The search employed

a list of relevant keywords and concepts as well as the relevant "AND" and "OR" Boolean operators to obtain full-text articles. The search terms consisted of "children", "infant", "adolescents", "HIV-positive", "antiretroviral therapy", "viral load", "suppression", "unsuppressed", "virological failure", "risk factors", "determinants", and "predictors". The search strategies used for the selected databases are provided in the online supplementary material titled "ALL Database search Results" (for full search terms see APPENDIX L).

2.2.4. Study selection

This systematic review considered studies conducted globally but with specific geographic restrictions limited to SSA countries. The screening, selection, and reporting of this review followed the PRISMA Protocol 2020 guidelines. Only quantitative studies (cohort, case-control, and cross-sectional) were included in this review. The identified studies were compiled and imported into Covidence, an online software tool. Covidence was used to manage the references, track the number of hits for each article from all databases, and identify and remove duplicate records.

We conducted data searches from November 1st, 2023 to April 30th, 2024, with an update in November 30th, 2024 to include any new publication. This timeframe included repeat searches to account for articles published after the initial search.

Each reference and abstract retrieved was independently examined and selected by two investigators. Any disagreement between the reviewers' decisions was resolved through discussion. The full texts of potentially eligible studies were retrieved and assessed for inclusion criteria using a PRISMA 2020 flow diagram to document the selection process. The two reviewers independently evaluated the full texts of the selected publications to

determine eligibility for the final analysis. In case of discrepancies, a third qualified reviewer was consulted to resolve disagreements regarding study inclusion or exclusion.

2.2.5. Quality assessment, risk of bias, and data extraction in individual studies

We appraised the methodological quality of the studies included in this systematic review and meta-analysis using the Joanna Briggs Institute (JBI) critical appraisal tool (Munn et al., 2023). Two reviewers independently assessed each study using JBI's structured checklist, marking each item as "Yes", "No", or "Unclear". Discrepancies were resolved through discussion, with assistance from a third reviewer when necessary. Each item received a score: 1 point for "Yes", 0 for "No", and "Unclear" as noted. These scores were converted to a percentage to classify the risk of bias as follows: studies scoring ≤ 49% were considered to have a high risk of bias, those scoring between 50% and 69% were categorized as having a moderate risk of bias, and studies scoring above 70 % were classified as having a low risk of bias. We included only studies with a moderate or low bias risk, defined as scores of 50 % or higher.

We used a Microsoft Excel matrix for data extraction, capturing details such as author, study year, location, objective, design, population, sample size, exposure factors, methods, outcomes, and findings. In longitudinal studies, only one VL measurement taken at 6 months of ART was included in the analysis to ensure that each participant contributed only once to the meta-analysis, thereby preventing inflation of the sample size due to repeated measures. During data extraction, we carefully recorded and incorporated the adjusted variables from each study to account for confounding and ensure a more accurate representation of the associations with VLS. USVL prevalence and associated risk factors were documented, and data quality was verified against published sources, with attempts to reach out to authors for clarifications.

2.2.6. Statistical analysis

Abstracted data were saved in Microsoft Excel (MS Office 2019) and then exported to Stata 16 (Stata Corp., College Station, TX, USA) for meta-analysis. The event and non-event counts were extracted from the various studies to obtain the meta-analyzed prevalence and odds ratios reported in this review. A random-effects model using the STATA command 'meta' was applied to estimate the meta-analyzed prevalence and risk factors associated with USVL among CALHIV. Significant associations with USVL were reported using a meta-analyzed odds ratio (OR) with 95 % confidence intervals (95 % CIs). Forest plots were used to display the meta-analyzed prevalence of USVL and its associated factors, along with 95 % CIs.

Subgroup analysis was conducted by study sub-region, study design, and study age group to examine variations in the meta-analyzed prevalences. For the meta-analysis of studies on risk factors for USVL, we applied the random-effects model using the Hartung-Knapp-Sidik-Jonkman method to ensure a more accurate estimation of between-study heterogeneity (Röver et al., 2015; IntHout et al., 2014). Heterogeneity across studies was quantified using the I^2 statistic, where values of 25 %, 50 %, and 75 % indicated low, moderate, and high heterogeneity, respectively. A p-value less than 0.05 from Cochrane's Q test was used to determine the presence of significant heterogeneity.

For the assessment of publication bias, we applied a logit transformation of the prevalences to stabilize variance and improve normality, followed by a visual inspection using a funnel plot and statistical evaluation with Egger's regression test, where a p-value < 0.05 indicated significant publication bias. We included a total of 52 studies in the assessment of publication bias.

2.3. Results

2.3.1. Search results

The search strategy yielded a total of 8,101 articles from Web of Science, 1,820 from Google Scholar, 1,070 from Scopus, 930 from PsycINFO, 601 from Embase, 419 from PubMed, 151 from EBSCOhost Research Databases, 29 from Wiley Online Library, and 20 from grey literature. After removing 2,082 duplicate articles and using the online software Covidence to identify 7,500 articles as ineligible, 3,559 articles remained.

Of these, 3,470 articles were excluded, leaving 89 articles for full-text review. Among these, 2 articles could not be retrieved, 21 were excluded due to incorrect outcome measures, 11 were excluded due to an incorrect study population, and 2 were excluded due to an inappropriate study design (APPENDIX O). Ultimately, 52 articles were included in this systematic review and meta-analysis to estimate the burden of unsuppressed viral load and its associated factors among children and adolescents living with HIV on antiretroviral therapy in sub-Saharan Africa (Figure 2.2).

2.3.2. Reliability between data extractors

During the data extraction process, we noted variations in the data extracted by different team members. These discrepancies, which could arise from differences in interpretation or approach, were carefully addressed through collaborative discussions among the data extractors. Each variation was critically examined, and through these deliberations, a consensus was reached regarding the most accurate and reliable data representation. Once agreement was achieved, the data was thoroughly reviewed and analyzed, ensuring consistency and minimizing the potential for bias in the subsequent analysis. This rigorous process helped ensure the robustness and reliability of the findings.

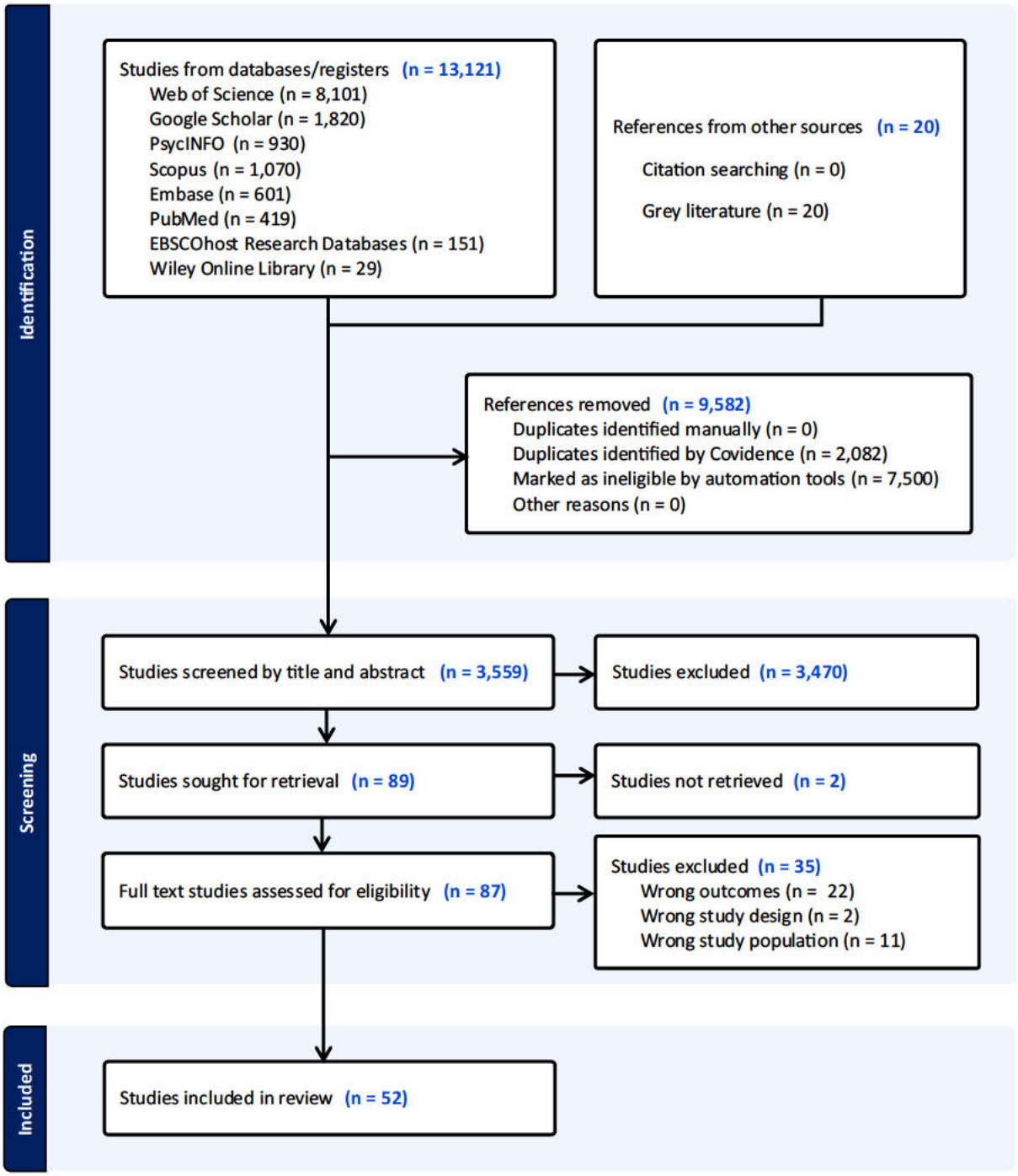

Figure 2.2 PRISMA 2020 flow diagram of studies included to estimate meta-analyzed prevalence of USVL among children and adolescents living with HIV on antiretroviral therapy in Sub-Saharan Africa.

2.3.3. Included studies' characteristics

Among the 52 studies included in this systematic review (Table 2.1), the geographical distribution of the sub-regions of SSA is as follows: Eastern Africa represents the majority of the studies with 29 articles, followed by Southern Africa with 14 articles. Western Africa is represented by 5 studies, while Central Africa includes 5 studies. Eleven studies were from Ethiopia (Sibhat et al., 2020; Mena et al., 2023; Bayleyegn et al., 2021; Abera et al., 2023; Shumitie et al., 2021; Tafere et al., 2023; Shiferaw et al., 2019; Osman & Yizengaw, 2020; Getawa et al., 2021; Fenta et al., 2021 ; Berihun et al., 2023), nine from Tanzania (Mageda et al., 2023; Muri et al., 2017; Bitwale et al., 2021; Khamadi et al., 2023; Ally et al., 2023; Mchomvu et al., 2022; Quaker et al., 2024; Mushy et al., 2024), six in Kenya (Kadima et al., 2018; Tsikhutsu et al., 2022; Gachoka & Njoroge, 2024; Kabogo et al., 2017; Mwangi & van Wyk, 2021; Onyango et al. 2023), five in Cameroon (Djiyou et al., 2023; Ndongo et al., 2024; Soudebto et al., 2024; Fokam et al., 2021; Mbébi-Enoné et al., 2023), four studies in South Africa (Teasdale et al., 2018; Mabizela & van Wyk, 2022; Elashi et al., 2022; Okonji et al., 2021), three studies in Zimbabwe (Simms et al., 2021; Jackson et al., 2022; Makadzange et al., 2015), Malawi (Jackson et al., 2022; Tweya et al., 2020; Bacha et al., 2022), Uganda (Bacha et al., 2022; Gordon et al., 2021; Nabukeera et al., 2021), and Nigeria (Mugo et al., 2023; Isaac et al., 2020; Yiltok et al, 2020). Two studies in Mozambique (Fataha et al., 2024; Lorenzetti et al., 2024), and Eswatini (Bacha et al., 2022; Chouraya et al., 2019). Additionally, one article was found for each of the following countries: Botwana (Bacha et al., 2022), Ivory Coast (Tanoh-Aka et al., 2021), Ghana (Afrane et al., 2021), Lesotho (Bacha et al., 2022), Namibia (Munyayi et al., 2022), Rwanda (Rwabukwisi et al., 2016), and Zambia (Mukumbuta et al., 2024).

In the 52 studies included, USVL was defined by a VL ≥ 1,000 copies/mL (Table 1). The WHO recommends VL ≥ 1,000 copies/mL to identify individuals needing closer

monitoring or treatment interventions to prevent HIV transmission and manage ART effectiveness (WHO, 2023).

Thirty-eight of the studies used a cross-sectional design (Gordon et al., 2022; Djiyou et al., 2023; Mageda et al., 2023; Bayleyegn et al., 2021; Tafere et al., 2023; Shiferaw et al., 2019; Osman et Yizengaw, 2020; Getawa et al., 2021; Fenta et al., 2021; Berihun et al., 2023; Bitwale et al., Khamadi et al., 2023; Ally et al., 2023; Quaker et al., 2024; Kadima et al., 2018; Tsikhutsu et al., 2022; Gachoka & Njoroge, 2024; Mwangi & van Wyk, 2021; Onyango et al., 2023; Ndongo et al., 2024; Soudebto et al., 2024; Fokam et al., 2021; Mabizela & van Wyk, 2022; Elashi & van Wyk, 2022; Okonji et al., 2021; Simms et al., 2021; Makadzange et al., 2015; Bacha et al., 2022; Mugo et al., 2023; Isaac et al., 2020; Yiltok et al., 2020; Fataha et al., 2019; Lorenzetti et al., 2024; Chouraya et al., 2019 ; Tanoh-Aka et al., 2021; Afrane et al., 2021; Mukumbuta et al., 2024; Shumitie et al., 2021), and fourteen employed a cohort study design (Nabukeera et al., 2021; Sibhat et al., 2014; Mena et al., 2023; Abera et al., 2023; Muri et al. 2017; Mchomvu et al. 2022; Mushy t al., 2024 ; Kabogo et al., 2017; Mbébi-Enoné et al., 2023; Teasdale et al., 2018; Jackson et al., 2022 ; Tweya et al., 2020; Munyayi & van Wyk, 2022; Rwabukwisi et al., 2016). We included all studies published in internationally recognized journals between December 2015 and August 2024. This meta-analysis encompassed a total of 169,949 CALHIV on ART. The sample sizes of the included studies ranged from 140 (Osman & Yizengaw, 2020) to 34,400 (Quaker et al., 2024).

2.3.4. Studies quality assessment

The quality of the included studies was rigorously assessed using the JBI quality appraisal criteria, and the results were converted to percentage scores for classification. Based on these scores, the risk of bias was categorized as follows: ≤ 49 % indicated high risk, 50 – 69

% moderate, and above 70 % low. In line with our inclusion criteria, only studies with a moderate or low risk of bias, defined by scores of 50 % or higher, were included in the review. The majority of studies in this analysis demonstrated strong methodological rigor, with an average quality score of 91.7%. Specifically, 38 studies achieved a score of 100%, reflecting high methodological quality and low bias risk.

However, some studies did exhibit slightly lower quality scores. For example, the study by Munyayi & van Wyk (2022) received a score of 64%, which indicates a moderate risk of bias. Additionally, studies such as Jackson et al. (2022), Kabogo et al. (2017), and others scored between 73% and 82%, placing them in the low risk of bias category but suggesting some methodological limitations. Despite these variances, the overall quality of the studies included in the review remains high, strengthening the reliability of the conclusions drawn. A detailed breakdown of each study's quality score can be found in Table 2.1.

By ensuring that only studies with a moderate or low risk of bias were included, the validity and reliability of the findings from this systematic review and meta-analysis are reinforced. This approach allows for a clearer understanding of the burden of unsuppressed viral load and its associated factors among children and adolescents living with HIV on ART in Sub-Saharan Africa.

Table 2.1 Studies meeting inclusion criteria

Author and year of publication	Sub-region of SSA	Country in which the study was conducted	Study area (city/ village/ region)	Study design	Start year	End year	Population group	Age group	Risk factors founded	Total number of participants included	Number of patients with unsuppressed viral load	JBI score (%)
Abera et al (2023)	Eastern	Ethiopia	Oromia Region	Cohort study	2015	2019	Children and adolescents	0 - 19 years	Poor ART adherence, Male sex, No disclosure, Opportunistic infection, Rural residence, Low CD4, Advanced WHO stage	492	85	91
Afrane et al (2021)	Western	Ghana	Accra	Cross sectional study	October 2017	July 2018	Children	< 15 years	Female sex, Low CD4, Past treatment of tuberculosis, Nevirapine	250	96	100
Ally et al (2023)	Eastern	Tanzania	Arusha, Dar-es-Salaam, Dodoma, Geita, Iringa, Kagera, Katavi, Kigoma, Kilimanjaro, Mara, Mbeya, Mjini Magharibi, Morogoro, Mtwara, Mwanza, Njombe, Pwani, Rukwa, Ruvuma, Shinyanga, Simiyu, Singida, Songwe, Tabora, and Tanga.	Cross sectional study	October 2018	September 2020	Children	0 - 14 years	Poor ART adherence, No disclosure	1980	292	100
Bacha et al (2022)	Southern and Eastern	Botswana, Eswatini, Lesotho, Malawi, Tanzania, and Uganda	Gaborone, Mbabane, Maseru, Lilongwe, Kampala, Mbeya and Mwanza	Cross sectional study	January 2014	December 2019	Children and adolescents	0 – 19 years	History of tuberculosis	18376	4661	75
Bayleyegn et al (2021)	Eastern	Ethiopia	Gondar	Cross sectional study	January 2020	April 2021	Children	<15 years	Children with unemployed family, Orphan status, Malnutrition, Anemia, Lymphopenia	253	79	100
Berihun et al (2023)	Eastern	Ethiopia	Dessie Branch	Cross sectional study	March 2022	June 2022	Children	< 15 years	Regimen substitution, Duration on ART < 12 months	522	143	100

Bitwale et al (2021)	Eastern	Tanzania	Dodoma	Cross sectional study	November 2018	February 2019	Children and adolescents	1 - 19 years	Tuberculosis, No disclosure, Nevirapine, Orphan, Poor ART adherence, No cotrimoxazole prophylaxis	300	102	100
Chouraya et al (2019)	Southern	Eswatini	Hhohho region	Cross sectional study	September 2017	October 2018	Children	< 15 years	Nevirapine based regimen	358	79	100
Djiyou et al (2023)	Central	Cameroon	Douala	Cross sectional study	February 2021	September 2021	Adolescents	10 - 19 years	Second line ART regime, Baseline VL ≥ 1000 copies/mL, Poor ART adherence	279	59	100
Elashi & van Wyk (2022)	Southern	South Africa	Thabo Mofutsanyane District	Cross sectional study	2019	2019	Adolescents	10 - 19 years	Low CD4, Age at ART initiation, Retention in care	4520	983	100
Fataha et al (2019)	Southern	Mozambique	Whole the country	Cross sectional study	January 2019	December 2019	Children	< 15 years	Male sex, Age < 5 years, living out of Maputo City, Duration on ART < 6 years	33559	18671	100
Fenta et al (2021)	Eastern	Ethiopia	Hawassa	Cross sectional study	July 2019	December 2019	Children	< 15 years	Rural, Advanced WHO stage, Malnutrition, Baseline VL ≥ 1000 copies/mL, Low CD4, Female, Poor ART adherence, Nevirapine	273	113	100
Fokam et al (2021)	Central	Cameroon	Yaounde	Cross sectional study	December 2018	May 2019	Adolescents	10 - 19 years	Advanced clinical staging, Poor ART adherence, NNRTI-based regime	196	106	100
Gachoka & Njoroge (2024)	Eastern	Kenya	Nairobi	Cross sectional study	October 2022	October 2022	Children	< 15 years	Tuberculosis, ART side effects, Enhanced adherence counselling, No DTG-based regimen, Caregiver < 40 years	252	63	100
Getawa et al (2021)	Eastern	Ethiopia	Gondar	Cross sectional study	March 2017	May 2017	Children	< 15 years	Male, Regimen change, Being on ART for a long period > 36 months, history of tuberculosis	200	25	100
Gordon et al (2022)	Eastern	Uganda	Kabale district	Cross sectional study	September 2019	October 2019	Adolescents	10 - 19 years	Opportunistic infection, Orphan, Misses all meals in some days, Traitment interruption, No cotrimoxazole prophylaxis, Malnutrition	249	47	100

Isaac et al (2020)	Western	Nigeria	North of Nigeria	Cross sectional study	December 2017	December 2019	Children and adolescents	0 - 18 years	Male, Nevirapine based regimen, Low CD4	663	340	75
Jackson et al (2022)	Southern	Zimbabwe and Malawi	Harare and Blantyre	Cohort study	2016	2019	Children and adolescents	6 - 19 years	Age at ART initiation >15 years, Not switching ART regimen	347	114	73
Kabogo et al (2017)	Eastern	Kenya	Nairobi	Cohort study	January 2011	December 2013	Children and adolescents	1 - 18 years	Suboptimal adherence to ART	146	64	73
Kadima et al (2018)	Eastern	Kenya	Migori and Kisumu counties	Cross sectional study	June 2014	May 2015	Children	≤ 15 years	Malnutrition, Second line ART regime, Male sex	1190	442	100
Khamadi et al (2023)	Eastern	Tanzania	Southern Highland zone	Cross sectional study	January 2019	December 2021	Children and adolescents	1 - 19 years	Age < 5 years, Poor ART adherence, Attending a level 1 or 2 health facility	707	112	100
Lorenzetti et al (2024)	Southern	Mozambique	Inhambane, Maputo City, Tete, and Nampula	Cross sectional study	October 2020	September 2021	Children and adolescents	0 – 19 years	-	12231	3338	89
Mabizela & van Wyk (2022)	Southern	South Africa	Gauteng	Cross sectional study	January 2015	December 2018	Adolescents	10 - 19 years	Poor ART adherence	192	50	75
Mageda et al (2023)	Eastern	Tanzania	Simiyu	Cross sectional study	October 2021	November 2021	Children	2 - 14 years	Older age at ART initiation, Poor ART adherence	253	17	100
Makadzange et al (2015)	Southern	Zimbabwe	Harare	Cross sectional study	May 2012.	December 2012.	Children	0 - 19 years	Age at ART initiation, Nevirapine based regimen	599	183	100
Mbébi-Enoné et al (2023)	Central	Cameroon	Littoral region	Cohort study	November 2018	October 2019	Children	0 - 19 years	Orphan status	1029	307	82
Mchomvu et al (2022)	Eastern	Tanzania	Tabora region	Cohort study	January 2018	April 2022	Children and adolescents	0 - 19 years	Low CD4, Second line regimen, Nevirapine based regimen, Poor ART adherence	378	124	82
Mena et al (2023)	Eastern	Ethiopia	Wolaita	Cohort study	January 2017	December 2021	Children	< 15 years	Single caregiver, Divorced caregiver, Low CD4, Follow up < 36 months	388	42	91
Mugo et al (2023)	Western	Nigeria	Adamawa, Bauchi, Borno, Jigawa, Kano, Kebbi, Kwara, Niger, Sokoto, Yobe, and Zamfara.	Cross sectional study	April 2019	June 2021	Children	0 - 15 years	Poor ART adherence, Being in a support group	2490	911	100

Mukumbuta et al (2024)	Southern	Zambia	Lusaka District	Cross sectional study	July 2021	September 2021	Adolescents	10 - 19 years	Poor ART adherence, low CD4, No sexually active, Missed clinical visits in 6 months	294	154	100
Munyayi & van Wyk (2022)	Southern	Namibia	Windhoek	Cohort study	January 2019	December 2021	Adolescents	10 - 19 years	Duration on ART < 24 months, Second Line ART regime	695	78	64
Muri et al (2017)	Eastern	Tanzania	Kilombero district	Cohort study	2013	2015	Children and adolescents	< 18 years	Female, Low CD4, Poor ART adherence, Nevirapine based regimen	213	54	82
Mushy et al (2024)	Eastern	Tanzania	Tanga region	Cohort study	October 2018	April 2022	Adolescents	10 - 19 years	No DTG-based regimen, dispensary facility level, Age 10 - 14 years	2250	226	73
Mwangi & van Wyk (2021)	Eastern	Kenya	Homa Bay County	Cross sectional study	November 2017	November 2017	Adolescents	10 - 19 years	Poor ART adherence, Low CD4, Second line regimen	908	182	100
Nabukeera et al (2021)	Eastern	Uganda	Kampala	Cohort study	January 2017	March 2019	Children	0 - 14 years	Advanced WHO stage, ART-induced side effects, Age < 5 years	300	69	73
Ndongo et al (2024)	Central	Cameroon	Yaoundé	Cross sectional study	December 2021	March 2022	Adolescents	10 - 19 years	Orphan status, ART regimen	247	33	100
Okonji et al (2021)	Southern	South Africa	Ehlanzeni district	Cross sectional study	September 2002	October 2019	Adolescents	10 - 19 years	Male sex, Low CD4, Second line regimen	9386	2411	100
Onyango et al (2023)	Eastern	Kenya	34 counties	Cross sectional study	October 2019	September 2020	Children and adolescents	< 18 years	Male sex, child's education status, caregiver sex, non-membership of a psychosocial support group, non-membership of a voluntary savings and lending association,	31291	4404	100
Osman et al (2020)	Eastern	Ethiopia	Jimma	Cross sectional study	April 2019	May 2019	Children	< 15 years	Advanced WHO stage	140	16	100
Quaker et al (2024)	Eastern	Tanzania	Whole the country	Cross sectional study	2018	2021	Adolescents	10 - 19 years	Male sex, Second or third line ART regimen, Poor ART adherence, Attending level 1 - 2 health facility, Advanced WHO stage	34400	3350	100
Rwabukwisi et al (2016)	Eastern	Rwanda	Kirehe and Southern Kayonza Districts	Cohort study	January 2005	December 2008.	Children	< 15 years	None	235	34	82

Shiferaw et al (2019)	Eastern	Ethiopia	Bahir Dar	Cross sectional study	July 2017	June 2018	Children	< 15 years	Nevirapine based regimen	1567	444	100
Shumetie et al (2021)	Eastern	Ethiopia	West Gojjam Zone and Amhara Region.	Cross sectional study	October 1, 2020	October 15, 2020	Children	< 15 years	No disclosure, Advanced WHO stage, Enrollment VL ≥ 1000 copies/mL, Poor adherence, Missed clinical appointment	370	76	90
Sibhat et al (2020)	Eastern	Ethiopia	Tigray	Cohort study	December 2018	June 2019	Children and adolescents	< 18 years	Poor adherence, Advanced WHO stage, Tuberculosis, Follow up duration	404	96	73
Simms et al (2021)	Southern	Zimbabwe	Mashonaland West, Mashonaland East, Mashonaland North, Mashonaland South, Midlands, and Masvingo	Cross sectional study	January 2019	March 2019	Adolescents	10 - 19 years	Male sex, No disclosure	833	292	100
Soudebto et al (2024)	Central	Cameroon	Yaoundé	Cross sectional study	January 2017	December 2020	Children and adolescents	0 - 19 years	Rural residence	272	124	75
Tafere et al (2023)	Eastern	Ethiopia	Addis-Ababa	Cross sectional study	July 2021	July 2021	Adolescents	10 - 19 years	ART regimen, Alcohol use, Smoke cigarette, Discrimination, Biological mother not alive, Have a history of admission last year	446	52	100
Tanoh-Aka et al (2021)	Western	Ivory Coast	Gbeke Region	Cross sectional study	July 2015	December 2019	Children	0 - 15 years	Malnutrition, Poor ART adherence, Unschooled mother, No prevention of mother to child transmission	329	118	75
Teasdale et al (2018)	Southern	South Africa	Eastern Cape	Cohort study	2012	2015	Children	<12 years	Enrollment VL ≥ 1,000 copies/mL, Low CD4 counts cells, ART regimen	349	92	91
Tsikhutsu et al (2022)	Eastern	Kenya	South Rift Valley and Kisumu	Cross sectional study	December 2018	March 2020	Children and adolescents	1 - 19 years	Duration on ART < 24 months, Poor ART adherence	935	185	100
Tweya et al (2020)	Southern	Malawi	Lilongwe	Cohort study	January 2014	December 2017	Children and adolescents	≤ 18 years	Malnutrition, Nevirapine based regimen, Male	1312	208	82
Yiltok et al (2020)	Western	Nigeria	Jos	Cross sectional study	June 2018	November 2018	Adolescents	10 - 19 years	Poor ART adherence	143	62	100

2.3.5. Variations in defining unsuppressed viral load: Thresholds and their rationale in HIV monitoring

The use of different criteria for defining USVL is influenced by a variety of factors, including clinical context, study objectives, and available resources. The most commonly employed threshold for USVL, which is VL ≥ 1,000 copies/mL, is largely derived from the WHO recommendations (2023). This threshold is widely used because it serves as an important marker for identifying individuals who require closer monitoring and more intensive treatment interventions. Such individuals are at risk of HIV transmission or may be failing to achieve optimal treatment outcomes from ART. The rationale behind this specific cut-off is to provide clinicians with a clear indication of when ART efficacy may be compromised, signaling the need for more immediate or adjusted therapeutic strategies.

In addition to the WHO's guideline of VL ≥ 1,000 copies/mL, a lower threshold of < 1,000 copies/mL is also frequently used to identify individuals who are considered virologically suppressed. Achieving a viral load below this threshold is critical in reducing the risk of HIV transmission and improving the overall health of individuals living with HIV. Virologic suppression plays a pivotal role in the long-term management of HIV, not only enhancing individual health outcomes but also minimizing the broader public health impact of the disease. By maintaining viral suppression, patients can live longer, healthier lives while simultaneously reducing the likelihood of transmitting the virus to others.

However, variations in study designs, populations, and clinical objectives have led to the adoption of alternative thresholds for USVL. Some studies may utilize VL ≥ 80 copies/mL or ≥ 400 copies/mL as indicators of unsuppressed viral load, particularly in contexts where even low levels of viral replication are important to monitor. For example, a threshold of ≥ 80 copies/mL has been used in studies focused on more stringent control of viral

replication, especially in populations where there may be heightened concern about the possibility of developing drug resistance or treatment failure even with minimal detectable viremia (Puga et al., 2016; Dow et al., 2014). This approach aligns with national HIV treatment guidelines in some regions, which recommend close monitoring of even low-level viremia to ensure that ART is functioning effectively.

Conversely, some studies have applied higher thresholds for USVL, such as VL ≥ 5,000 copies/mL, particularly in resource-limited settings. In these environments, where access to highly sensitive diagnostic tools may be limited, it is often more feasible to monitor higher levels of viral replication. For instance, in a study conducted in Cameroon between 2009 and 2013, VL ≥ 5,000 copies/mL was used as the cut-off for determining unsuppressed viral load. This higher threshold was necessitated by the logistical challenges of detecting lower levels of viremia in such settings, where advanced laboratory technologies or infrastructure for HIV monitoring may not be readily available (Nlend et al., 2017).

The selection of an appropriate threshold for USVL is thus contingent upon a combination of clinical priorities, available resources, and the specific goals of a given study or treatment regimen. These varying thresholds underscore the complexity of HIV monitoring and highlight the importance of context when interpreting virological data. Ultimately, the choice of threshold must be guided by both the need for accurate detection of USVL and the practical considerations of implementing HIV care in diverse healthcare settings.

2.3.6. Meta-analysis

2.3.6.1. Publication bias and pooled prevalence of unsuppressed viral load in children and adolescents living with on antiretroviral therapy in sub-Saharan Africa

We included 52 articles with 169,949 CALHIV on ART to estimate USVL prevalence in SSA, , with 44,408 of these CALHIV reporting USVL; grouping studies into three population-based subgroups (Table 2.1): 20 studies including only children (< 15 years) with 45,248 participants (Nabukeera et al., 2021; Mageda et al., 2023; Mena et al., 2023; Bayleyegn et al., 2021; Shumetie et al., 2021; Shiferaw et al., 2019; Osman & Yizengaw, 2020; Getawa et al., 2021; Fenta et al., 2021; Berihun et al., 2023, Ally et al., 2023; Kadima et al., 2018; Gachoka & Njoroge, 2024; Teasdale et al., 2018; Mugo et al., 2023; Fataha et al., 2019; Chouraya et al., 2019; Tanoh-Aka et al., 2021; Afrane et al., 2021; Rwabukwisi et al., 2016), 15 studies including only adolescents (10 to 19 years) with 55,038 participants (Gordon et al., 2022; Djiyou et al., 2023; Tafere et al., 2023; Quaker et al., 2024; Mushy et al., 2024; Mwangi et al., 2021; Ndongo et al., 2024; Fokam et al., 2021; Mabizela et al., 2024; Elashi & van Wyk, 2022; Okonji et al., 2021; Simms et al., 2021; Yiltok et al., 2020; Munyayi & van Wyk, 2022; Mukumbuta et al., 2024), and 17 studies including both children and adolescents (0 to 19 years) with 69,663 participants (Sibhat et al., 2020; Abera et 2023; Muri et al., 2017; Bitwale et al., 2021; Khamadi et al., 2023; Mchomvu et al., 2022; Tsikhutsu et al., 2022; Kabogo et al., 2017; Onyango et al., 2023; Soudebto et al., 2024; Mbébi-Enoné et al., 2023; Jackson et al., 2022; Makadzange et al., 2015; Tweya et al., 2020; Bacha et al., 2022; Isaac et al., 2020; Lorenzetti et al., 2024). Accordingly, the meta-analyzed prevalence of USVL among CALHIV in SSA was 26.47 % (95 % CI: 23.06 % – 29.87 %). However, this meta-analysis showed a significant heterogeneity across the included studies as evidenced with I^2 = 99.66 %, p < 0.0001 (Figure 2.3).

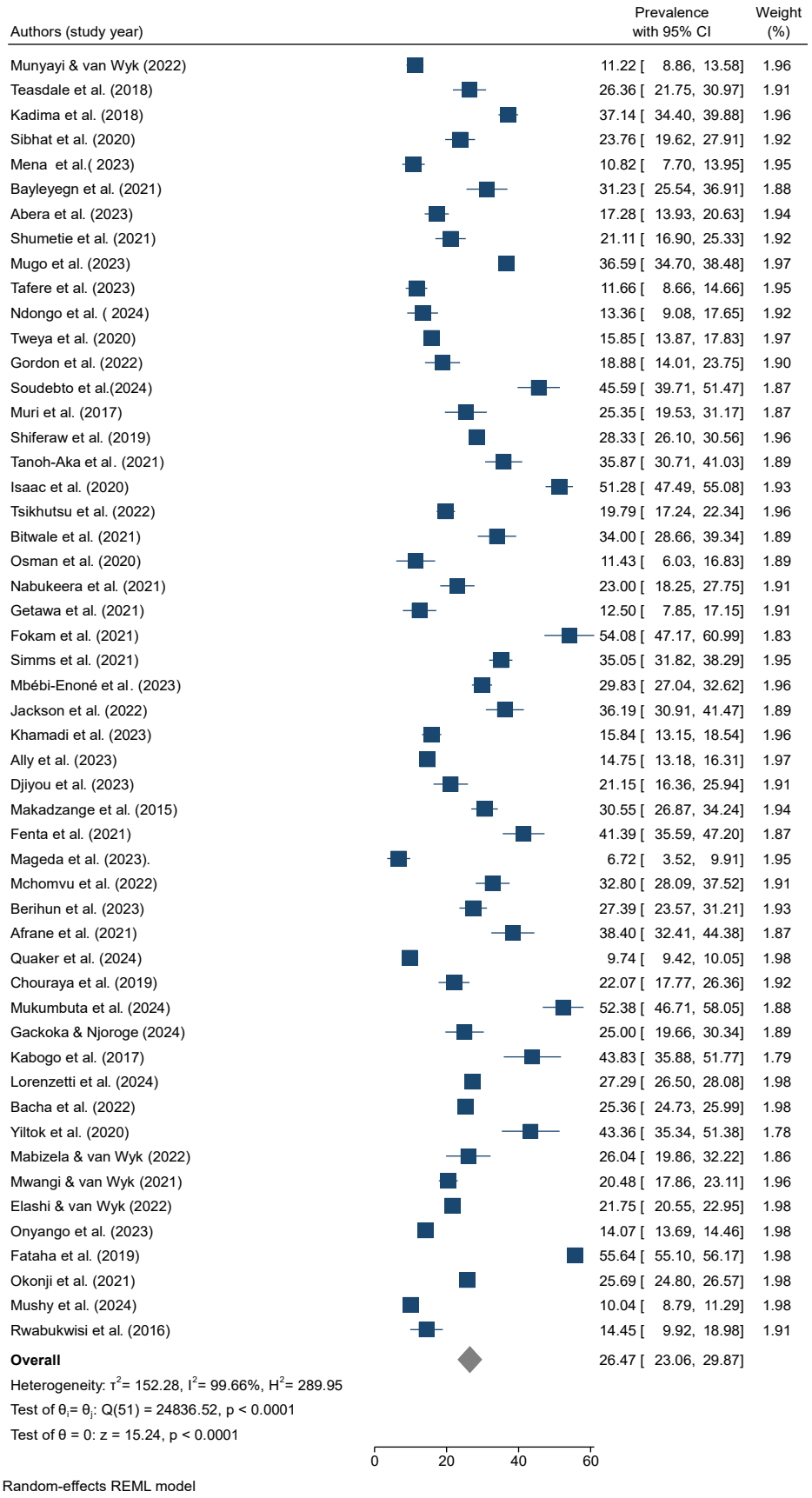

Figure 2.3 Forest plot of the meta-analyzed prevalence of unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa.

Whereas non-significant Egger's test (β1 = -2.74, p = 0.093) excludes presence of publication bias (Figure 2.4).

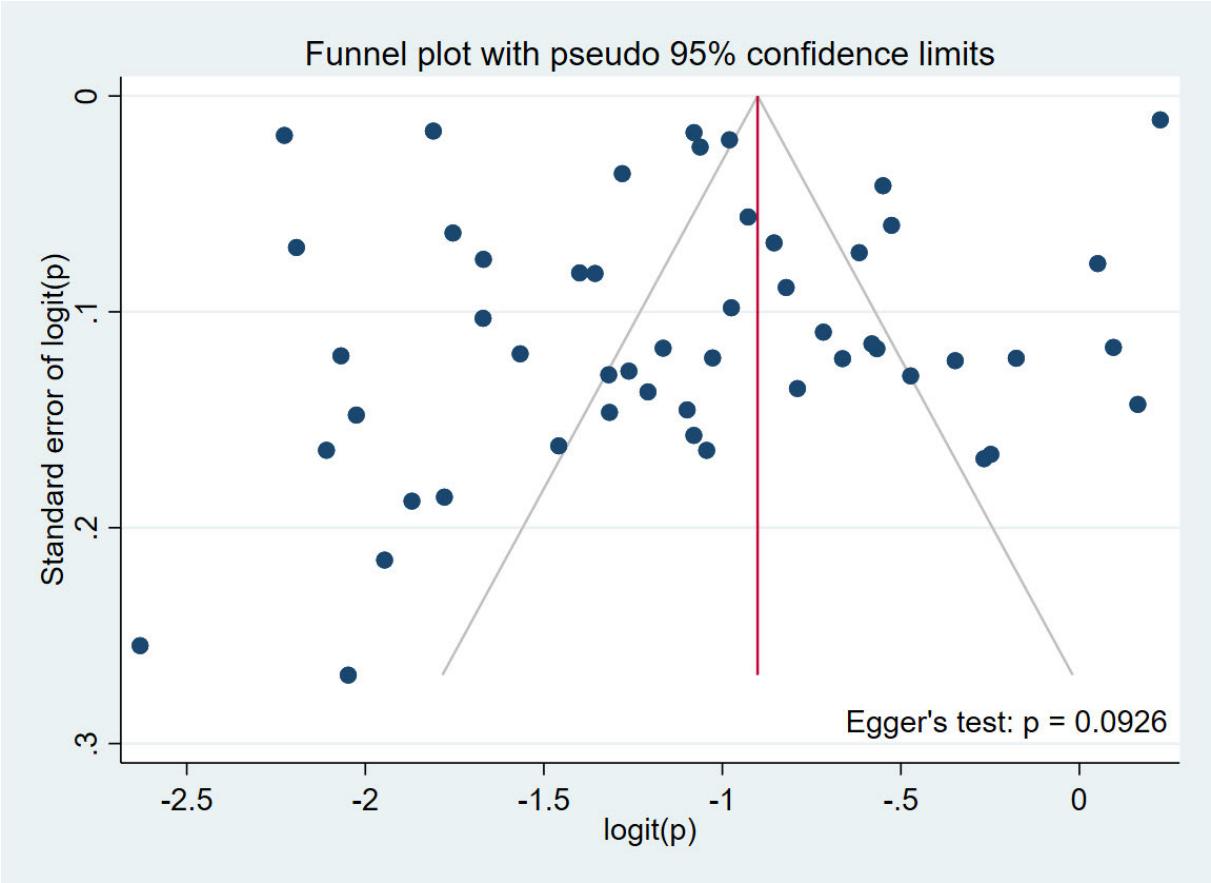

Figure 2.4 Funnel plot assessing publication bias for the prevalence of unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa

We performed subgroup analysis based on study sub-region, study design, and study age group. the analysis by study sub-region revealed differences in prevalence rates across the regions. The Central Africa had a meta-analyzed prevalence of 32.65% (95% CI: 17.95% – 47.35%), while the Eastern Africa showed a lower meta-analyzed prevalence of 21.32% (95% CI: 17.66% – 24.97%). In the Southern Africa, the prevalence was 29.33 % (95% CI: 22.86% – 35.80%), and the Western Africa had the highest meta-analyzed prevalence at 41.06% (95% CI: 35.11% – 47.02%). The test for group differences (Q = 31.72, p < 0.0001) revealed significant variations in prevalence rates between the SSA sub-regions (Figure 2.5).

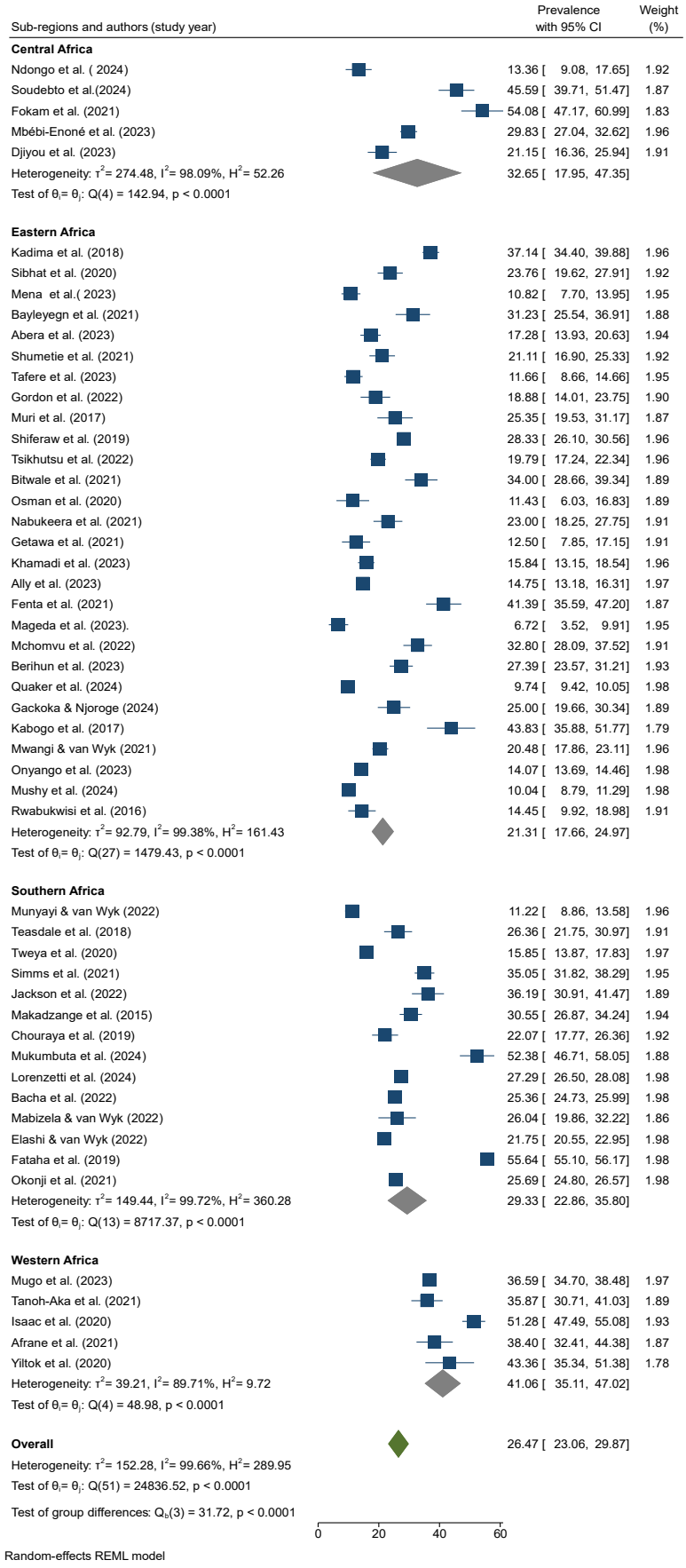

Figure 2.5 Forest plot of the prevalence of unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa by sub-region.

The analysis by study design revealed variations in the prevalence rates across different types of studies. In cohort studies, the meta-analyzed prevalence was higher at 22.62% (95% CI: 17.34% – 27.90%), while cross-sectional studies showed the highest meta-analyzed prevalence of 27.86% (95% CI: 23.68% – 32.03%). The test for group differences (Q = 2.32, p = 0.13) indicated that there were no statistically significant variations in prevalence rates across the study designs, suggesting a relatively consistent effect across these different study designs (Figure 2.6).

Additionally, the analysis by study age group demonstrated that the prevalence of USVL was higher in studies focusing on children (< 15 years) [26.01% (95% CI: 20.51% – 31.52%)] compared to those focusing on adolescents (10 to 19 years) [24.76% (95% CI: 17.36% – 32.16%)] (Figure 2.7). Studies combining both children and adolescents (0 to 19 years) had the highest meta-analyzed prevalence at 28.52% (95 % CI: 23.33 % – 33.72 %). Despite the observed variations in prevalence across age groups, the test for group differences (Q = 0.79, p = 0.67) showed no significant statistical variation in the prevalence rates between the three age groups.

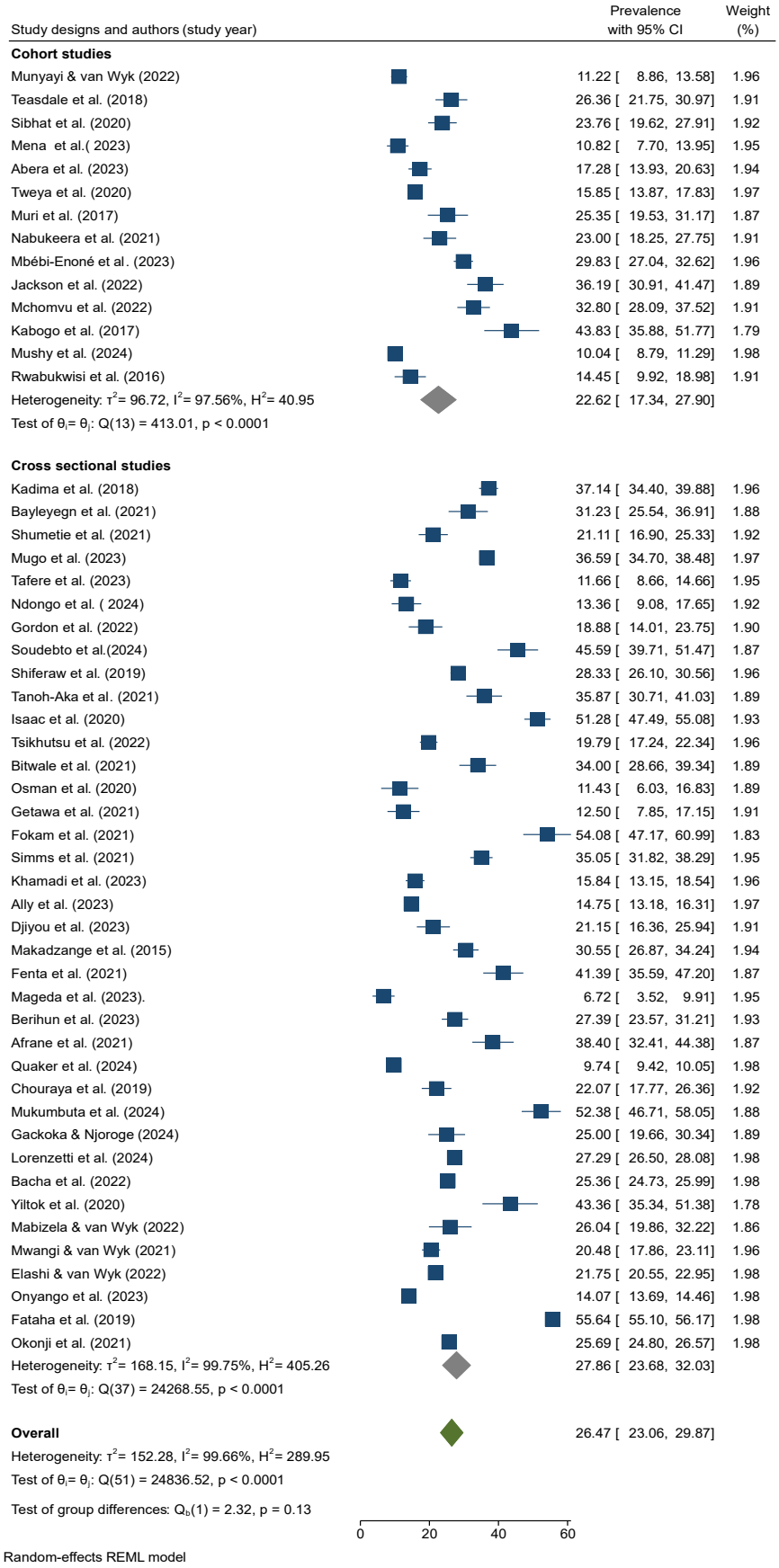

Figure 2.6 Forest plot of the prevalence of unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa by study design.

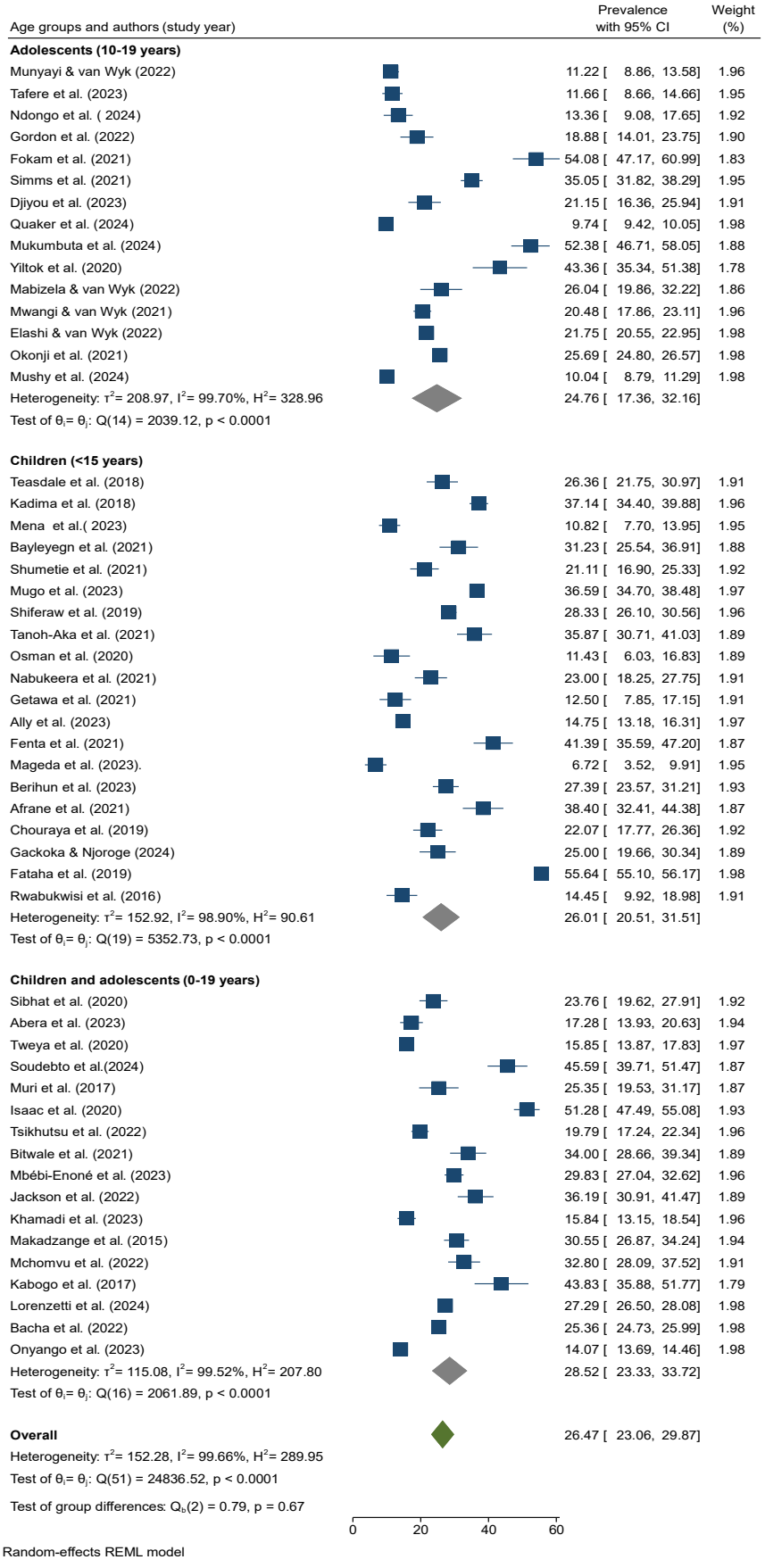

Figure 2.7 Forest plot of the prevalence of unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa by age group

2.3.6.2. Associated factors with unsuppressed viral load in children and adolescents living with HIV on antiretroviral therapy in sub-Saharan Africa

This meta-analysis calculated the meta-analyzed prevalence of USVL in CALHIV on ART in SSA and examined factors associated with USVL like age, sex, residence, orphan status, health facility level, disclosure, nutritional status, ART-adherence, WHO stage, CD4+ T-cell count, OIs, ART duration, ART-regimen, cotrimoxazole prophylaxis, and drug substitution. Factors were grouped into sociodemographic characteristics, HIV care management, clinical and immunological factors, and treatment-related factors.

CALHIV < 5 years were twice as likely to have USVL compared to their older counterparts (OR = 1.77; 95 % CI: 1.46 – 2.15) (Khamadi et al., 2023; Ally et al., 2023; Fataha et al., 2024). Those living in rural areas (Abera 2023; Tafere et al., 2023) were more likely to have USVL than those in urban areas (OR = 2.37; 95 % CI: 1.55 – 3.61). Males (Abera et al., 2023; Getawa et al., 2021; Quaker et al., 2024; Kadima et al., 2018; Onyango et al., 2023; Okonji et al., 2021; Simms et al., 2021; Tweya et al., 2020; Isaac et al., 2020; Fataha et al., 2024) showed a higher likelihood of USVL than females (OR = 1.37; 95 % CI: 1.18 – 1.58). Additionally, orphaned CALHIV (Gordon et al., 2022; Bayleyegn et al., 2021; Bitwale et al., 2021; Ndongo et al., 2024; Mbébi-Enoné et al., 2023) had increased odds of USVL compared to non–orphaned (OR = 1.80; 95 % CI: 1.32 – 2.47) (Figure 2.8).

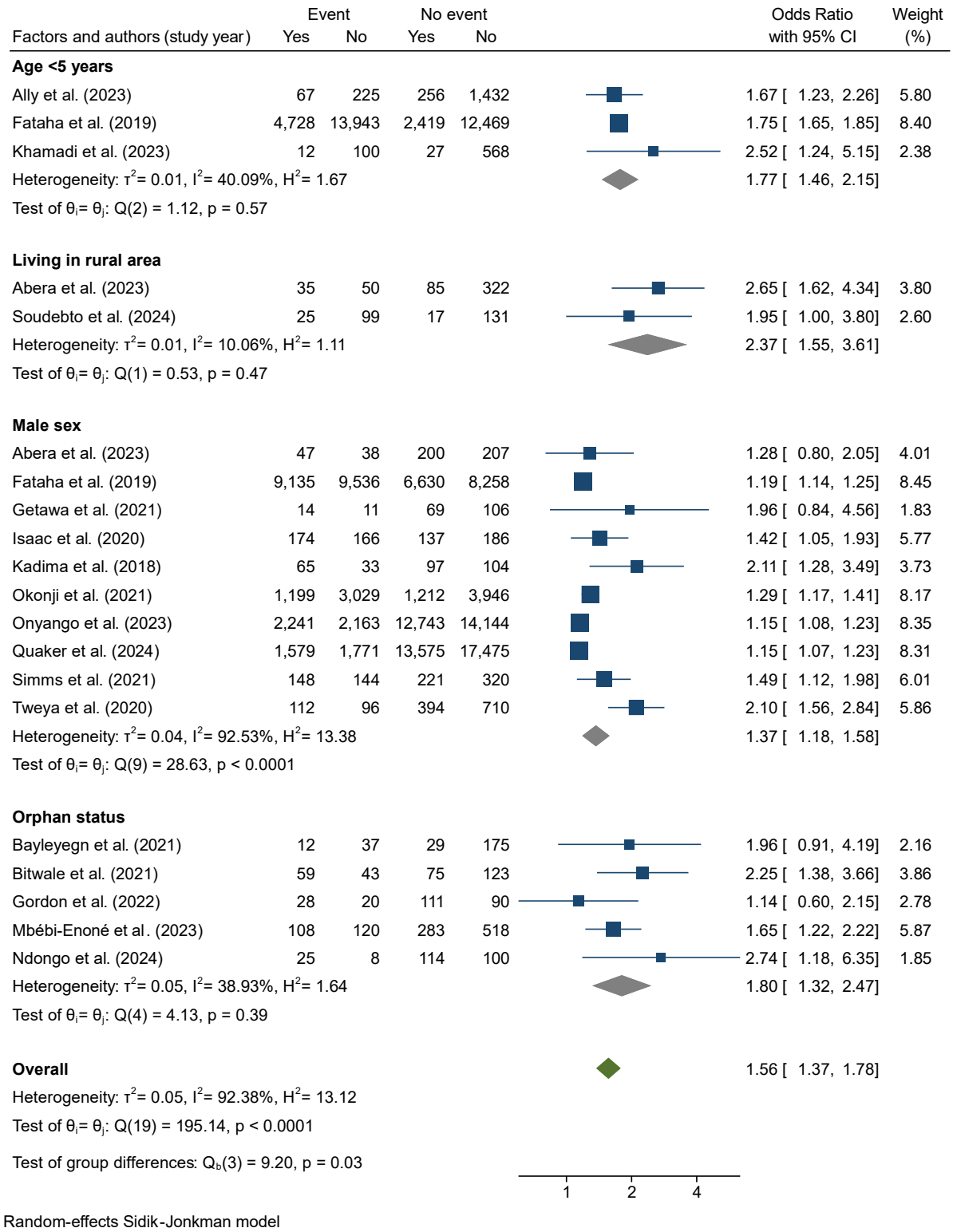

Figure 2.8 Forest plot which describe association between sociodemographic characteristics and unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa

Based on the findings of three studies (Khamadi et al., 2023; Quaker et al., 2024; Tsikhutsu et al., 2022), CALHIV who attended a level 1 or 2 healthcare facility were 1.58 times more likely to have an USVL than their counterparts (OR = 1.58; 95 % CI: 1.07 – 2.35). Similarly, CALHIV who had not been disclosed their HIV status (Shumetie et al., 2021; Bitwale et al., 2021; Ally et al., 2023; Simms et al., 2021) were at a high risk (OR = 4.48; 95 % CI: 1.06 – 18.84) of developing USVL compared to those who had been disclosed. The meta-analyzed OR revealed that CALHIV with poor ART adherence (Djiyou et al., 2023; Mageda et al., 2023; Sibhat et al., 2020; Abera et al., 2023; Muri et al., 2017; Bitwale et al., 2021; Khamadi et al., 2023; Ally et al., 2023; Mchomvu et al., 2022; Quaker et al., 2024; Tsikhutsu et al., 2022; Mwangi et al., 2021; Mabizela & van Wyk, 2022; Mugo et al., 2023; Yiltok et al., 2020; Tanoh-Aka et al., 2021; Mukumbuta et al., 2024) were 6.50 times more likely to experience USVL compared to their counterparts (OR = 6.50; 95 % CI: 3.48 – 12.14) (Figure 2.9).

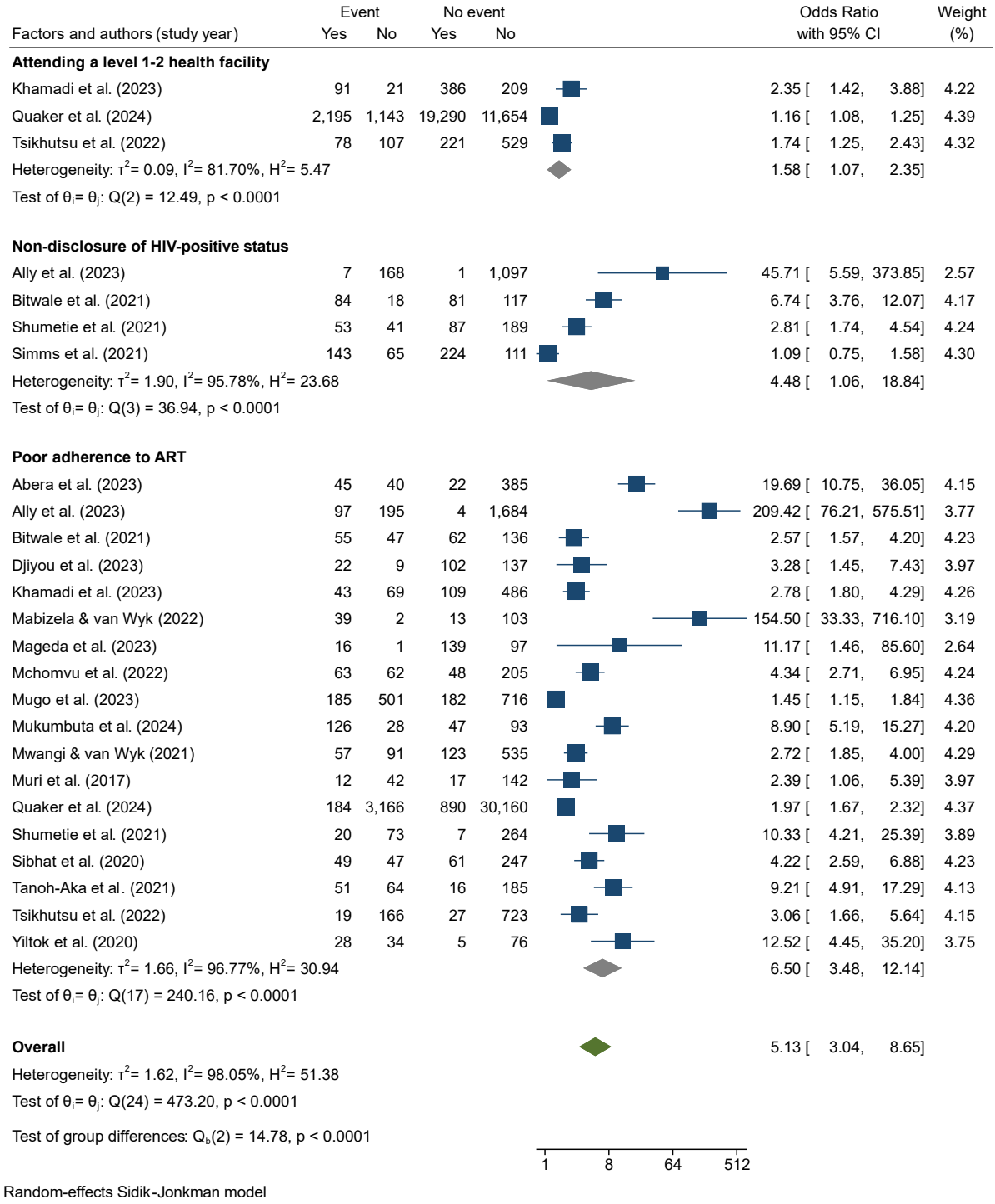

Figure 2.9 Forest plot which describe association between factors related to the management of HIV care and unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa

CALHIV who were in advanced WHO clinical stage (3 / 4) (Nabukeera et al., 2021; Sibhat et al., 2020; Abera et al., 2023; Shumetie et al., 2021; Osman & Yizengaw, 2020; Quaker et al., 2024) were at a high risk (OR = 5.18; 95 % CI: 1.85 – 14.47) of developing USVL compared to those in WHO clinical stage 1 / 2. Additionally, CALHIV with low CD4+ T-cells (Mena et al., 2023; Abera et al., 2023; Mchomvu et al., 2022; Mwangi et al., 2021; Elashi & van Wyk, 2022; Okonji & van Wyk, 2021; Isaac et al., 2020; Afrane et al., 2021; Mukumbuta et al., 2024) were at a high risk (OR = 2.28; 95 % CI: 1.48 – 3.51) of experiencing USVL. The meta-analyzed OR of malnutrition on USVL (Gordon et al., 2022; Bayleyegn et al., 2021; Kadima et al., 2018; Tweya et al., 2020; Tanoh-Aka et al., 2021) was 2.57 times higher compared to good nutritional status (OR = 2.57; 95 % CI: 1.20 – 5.50). Based on this finding, CALHIV with a history of OIs (Gordon et al., 2022; Sibhat et al., 2020; Abera et al., 2023; Getawa et al., 2021; Bitwale et al., 2021; Bacha et al., 2022; Afrane et al., 2021) were 3.70 times more likely to have USVL compared to their counterparts (OR = 3.70; 95 % CI: 1.53 – 8.93) (Figure 2.10).

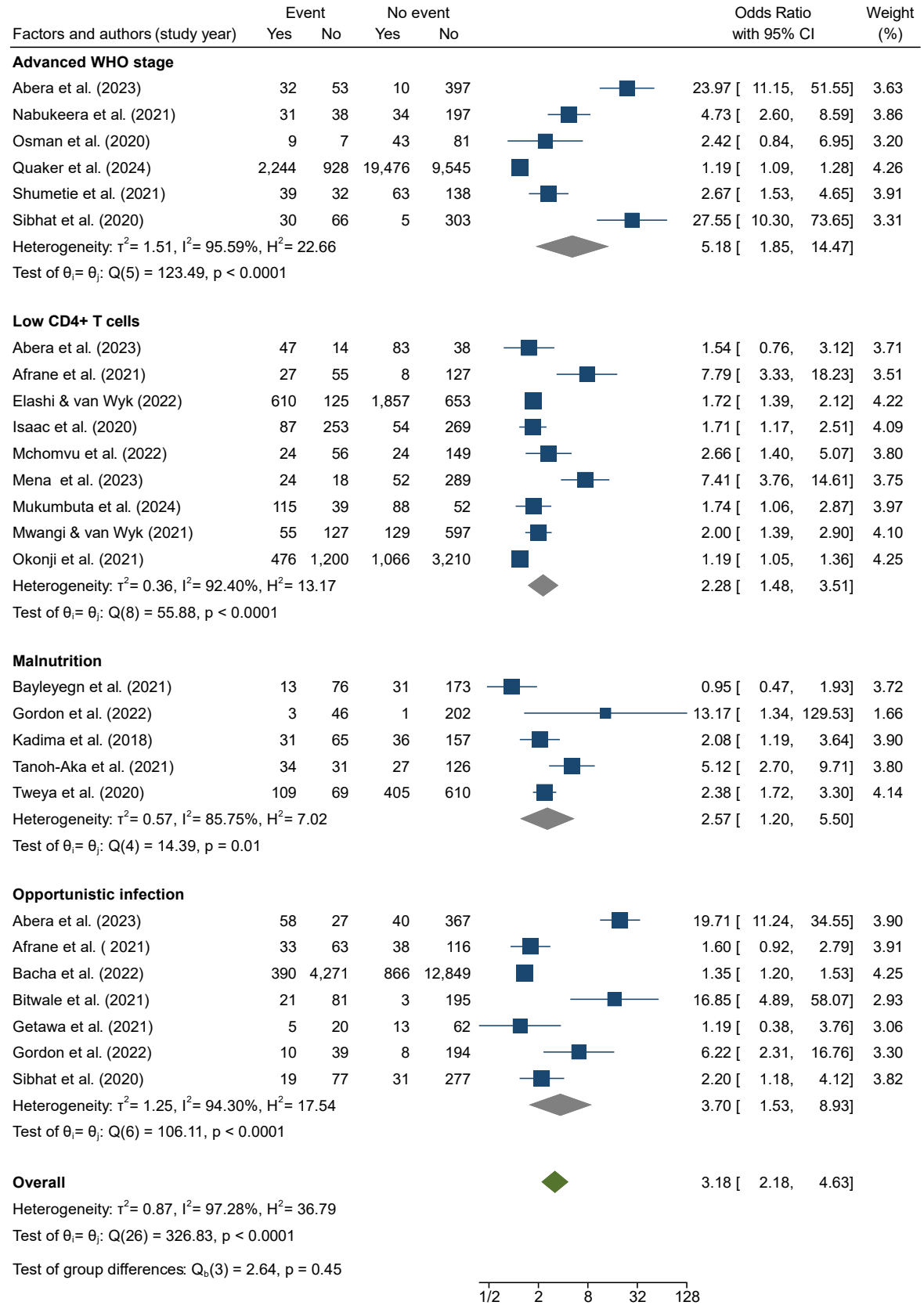

Figure 2.10 Forest plot which describe association between clinical and immunological factors and unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa

Report from two studies (Gordon et al., 2022; Bitwale et al., 2021) showed that CALHIV who did not receive cotrimoxazole prophylaxis were 2.61 times more likely to be diagnosed with USVL when compared to their counterparts (OR = 2.61; 95 % CI: 1.53 – 4.46). Once more, CALHIV who had drug substitution history (Djiyou et al., 2023; Getawa et al., 2021; Mchomvu et al., 2022; Quaker et al., 2024; Kadima et al., 2018; Mwangi et al. 2021; Okonji & van Wyk, 2021; Munyayi et al., 2022) were 3.81 times more positively associated with USVL (OR = 3.81; 95 % CI: 2.67 – 5.44). Results revealed that duration on ART < 24 months (Tsikhutsu et al., 2022; Munyayi et al., 2022) (OR = 5.20; 95 % CI: 2.79 – 9.67) and nevirapine-based regimen (Shiferaw et al., 2019; Muri et al., Bitwale et al., 2021; Mchomvu et al., 2022; Tweya et al., 2020; Isaac et al., 2020; Chouraya et al., 2019; Afrane et al., 2021) (OR = 2.59; 95 % CI: 1.70 – 3.95) were reported significantly associated factors of USVL (Figure 2.11).

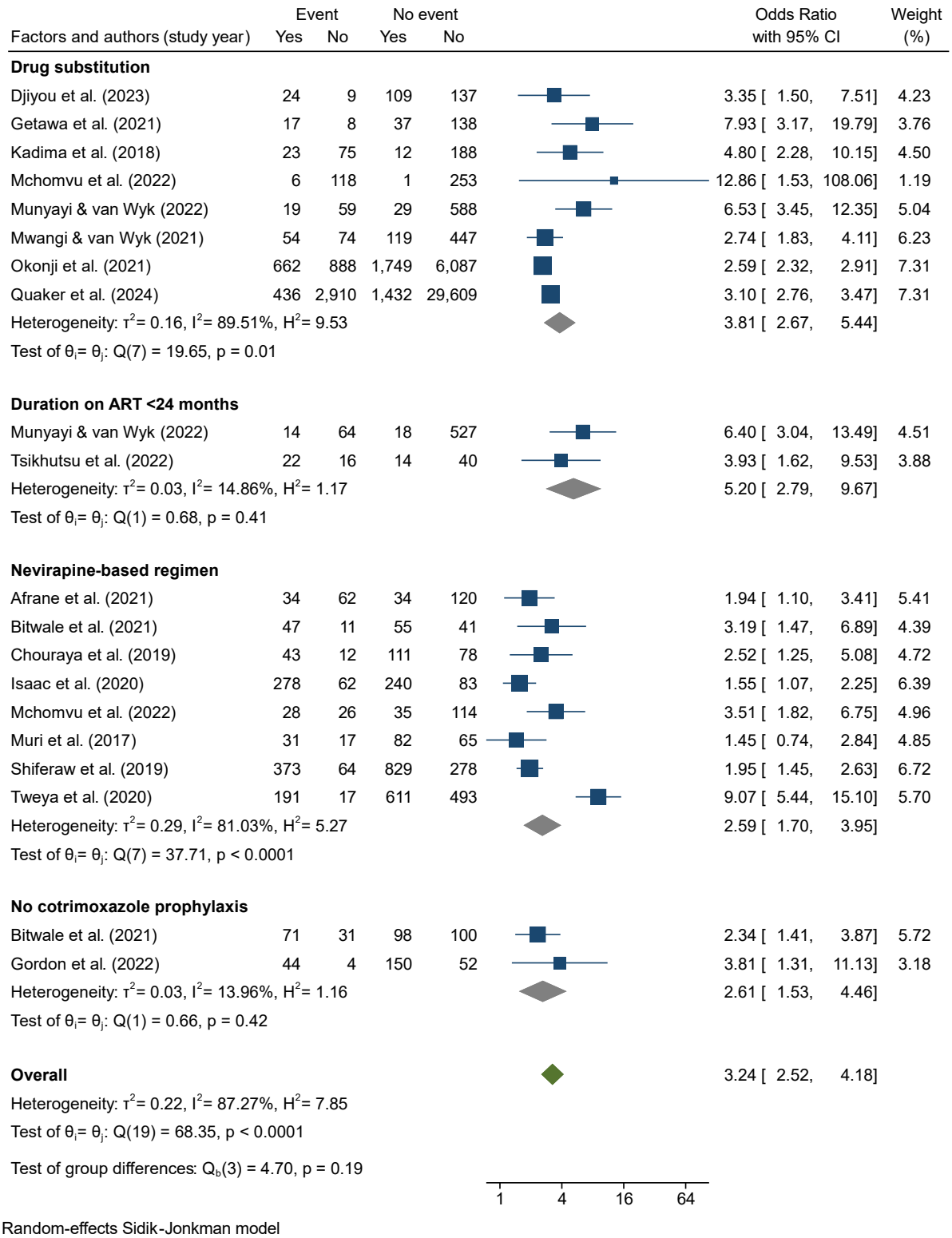

Figure 2.11 Forest plot which describe association between antiretroviral treatment related factors and unsuppressed viral load among children and adolescents living with HIV in sub-Saharan Africa

2.4. Discussion

2.4.1. Prevalence of unsuppressed viral load among children and adolescents living with HIV on antiretroviral therapy in sub-Saharan Africa

The magnitude of CALHIV in SSA is substantial, as evidenced by this meta-analysis of 52 studies (169,949 CALHIV on ART) which revealed a meta-analyzed prevalence of USVL at 26.01% for children under 15, 24.76% for adolescents aged 10-19, and 28.52% overall. These statistics, falling significantly below UNAIDS' 95% VLS target, underscore the pressing need for targeted interventions to tackle this public health issue (UNAIDS, 2014; Muri et al., 2017).

Our results show that, in studies of children alone, prevalence ranged from 6.72% in Simiyu (Tanzania) (Mageda et al., 2023) to 55.64% in Mozambique (Fataya et al., 2024). For studies conducted among adolescents alone, the lowest prevalence recorded was 9.74% in Tanzania (Quaker et al., 2024) and the highest was 54.08% in Yaoundé (Cameroon) (Fokam et al., 2021). Studies of children and adolescents have reported prevalences ranging from 14.07% in Kenya (Onyango et al., 2023) to 51.28% in in North Nigeria (Isaac et al., 2020). Differences in methodology and sample sizes used for diagnosis in individual studies conducted in each country, as well as differences in socioeconomic status, the quality of medical services, and geographical areas, can all have a significant impact on the accuracy of diagnosing USVL. These factors could explain the observed variations in the prevalence of USVL in CALHIV in SSA. The substantial heterogeneity observed across the studies ($I^2 > 97\%$, $p < 0.0001$) indicates a complex interplay of factors affecting USVL, with the likelihood of considerable geographic and demographic variation. However, the lack of notable publication bias — as demonstrated by insignificant Egger's test — strengthens the validity and dependability of our meta-analyzed prevalence estimates.

2.4.2. Associated factors with unsuppressed viral load among children and adolescents living with HIV on antiretroviral therapy in sub-Saharan Africa

This meta-analysis aimed to comprehensively examine the factors associated with USVL among children and adolescents living with HIV receiving antiretroviral therapy in SSA. The findings highlight the multifactorial nature of USVL, influenced by a complex interplay of sociodemographic determinants, healthcare system-related factors, clinical and immunological features, and treatment-related aspects. These determinants include disparities in the level of healthcare services, variations in treatment adherence, the presence of opportunistic infections, immunological markers such as CD4+ count, and the specific ART regimens utilized. Understanding these contributing factors is crucial for optimizing ART outcomes in this vulnerable population, informing targeted interventions, and strengthening healthcare policies to enhance VLS rates across diverse settings in SSA.

2.4.2.1. Influence of residence on viral load suppression among children and adolescents living with HIV

This study highlights the crucial role of residence in determining virological outcomes among CALHIV. Specifically, CALHIV residing in rural areas showed a notably higher prevalence of USVL compared to those in urban settings. Recent studies support these findings, showing a strong link between rural residence and an increased risk of virological failure. Abera et al. (2023) discovered that children and adolescents in rural areas had a hazard ratio of 1.97 (95% CI: 1.15–3.36), nearly double that of their urban counterparts. This aligns with research from South Africa (Fatti et al., 2010) and Ethiopia (Tafere et al., 2023; Fenta et al., 2021), which also highlighted the heightened vulnerability to treatment failure among rural children on ART. These studies underscore the disparities in healthcare

access and quality between urban and rural areas as pivotal in the effectiveness of ART, with rural populations facing more challenges in both accessing and adhering to therapy.

This disparity is driven by a combination of structural, systemic, and socio-economic barriers that limit access to optimal healthcare in rural areas. Factors such as the limited availability and accessibility of healthcare services, the potentially lower quality of healthcare infrastructure, shortages of experienced clinicians—particularly those with expertise in HIV care—and the logistical complexities associated with consistent ART distribution in remote settings all contribute to poorer health outcomes in rural populations (Amzat & Razum, 2018; Masiano et al., 2019; Ngene et al., 2023; Bono et al., 2021; Moon et al., 2010). These structural challenges not only hinder timely access to medical care but also exacerbate treatment disparities, ultimately impacting the effectiveness of HIV management in these areas.

The impact of geographic isolation on adherence to ART is compounded by several factors inherent to rural life. Long travel distances to healthcare facilities, combined with a lack of transportation options, poor road conditions, and high travel costs, place a heavy burden on patients residing in rural areas (Sovershaeva et al., 2019; Gaede & Versteeg, 2011; Bono et al., 2023; Moon et al., 2010). This can significantly reduce the likelihood of regular health check-ups, including viral load monitoring, and ultimately hinder treatment adherence. As a result, individuals in rural areas are more likely to experience interruptions in their treatment or delayed access to care (Kalichman et al., 2020), increasing their susceptibility to virological failure. In contrast, individuals living in urban areas may have better access to healthcare services, more frequent follow-ups, and a greater level of awareness regarding HIV and its management. Urban dwellers often benefit from improved transportation, better healthcare infrastructure, and a greater concentration of

healthcare professionals, which can facilitate more consistent monitoring and treatment adherence (Fatti et al., 2010; Foster & Frazier, 2008). Furthermore, urban populations may have more access to educational resources about HIV/AIDS, enabling them to make more informed decisions about their health. Rural areas are frequently characterized by geographic isolation, which introduces significant logistical challenges in providing consistent antiretroviral therapy and ensuring the regular monitoring of virological suppression. The healthcare infrastructure in rural areas often struggles to maintain a continuous and adequate supply of ART, heightening the risk of treatment interruptions and subsequent treatment failure (Moon et al., 2010). Furthermore, rural healthcare facilities may lack essential medical equipment, laboratory capabilities, and specialized expertise necessary for the management of PLHIV patients (Moon et al., 2010; Cohen, 2007). This can lead to delays in diagnosis, inappropriate treatment regimens, and suboptimal ART adherence.

In addition to these logistical challenges, children and adolescents in rural areas often face additional psychosocial obstacles, including social stigma, behavioral and emotional problems, limited assistance and support from caregivers, and economic hardships (Moon et al., 2010; Li et al., 2018; Kalichman et al., 2020; Zhou et al., 2023; Gumede et al., 2023). These factors can further impede their ability to adhere to ART and achieve optimal viral suppression. Moreover, disparities in HIV knowledge between urban and rural populations leave young people in rural areas less informed about transmission, prevention, and treatment (Ayodele & Ayodele, 2016), potentially contributing to the high rate of unsuppressed viral load in rural settings. The compounded effects of these structural, psychosocial, and educational barriers highlight the need for targeted interventions that address both systemic healthcare inequalities and gaps in HIV awareness. Therefore, improving ART adherence and reducing the burden of HIV among rural populations,

particularly children and adolescents, requires a comprehensive approach that integrates healthcare accessibility, psychosocial support, and educational programs tailored to rural communities (Moon et al., 2010).

In light of these findings, it is evident that targeted interventions are urgently needed to address the urban–rural divide in HIV care. One frequently proposed strategy is the decentralization of HIV care services, which aims to bring ART and related services closer to remote populations (Reidy et al., 2014). However, in practice, decentralization in SSA faces significant challenges, particularly due to chronic shortages of qualified health personnel, weak infrastructure, and limited diagnostic capacity in rural areas. Rather than attempting to replicate full-scale tertiary care in remote settings, decentralization in this context often refers to the integration of HIV services into existing primary care facilities, supported by simplified clinical guidelines and task-shifting to nurses or trained community health workers (Callaghan et al., 2010).

Mobile health units have also shown promise by delivering ART and conducting regular virological monitoring in hard-to-reach communities (Sloot et al., 2020), although their sustainability depends on continued funding and logistical support. Task-shifting—delegating certain tasks from doctors to less specialized providers—has been effective in increasing access and improving retention in care, though it must be accompanied by proper training, supervision, and remuneration to be viable long-term (Callaghan et al., 2010). Strengthening ART supply chains in rural regions is equally crucial to prevent stockouts and minimize treatment interruptions (Itiola & Agu, 2018; USAID, 2020).

While these approaches do not resolve all the systemic issues, they represent pragmatic steps toward improving healthcare access and equity in rural SSA. By adapting decentralization to local realities and combining it with strong community engagement

and health system support, it is possible to make meaningful progress in reducing HIV-related morbidity and mortality among CALHIV in rural areas.

2.4.2.2. Age-related factors play a crucial role in determining virological suppression outcomes among children living with HIV

The study revealed a significant association between younger age and virological outcomes, highlighting that children under the age of five are particularly vulnerable to USVL. Recent studies further corroborate these findings, demonstrating that children under five years of age are likely to experience unsuppressed viral load compared to their older counterparts. Studies by Nabukeera et al. (2021) and Fataha et al. (2024) reinforce the notion that younger children face a disproportionate burden of virological failure, highlighting the need for age-specific strategies in pediatric HIV care.

These findings underline the necessity of addressing the specific challenges faced by children under five years old in order to reduce the risk of treatment failure and improve long-term health outcomes. This age group appears to be at an elevated risk of virological failure, which can be attributed to a complex interplay of biological, pharmacological, and healthcare-related factors. Understanding the unique challenges faced by this subgroup is crucial for developing targeted interventions aimed at improving their treatment outcomes. From a clinical standpoint, infants and young children encounter distinct obstacles in adhering to ART. Developmental limitations within this age group significantly contribute to the challenges of treatment adherence. For example, children under the age of 5 often experience difficulties swallowing pills, particularly those larger than 10 mm (Standing and Tuleu, 2005), and may find the taste of pediatric ART formulations unpalatable. These challenges can lead to poor adherence, which in turn reduces the likelihood of achieving viral load suppression. However, research has shown that minitablets smaller than 4 mm

are suitable for children aged 2 to 5 years (Mistry and Batchelor, 2017), and clinical studies have shown that children as young as 6 months to 5 years are capable of swallowing several minitablets at once (Kluk et al., 2015; Klingmann, 2017; Klingmann et al., 2018). Furthermore, this format is often preferred over other forms such as syrups, suspensions, or powders (Thomson et al., 2009; Spomer et al., 2012; Riet-Nales et al., 2013; Klingmann et al., 2013; 2015), highlighting the potential of minitablets as a more effective solution to enhance adherence in young children (VandenBerg et al., 2022). However, preferences for one form over another should be assessed individually for each child, as suggested by Miyazaki et al. (2022) and Avila-Sierra et al. (2023), syrup and pellets are more easily tolerated and swallowed than minitablets.

Additionally, infants and young children experience significant pharmacokinetic and pharmacodynamic differences compared to older children and adults. The developing gastrointestinal tract, liver, and renal systems in this age group can impact the absorption, metabolism, and elimination of ART drugs, potentially leading to suboptimal drug concentrations in the bloodstream. This may increase the risk of suboptimal viral suppression and treatment failure (Schlatter et al., 2016).

HIV progression is often more aggressive in young children due to the immaturity of their immune system, which impedes their ability to mount a robust defense against the virus. This immune deficiency significantly increases the urgency of achieving timely and effective viral suppression. Delayed or inadequate viral suppression during this critical period can result in rapid disease progression, posing substantial risks to the child's health and development. Therefore, the timely initiation of ART is crucial for this vulnerable age group. The innate and adaptive immune responses in infants are more tolerogenic, which contributes to the failure to control viral replication in early life (Muenchhoff et al., 2014).

This immunological immaturity leads to faster disease progression, with a shorter time to AIDS and death compared to adults (Muenchhoff et al., 2014). Early initiation of antiretroviral therapy not only reduces viral diversity and evolution, preventing the emergence of new viral variants and enhancing viral suppression, but also plays a crucial role in modulating the immune system (Palma et al., 2016). In infants with perinatal HIV infection, early ART reduces immune activation, preserves the early expansion of naive T-cells, and maintains innate cell levels, ultimately leading to more substantial immune reconstitution compared to delayed ART (Azzoni et al., 2015). The literature review conducted by Berendam et al. (2020) showed that immune-based interventions targeting HIV replication have shown promise in reducing the viral reservoir size and maintaining viral suppression in preclinical studies and clinical trials. However, most of these studies have focused on carefully selected HIV-positive adults, highlighting the need to assess their efficacy in children and adapt them to the developing immune system in early childhood (Berendam et al., 2020).

In light of these disparities, it is crucial to implement targeted interventions aimed at improving adherence to ART and virological suppression in this age group. One of these interventions involves the development of ART formulations specifically designed for children and adolescents, which are not only easier to administer but also more palatable, in order to promote better treatment adherence. These interventions include the use of a flavored throat spray, in situ coating of tablets or capsules, behavioral therapies, and mini-tablets (VandenBerg et al., 2022; Schlatter et al., 2016; Penazzato et al., 2019). Furthermore, caregiver support programs should be strengthened to provide caregivers with the necessary tools and resources to manage pediatric ART more effectively. This includes education on the importance of consistent ART administration, strategies for managing side effects, and guidance on addressing adherence challenges. In addition,

regular and more frequent viral load monitoring is essential in this vulnerable population, as it allows for the early detection of treatment failure and the timely adjustment of ART regimens. Strengthening early infant diagnosis programs and ensuring that ART is initiated as soon as an HIV diagnosis is confirmed remain fundamental strategies to reduce the risk of virological failure and improve the prognosis of children living with HIV (Essajee et al., 2015; Modi et al., 2018; Obeagu et al., 2024). By ensuring that these children receive the appropriate care at the earliest stages of their disease, it is possible to mitigate the impact of HIV on their long-term health and development.

2.4.2.3. Sex as a key determinant of viral load suppression among children and adolescents living with HIV

Sex emerged as a significant determinant of VLS among CALHIV, with evidence indicating that male CALHIV faced a higher risk of USVL compared to their female counterparts. This trend, consistently observed across multiple settings in SSA, has been reinforced by recent studies showing that male CALHIV are at a higher risk of USVL than their female peers (Abera et al. 2023; Fataha et al., 2019; Getawa et al., 2021; Isaac et al., 2020; Desalegn et al., 2024; Quaker et al., 2024; Okonji et al., 2021; Umar et al., 2019; Cissé et al., 2019; Kadima et al., 2018; Zoufaly et al., 2013; Getaneh et al., 2019). The underlying causes of this sex-based disparity are multifactorial, involving behavioral, pharmacological, and biological factors. In sub-Saharan Africa, several studies conducted in adults living with HIV have reported that men on ART are at a higher risk of treatment failure compared to women, regardless of their later initiation of treatment. Men are more likely to interrupt ART, be lost to follow-up, have weaker immunological and virological responses, and face a higher risk of mortality than women (Kamya et al., 2007; Muwonga et al., 2011; Hawkins et al., 2011; Maskew et al., 2013; Kranzer et al., 2010; Cornell et al.,

2012; Maman et al., 2012; Ochieng-Ooko et al., 2010; Druyts et al., 2013; Mosha et al., 2013; Cohn et al., 2020). In Burkina Faso, Penot et al. (2014) demonstrated that, after adjustment, male gender remained strongly associated with virologic failure (adjusted OR = 2.52; 95 % CI: 1.77 – 3.60; p<0.001).

Two key factors may explain why men are more vulnerable to virologic failure. The first concerns gender differences in the pharmacokinetic and pharmacodynamic profiles of antiretroviral drugs (Ofotokun et al., 2007; Gandhi et al., 2004). It has been observed that women have higher concentrations of antiretroviral drugs, which improves virological efficacy (Veldkamp et al., 2001; Marzolini et al., 2001; Shiau et al., 2014). These differences could be attributed to variations in drug absorption, distribution, metabolism, and excretion, influenced by factors such as body composition, hormonal fluctuations, and enzymatic activity (Mank & Rideout, 2021).

The second factor is suboptimal adherence to HIV care and treatment among men, which has often been observed in SSA (Bastard et al., 2011; Nachega et al., 2006; Kranzer et al., 2010; Colvin, 2019). The lower adherence to treatment in men may be influenced by socio-cultural gender norms, as highlighted by Bila and Egrot (2009) in their study on gender asymmetry in healthcare facility attendance by PLHIV in Burkina Faso. We believe that, for male CALHIV, adherence to ART may be hindered by societal views on masculinity, particularly during adolescence. As boys grow older, they may become more reluctant to seek medical care or discuss their health due to social pressure to appear strong and avoid showing vulnerability. Studies have shown that adolescent males tend to exhibit lower levels of adherence, miss more clinic visits, and engage less in treatment support programs (Umar et al., 2019; Colvin, 2019). Communication barriers with female healthcare

providers and the lack of male-friendly services also contribute to reduced healthcare engagement among males (Schneider et al., 2012; Mukumbang, 2021).

However, some of these factors are more applicable to older children and adolescents than to younger ones. In early childhood, particularly under the age of five, adherence and treatment outcomes are primarily influenced by caregiver behavior rather than the child's sex or gender identity. While there is limited research specifically examining whether caregivers treat very young boys and girls differently in terms of ART adherence, some studies have suggested that boys may receive less supervision or caregiving support than girls, potentially leading to inconsistent ART use (Somi et al., 2009). Yet, the evidence remains mixed. For example, some studies have reported no significant gender differences in adherence among CALHIV (Ioannides et al., 2017; Vreeman et al., 2014), whereas others have found higher rates of viral non-suppression in female CALHIV (Afrane et al., 2021; Fenta et al., 2021; Muri et al., 2017). These inconsistencies highlight the need for more age-stratified analyses to better understand how gender and age interact to influence treatment outcomes among CALHIV.

These disparities underscore the necessity for sex-specific interventions aimed at improving ART adherence and viral suppression among male CALHIV. Strategies such as enhanced adherence counseling, targeted psychosocial support, and male-centered healthcare engagement approaches could play a crucial role in mitigating these differences and optimizing treatment outcomes for all CALHIV.

2.4.2.4. Impact of orphan status on virological suppression rates among children and adolescents living with HIV

Orphan status significantly influences viral suppression rates among CALHIV. Several studies have shown that orphaned children living with HIV are more likely to have an unsuppressed VL compared to non-orphaned children. Both simple and double orphan status have been associated with higher chances of virologic failure (Vreeman et al., 2018; Yiman et al., 2019; Haile & Berha, 2019; Bayleyegn et al., 2021; Getaneh et al., 2022; Bitwale et al., 2021; Gordon et al., 2022; Mbébi-Enoné et al., 2023; Ndongo et al., s2024). In their study, Bayleyegn et al. (2021) found that children on antiretroviral therapy living with caregivers had a fourfold higher risk of virologic failure compared to those living with their immediate family (AOR = 3.63; 95% CI: 1.27 – 10.24). Similar results were observed in several studies conducted in Ethiopia, where children without a family as a primary caregiver were more likely to experience treatment failure (Yiman et al., 2019; Haile & Berha, 2019).

The vulnerability of CALHIV, resulting from the loss of a biological parent or lack of adequate support from non-biological caregivers, places them at increased risk of poor treatment adherence and failure to achieve and maintain viral suppression. This vulnerability is multifaceted, involving not only emotional and psychological distress but also socio-economic uncertainties and inconsistent care often associated with the loss of a parent (Gordon et al., 2022; Nyogea et al., 2015; Kikuchi et al., 2012; Bayleyegn et al., 2021). These complex factors create an environment where the ability of CALHIV to manage their HIV infection becomes increasingly compromised, leading to poorer health outcomes.

The intricate interplay of emotional trauma, disrupted family structures, and socio-economic challenges commonly associated with orphanhood can significantly heighten the risk of failing to achieve sustained viral suppression. Psychological distress, such as anxiety and depression stemming from parental loss, often hinders adherence to ART, exacerbated by financial constraints and inconsistent caregiving (Bayleyegn et al., 2021). The absence of stable and supportive care further compounds the emotional strain, impeding CALHIV's access to necessary medical care and adherence to treatment protocols crucial for attaining viral suppression. The obstacles confronting orphaned children, spanning from the emotional repercussions of parental loss to inadequate care, can severely undermine the efficacy of ART regimens. Additionally, the socio-economic circumstances in which many orphans are situated frequently result in limited healthcare access, insufficient nutritional support, and inadequate emotional assistance, all of which are vital for effective HIV treatment (Shah et al., 2022; Mufalali et al., 2022). This underscores the significance of recognizing orphan status as a pivotal determinant in the care and management of CALHIV.

Interventions aimed at improving virologic outcomes for orphaned CALHIV must take a holistic approach, addressing not only medical and therapeutic needs but also the psychological and social factors that influence their treatment adherence (Shah et al., 2022; Mufalali et al., 2022). Comprehensive support, including emotional counseling, financial assistance for families or caregivers, as well as stable and consistent care, can reduce barriers to treatment and improve the health of this vulnerable population (Coard et al., 2022). In Onyango et al.'s (2023) study, the intervention of empowering families of orphaned and vulnerable children by providing income-generating activities was identified as a factor associated with viral load suppression. Social protection and community-based interventions, such as cash transfers, mentorship, and family therapy, have shown

potential to improve the cognitive, psychosocial, and behavioral outcomes of orphaned and vulnerable children, including those living with HIV (Thomas et al., 2020). Community-based art therapy interventions (Mueller et al., 2011) and community-based culturally grounded interventions (Thomas et al., 2020) have also had positive effects, although their effectiveness varies, requiring further research to identify the most effective practices and assess their cost-effectiveness.

According to Patel et al. (2011), a community-based play center model enhances the overall care of orphaned and vulnerable children under five years old by promoting their emotional, cognitive, and physical development, while offering caregivers the opportunity to access HIV testing, care, and treatment for children exposed, affected, or HIV-positive in a secure and supportive environment. This holistic approach, which addresses the needs of orphaned children and supports their psychological adaptation, is crucial for improving their well-being and optimizing their treatment (Mufalali et al., 2022). Finally, the association between social interventions providing economic support to families and psychosocial support is vital for ensuring quality care. Indeed, caring for a CALHIV is challenging for the caregiver and impacts the entire family system (Onyango et al., 2023).

2.4.2.5. Impact of healthcare facility level on viral load suppression among children and adolescents living with HIV

The findings of this meta-analysis reveal a significant association between the level of healthcare facility and virological suppression outcomes among CALHIV. Specifically, CALHIV receiving treatment in lower-level health facilities (level 1 or 2) had a higher likelihood of unsuppressed viral load compared to their counterparts treated in higher-level facilities (OR = 1.58; 95% CI: 1.07–2.35). Tsikhutsu et al. (2022) found that receiving treatment in a level 3 facility was independently associated with better viral suppression

(aPR = 1.23; 95% CI: 1.11 – 1.36), highlighting a notable disparity in quality of care, resource availability, and expertise between lower- and higher-level facilities. In the study by Khamadi et al. (2023), seeking HIV care at a referral center (aPR = 1.12, 95% CI: 1.04 – 1.21) was associated with improved virological suppression. Similarly, Mushy et al. (2024) found that receiving HIV care at a dispensary-level facility was independently linked to a higher risk of viral load non-suppression (HR = 3.61, 95% CI: 1.44–7.03), further emphasizing the significant influence of facility level on treatment outcomes.

This relationship raises critical concerns about the adequacy of services provided in lower-level facilities, which may negatively impact virological outcomes. According to Tsikhutsu et al. (2022), it remains uncertain whether all healthcare facilities have the necessary resources to provide comprehensive adherence support. Their study suggests that access to level 3 facilities, which are better equipped, may explain the observed association between viral suppression and the quality of care in these settings. Furthermore, some differentiated care models in adolescent-specialized clinics have led to improved viral suppression. These models adopt a patient-centered approach and specifically address the unique needs and challenges of adolescents (Zanoni et al., 2017; Njuguna et al., 2020). In a study by Zanoni et al. (2017), a specialized clinic operating only on weekends demonstrated higher retention and viral suppression rates. This initiative aimed to reduce stigma, strengthen peer support, and minimize school absences for adolescents.

The association between lower-level healthcare facilities and virological failure can be attributed to several interconnected factors. Level 1 and 2 hospitals differ from level 3 hospitals in the resources and expertise they offer for managing HIV in children and adolescents. Level 1 and 2 facilities are often primary or secondary care centers with limited resources, restricting access to advanced diagnostics and complex antiretroviral

treatments in different pharmaceutical formulations suited for CALHIV (Kredo et al., 2013). As a result, the management of comorbidities and HIV-related complications in youth may be less specialized. Additionally, these hospitals often lack healthcare personnel specifically trained to treat CALHIV, which can affect the quality of care (Kredo et al., 2013). The absence of a comprehensive range of services in these facilities may contribute to suboptimal HIV management in CALHIV, leading to higher rates of virological failure (Tsikhutsu et al., 2022). In contrast, Level 3 hospitals are tertiary care centers offering more extensive resources, including advanced diagnostic tests and cutting-edge treatments (Kredo et al., 2013). They have pediatric specialists trained in managing pediatric and adolescent HIV, as well as programs tailored to the specific needs of this population, such as dedicated adolescent spaces and patient-centered approaches (Zanoni et al., 2017). These hospitals also tend to integrate a multidisciplinary approach, involving psychologists and social workers to support the psychological and social aspects of young people living with HIV (Kredo et al., 2013). The combination of these resources and expertise enables a more comprehensive and effective approach to HIV care, contributing to better viral suppression and improved disease management (Tsikhutsu et al., 2022). However, while Level 3 hospitals are theoretically better equipped and staffed, in practice across SSA, they often serve more complex cases and face their own systemic limitations. As such, the modest differences in odds of VLS observed in our study may reflect both the limited availability of truly specialized services and the multifactorial challenges affecting treatment outcomes among CALHIV.

This finding underscores the importance of reducing disparities in healthcare access and ensuring that CALHIV receive treatment in well-equipped facilities with qualified personnel for optimal care. In this regard, policymakers and program managers must focus on improving infrastructure and capacity in lower-level healthcare facilities (Nwabueze et

al., 2010). This includes enhancing access to essential medical resources, strengthening continuous training for healthcare providers—especially in pediatric HIV management—and promoting better coordination between different levels of care (Patel et al., 2013). The study by Patel et al. (2013) concluded that nurse-led, integrated HIV and tuberculosis care for children, implemented at primary healthcare levels in resource-limited settings, is feasible and effective in achieving positive outcomes such as high ART coverage, low mortality, and clinical and immunological improvements.

In this context, decentralization of healthcare services could play a key role in ensuring that specialized care, such as HIV treatment, is accessible to all. The decentralization of HIV care to local primary healthcare clinics has contributed to increasing the number of children receiving antiretroviral treatment (Kredo et al., 2013; Fayorsey et al., 2013; Sornillo et al., 2023) and has led to lower rates of virological failure, loss to follow-up, and mortality (Fayorsey et al., 2013; Mbébi Enoné et al., 2023). It would facilitate access to specialized care, relieve pressure on higher-level hospitals, and improve the distribution of resources and expertise across regions (Munderi et al., 2012). Addressing these disparities could help reduce virological failure among CALHIV and improve long-term health outcomes.

2.4.2.6. Impact of HIV status disclosure on viral load suppression among children and adolescents living with HIV

HIV status disclosure emerges as a key determinant of treatment success in this study. This meta-analysis found that children and adolescents living with HIV who were unaware of their status faced a significantly higher risk of treatment failure compared to those who had been informed of their diagnosis. Recent research further strengthens the link between non-disclosure of HIV status and virologic failure among CALHIV. Several studies, including

those by Bitwale et al. (2021), Shumetie et al. (2021), and Simms et al. (2021), indicate that CALHIV who had not been informed of their HIV-positive status were at a significantly higher risk of unsuppressed viral load compared to those whose status had been disclosed. These findings underscore the critical importance of HIV status disclosure as a key intervention to optimize treatment outcomes.

The study by Getaneh et al. (2022), which conducted a systematic review and meta-analysis on antiretroviral treatment failure and its associated factors in Ethiopia, also highlighted this association. Their findings indicated that the lack of HIV status disclosure was significantly linked to an increased risk of treatment failure (OR = 1.6; 95% CI: 1.0–2.5). Similarly, Shumetie et al. (2021) observed that HIV-positive children who were unaware of their status were 4.26 times more likely (AOR = 4.26; 95% CI: 2.09, 8.70) to experience virologic failure compared to those who had been informed. These results align with those of Emmett (2010) in Moshi, Tanzania, who demonstrated the protective effect of full HIV status disclosure against virologic failure ($p = 0.02$).

Furthermore, a study by Bitwale et al. (2021) in Dodoma, Tanzania, revealed that children who were not aware of their status were 7.74 times more likely (AOR = 7.741; 95% CI: 2.351–25.489) to have an unsuppressed viral load. Similarly, studies conducted in Ethiopia by Sisay et al. (2018) and Yimam et al. (2019) confirmed that HIV status disclosure served as a protective factor against virologic failure during medical consultations. Additionally, a study in Uganda (Atuyambe et al., 2014) found that disclosing HIV status to family and friends fostered better emotional support and positive behavioral changes among patients. Therefore, the absence of HIV status disclosure to family members could contribute to virologic failure due to the lack of these essential support mechanisms (Bitwale et al., 2021).

The primary explanation for this impact lies in the psychological and behavioral consequences of non-disclosure (Shumetie et al., 2021). Indeed, not being informed of their HIV status can lead to increased stress, especially when CALHIV are on ART without knowing the reason, resulting in lower adherence to treatment and difficulties in maintaining consistent medication schedules. This reduces treatment effectiveness and leads to therapeutic failure (Daskalopoulou et al., 2017; Shumetie et al., 2021). These studies suggest that awareness of one's HIV status plays a central role in improving treatment outcomes, likely by enhancing adherence to ART and enabling better disease management. The complex relationship between psychological well-being and treatment effectiveness underscores the importance of a comprehensive approach to CALHIV care, addressing their emotional and social needs. Treatment adherence is not solely dependent on the availability of antiretrovirals but also on the patient's mental and emotional state. In this context, HIV status disclosure becomes a crucial step in strengthening treatment engagement and improving health outcomes.

Although the study by García-Boyano et al. (2022) did not demonstrate that early disclosure leads to better adherence, it highlighted improvements in psychological outcomes, supporting WHO (2011) recommendations for disclosure before the age of 12. The optimal age for disclosure depends on cognitive development, not just age. However, data on the impact of disclosure on treatment adherence remain mixed. Most studies cited are cross-sectional and do not compare adherence before and after disclosure. Longitudinal evidence on the impact of disclosure remains limited. A systematic review by Nichols et al. (2017) revealed divergent findings: five studies found no association between disclosure and adherence, four reported a negative impact, while five showed positive benefits. The mixed findings likely reflect differences in study design, population, and quality. Some studies may have limited validity due to methodological weaknesses. Among the negative

effects, fear of stigma, denial of serological status, and increased depressive symptoms were identified as factors that could compromise adherence. Conversely, studies demonstrating positive effects emphasized that disclosure could strengthen collaboration between the child and their caregiver, improve understanding of treatment, and encourage open communication about adherence among healthcare providers, caregivers, and patients. These findings highlight the need to approach disclosure as a gradual and personalized process rather than a single event (Nichols et al., 2017). Gradual disclosure refers to a step-by-step sharing of HIV-related information tailored to the child's age and maturity. A disclosure approach tailored to the patient's cognitive development and emotional maturity is essential to minimize psychological risks and foster autonomy in managing their health (WHO, 2011).

The implementation of interventions that integrate both disclosure and adherence support in a culturally appropriate manner could optimize therapeutic benefits for CALHIV. Outcomes may differ depending on whether disclosure was well-managed or poorly implemented. Disclosure with adequate support tends to yield better psychological and adherence outcomes. Well-managed disclosure maximizes long-term treatment success and significantly improves CALHIV health outcomes. According to WHO (2011), a supportive and structured framework involving healthcare providers and caregivers is crucial for ensuring effective guidance. Pediatric HIV care programs should incorporate specific interventions aimed at strengthening trust and collaboration among healthcare systems, caregivers, and CALHIV. These interventions must be designed to support a well-structured disclosure process, essential for improving treatment adherence, promoting viral suppression, and ensuring overall well-being (WHO, 2011).

Age- and comprehension-appropriate information and awareness campaigns should be implemented to facilitate a gradual disclosure of HIV status, reduce stigma, and improve treatment adherence. Training healthcare providers in pediatric counseling is crucial for effective support and optimal psychological assistance (WHO, 2011). Psychological and social support, including support groups for children, families, and caregivers, help better manage emotional challenges and promote treatment adherence, which is key to viral load suppression. Strong community involvement and awareness campaigns are necessary to combat discrimination and create an environment conducive to pediatric HIV care. Individualized support, considering each child's specific needs, enhances treatment adherence and improves ART management. Strengthening policies on protection, confidentiality, and non-discrimination is crucial to securing the disclosure process and preventing stigma (WHO, 2011).

2.4.2.7. Role of adherence to antiretroviral therapy in viral load suppression among children and adolescents living with HIV

One of the most significant findings of this meta-analysis highlights the crucial role of adherence to ART in viral load suppression. The results clearly show that suboptimal adherence to ART is a major factor in the failure to achieve viral suppression, with individuals demonstrating poor adherence having 6.5 times higher odds of experiencing USVL. This finding is corroborated by several studies, which strengthen the significant association between low adherence and an increased risk of unsuppressed viral load in this population. Recent studies (Djiyou et al., 2023; Mageda et al., 2023; Sibhat et al., 2020; Abera et al., 2023; Desalegn et al., 2024; Khamadi et al., 2023; Ally et al., 2023; Quaker et al., 2024; Tsikhutsu et al., 2022) consistently show that poor adherence is a key predictor of treatment failure among CALHIV, exacerbating the challenges associated with

managing the infection in this vulnerable group. This finding, in line with existing literature, consistently demonstrates that inadequate adherence to antiretroviral regimens is one of the strongest predictors of virological failure, thereby compromising the effectiveness of treatment (Iacob et al., 2017; Nachega et al., 2018). ART is recommended for PLHIV to achieve VLS, maintain strong immunity, and improve long-term survival. However, its effectiveness relies on optimal adherence to the prescribed treatment regimen (WHO, 2016).

Non-adherence to antiretroviral treatment results from a series of complex and interconnected factors (Tsikhutsu et al., 2022). In pediatric settings, adherence to ART is influenced by various factors, including the child's current clinical status, cognitive and behavioral maturity, and the physical and psychosocial health of their primary caregivers. Additionally, factors such as socioeconomic status, cultural beliefs, the biological relationship with healthcare providers, and the social and cultural environment play a significant role in adherence (Haberer & Mellins, 2009; Tsikhutsu et al., 2022). Behavioral issues, religious beliefs, learning difficulties, hyperactivity disorders, food insecurity, treatment duration, ART formulation, and the patient's age are all factors that can negatively affect adherence (Shah, 2007; Malee et al., 2011; Young et al., 2014), thus hindering CALHIV from achieving VLS.

Even in the presence of targeted professional interventions, these factors may persist and undermine adherence to treatment. Jobanputra et al. (2015) reported that patients who had received multiple referrals to adherence counseling sessions due to non-adherence were less likely to achieve viral suppression. This suggests that adherence counseling strategies should be adjusted to more precisely identify the underlying causes of non-adherence. As recommended by current guidelines in the DRC (PNLS, 2021), the following measures

should be implemented: a thorough assessment of ART adherence barriers, individualized case management, home visits, mental health screening, and directly observed medication administration for patients experiencing therapeutic failure.

To enhance treatment adherence and achieve UNAIDS goals, Nachega et al. (2018) propose several strategies tailored to children and adolescents. For children, they recommend improved access to new pediatric formulations of antiretrovirals and a family-centered approach integrated into a community-based care model. Regarding adolescents, suggestions include peer support, both individual and collective, the establishment of guidelines for transitioning to adult care, youth-specific services, and anticipatory counseling on disclosure of HIV status for healthcare professionals, parents, and the adolescents themselves. Special emphasis is placed on a seamless transition to differentiated care tailored to the specific needs of this population (Nachega et al., 2018).

In interventions aimed at improving treatment adherence, Iacob et al. (2017) emphasize that adherence is a complex and dynamic process. As with other chronic conditions, PLHIV face difficulties in maintaining high levels of adherence to treatment over the long term. Therefore, it is essential for healthcare professionals to recognize that perfect and continuous adherence is rarely realistic. Regular adherence monitoring is crucial (Iacob et al., 2017). Even for patients who are generally considered adherent, discussions about adherence should not be minimized, as there is always the possibility that they may become non-adherent. Adherence monitoring should focus on three key areas: rapid identification of non-adherent patients, analysis of the underlying causes of non-adherence, and implementation of appropriate solutions (Iacob et al., 2017). In low-resource settings, where full multidisciplinary teams may not always be available, community health workers, peer educators, and caregivers can play a central role in adherence support.

Adapting the team approach to local capacities and leveraging existing human resources is essential. Such interventions, whether general or specifically tailored to certain groups, can still significantly improve treatment adherence among PLHIV (Iacob et al., 2017).

2.4.2.8. Impact of advanced WHO clinical stages, opportunistic infections, low CD4+ T-cell counts, and malnutrition on viral load suppression among children and adolescents living with HIV

The results of this meta-analysis indicate that CALHIV in advanced WHO clinical stages (3 or 4) were at a higher risk of developing USVL compared to those in WHO clinical stages 1 or 2. These findings align with previous SSA research (Fenta et al., 2021; Nabukeera et al., 2021; Osman & Yizengaw, 2020; Quaker et al., 2024; Shumetie et al., 2021; Sibhat et al., 2020), which also demonstrated that CALHIV in advanced WHO clinical stages are significantly more likely to experience unsuppressed viral load compared to those in earlier stages of HIV infection. This heightened risk reflects multifaceted challenges, including severe immune dysfunction, increased exposure to opportunistic infections, and difficulties with adherence to ART, creating a vicious cycle: poor adherence compromises the effectiveness of ART, weakening the immune system and increasing susceptibility to OIs and the development of drug resistance (Gelaw et al., 2021). Consequently, this accelerates viral replication, increases CD4 cell depletion, promotes the accumulation of resistant strains, and speeds up disease progression (Abera et al., 2023), ultimately resulting in virological failure. This is further confirmed by the findings of this meta-analysis, which shows that, as previously reported by other SSA studies (Mena et al., 2023; Abera et al., 2023; Mchomvu et al., 2022; Mwangi et al., 2021; Elashi & van Wyk, 2022; Okonji & van Wyk, 2021; Isaac et al., 2020; Afrane et al., 2021; Mukumbuta et al., 2024), CALHIV with low CD4+ T-cell counts (<200 cells/mm3) were more likely to experience USVL compared to those with higher CD4+ counts. Similarly, this meta-

analysis found that, consistent with previous studies (Gordon et al., 2022; Sibhat et al., 2020; Abera et al., 2023; Getawa et al., 2021; Bitwale et al., 2021; Bacha et al., 2022; Afrane et al., 2021), CALHIV with a history of OIs were more likely to experience USVL compared to those without a history of such infections. In addition to these clinical factors affecting VLS, malnutrition—demonstrated by several studies conducted in SSA (Gordon et al., 2022; Bayleyegn et al., 2021; Kadima et al., 2018; Tweya et al., 2020; Tanoh-Aka et al., 2021)—significantly increases the risk of USVL compared to CALHIV with normal nutritional status.

The results of this study emphasize the significant impact of advanced WHO clinical stages (3 and 4), OIs, low CD4+ T-cell counts, and malnutrition as key predictors of USVL in CALHIV, acting independently or in combination, potentially creating a vicious cycle if timely intervention measures are not initiated. Advanced WHO clinical stages are strongly associated with an increased risk of USVL due to profound immune system deterioration and substantial depletion of CD4+ T-cells. As HIV progresses, the continued decline in CD4+ T-cells weakens the immune system's ability to combat infections and regulate viral replication (Okoye & Picker, 2013). At these advanced stages, the immune system becomes severely compromised, preventing the body from mounting an effective immune response, leading to persistently high VLs and significantly reduced CD4+ counts. Consequently, CALHIV in advanced clinical stages are at a higher risk of ART failure and increased susceptibility to secondary infections, further complicating HIV management.

Advanced WHO clinical stages encompass severe HIV-related complications, often accompanied by OIs such as tuberculosis, pneumonia, and candidiasis. These infections place additional strain on an already weakened immune system, exacerbating viral replication and reducing the effectiveness of ART (Kervevan & Chakrabarti, 2021). The

increased burden of OIs in advanced clinical stages further complicates ART adherence, as the additional physiological stress contributes to negative health outcomes, including malnutrition. Malnutrition, particularly in the context of severe immune depletion, impairs ART absorption and its efficacy, thereby increasing the risk of virological failure (WHO, 2020). The interaction between malnutrition and HIV progression necessitates comprehensive care strategies that integrate nutritional support alongside ART to improve treatment outcomes. The presence of OIs not only accelerates HIV progression but also compromises immune recovery, underscoring the need for early diagnosis, prompt initiation of ART, and continuous monitoring of immune function in CALHIV. This approach aligns with the "test and treat" strategy, introduced in 2009, which emphasizes early and regular HIV testing and immediate access to ART, regardless of CD4 count, for anyone diagnosed as HIV-positive (Granich et al., 2009; Nah et al., 2017; Phanuphak et al., 2019). Officially recognized by the WHO in 2015 following randomized controlled trials demonstrating its clinical benefits, this strategy aims to optimize VLS and prevent disease progression (WHO, 2016). Its success relies on intensified efforts to rapidly identify individuals living with HIV and efficiently link them to care.

These results highlight the urgent need for early interventions to prevent the progression of HIV to advanced stages in CALHIV. A delayed or missed diagnosis is a critical factor contributing to the advanced stage of the disease at the time of initiating ART, with significant implications for treatment outcomes. The presence of OIs, low CD4+ T-cell counts, and malnutrition, in addition to advanced WHO clinical stages, are well-established predictors of USVL in CALHIV. However, a delayed diagnosis, often indicated by these factors, complicates the rapid initiation of ART and significantly hinders sustained VLS. In regions with limited access to healthcare, late HIV diagnosis often results in ART initiation at more advanced stages of the disease, exacerbating immune system

vulnerability and increasing the risk of USVL (Kervevan & Chakrabarti, 2021). The CHER study and others emphasize the critical importance of early ART initiation, particularly in infants and young children, where rapid treatment is essential for long-term VLS (Cotton et al., 2013; Payne et al., 2021). EID and prompt initiation of ART are crucial to improving long-term treatment outcomes, preventing complications, and increasing the likelihood of sustained VLS.

Comprehensive HIV care for CALHIV should not only focus on viral control through ART but also on managing OIs and nutritional deficiencies. A holistic approach that integrates ART adherence support, proactive immune function management, infection control, and nutritional interventions is imperative to optimizing treatment success (WHO, 2016). Strengthening healthcare systems to provide these integrated services is essential to improving treatment outcomes and preventing the escalation of HIV-related complications. Early interventions are crucial to reducing the burden of OIs, preventing virological failure, and ultimately ensuring long-term health outcomes for CALHIV. Removing barriers to EID and the rapid initiation of ART, following the "test and treat" strategy, will be critical in preventing the progression of HIV to advanced stages and improving the overall health of CALHIV. This approach, involving systematic screening and immediate treatment, enables early intervention, thereby reducing transmission risks and optimizing long-term health outcomes for this vulnerable population.

2.4.2.9. Role of cotrimoxazole prophylaxis in reducing the risk of unsuppressed viral load among children and adolescents living with HIV

This meta-analysis provides compelling evidence supporting the crucial role of cotrimoxazole prophylaxis in reducing the risk of USVL in CALHIV. Cotrimoxazole, a broad-spectrum antimicrobial agent recommended by the WHO (2016) for individuals

living with HIV, has been shown to significantly reduce the incidence of OIs in immunocompromised populations. The protective effect of cotrimoxazole prophylaxis is particularly relevant in settings where the burden of OIs, such as bacterial pneumonia, toxoplasmosis, and malaria, remains high (Bourke & Prendergast, 2020). By preventing these infections, cotrimoxazole contributes to better immune system preservation, which is essential for achieving and maintaining viral suppression. The absence of cotrimoxazole prophylaxis has been associated with a twofold increase in the likelihood of USVL, highlighting its importance in HIV treatment strategies.

Beyond its well-established role in preventing OIs, emerging evidence suggests that cotrimoxazole may enhance the efficacy of ART through several potential mechanisms. First, its antimicrobial properties could have a direct antiviral effect on HIV replication, thereby contributing to better virological outcomes. Second, by preventing secondary infections that could otherwise weaken the immune system, cotrimoxazole may facilitate immune recovery and support ART-mediated viral suppression. Third, improved overall health due to infection prevention may enhance adherence to ART, as patients experiencing fewer illnesses are more likely to consistently take their medications (Bourke & Prendergast, 2020). According to Church et al. (2015), cotrimoxazole prophylaxis reduces anemia and improves growth in children living with HIV, likely by reducing inflammation, either through direct immunomodulatory activity or through effects on the intestinal microbiota leading to reduced microbial translocation. The South African study by Hoffmann et al. (2010) demonstrated that cotrimoxazole prophylaxis reduced mortality among individuals initiating combined antiretroviral therapy, particularly among those with a CD4 count below 200 cells/µl or WHO clinical stage 3 or 4, highlighting its effectiveness in improving treatment outcomes in resource-limited settings.

Previous studies, particularly that of Bitwale et al. (2021), emphasize that the absence of cotrimoxazole prophylaxis is strongly associated with virological treatment failure among CALHIV, with an adjusted odds ratio of 25.56 (95% CI: 3.15–27.55; p = 0.002), indicating that these patients are much more likely to experience virological treatment failure compared to those receiving prophylactic treatment. These findings underscore the necessity of integrating cotrimoxazole prophylaxis as a standard component of HIV care for pediatric and adolescent populations, particularly in settings where access to comprehensive healthcare remains a challenge. Cotrimoxazole prophylaxis plays a crucial role in preventing opportunistic infections and improving virological outcomes among CALHIV. Its absence is strongly associated with an increased risk of USVL, highlighting the need for consistent implementation of prophylactic guidelines (WHO, 2016). Strengthening adherence to cotrimoxazole prophylaxis as part of a comprehensive HIV care strategy is essential for improving long-term health outcomes for CALHIV and reducing the burden of HIV-related complications.

2.4.2.10. Impact of drug substitutions on virological suppression in children and adolescents living with HIV

In this meta-analysis, it was observed that CALHIV with a history of drug substitutions were 3.81 times more likely to experience USVL (OR = 3.81; 95% CI: 2.67–5.44). Recent studies have strengthened this significant association between drug substitutions and virological outcomes in CALHIV (Berihun et al., 2023; Mwangi & van Wyk, 2021; Munyayi & van Wyk, 2022; Getawa et al., 2021; Mchomvu et al., 2022; Quaker et al., 2024; Kadima et al., 2018; Okonji et al., 2021). Indeed, CALHIV with a history of drug substitutions are more likely to experience USVL compared to those whose treatment regimen remained stable. In a systematic review and meta-analysis by Getaneh et al. (2022)

in Ethiopia, drug substitutions (OR = 2.0, 95% CI: 1.5–2.7) were identified as a significant factor associated with treatment failure in children living with HIV. This strong association suggests that therapeutic changes, although often necessary, may lead to periods of suboptimal viral control, particularly when they cause temporary interruptions in treatment, reduced regimen potency, or difficulties in adapting to new medications.

Therapeutic regimen changes are commonly recommended for PLHIV who face difficulties in achieving durable viral load suppression (WHO, 2016). Costenaro et al. (2015), in their cohort study from Mozambique and Uganda, found that a total of 202 out of 769 (26.3%) children receiving substituted drugs, with the main reported reasons for substitution being drug toxicity, drug availability, and interactions with tuberculosis drugs, accounting for 18.3%, 17.3%, and 25.7%, respectively. Only 9 (4%) patients switched ART due to clinical or immunological failure. In line with this, Buck et al. (2010) found that the discontinuation of first-line ART in 1,434 Malawian children was primarily driven by toxicities, ART failure, and other clinical factors. These findings underscore the importance of carefully monitoring treatment outcomes and adjusting regimens to address emerging issues, such as side effects and drug interactions, which can hinder long-term viral suppression. However, these changes introduce new challenges, including more complex management of side effects, reduced adherence due to the multiplicity of medications, or difficulties in adapting to new drug formulations, compromising viral suppression durability. The introduction of new drugs generally leads to new side effects until the usual adaptation and response phases are reached, which can affect treatment adherence and, consequently, the virological status under ART (Getaneh et al., 2022).

Drug substitutions in PLHIV are often triggered by clinical and behavioral factors, including the development of drug resistance, adverse effects, poor treatment tolerance,

metabolic variations, and difficulties in treatment adherence. Each of these factors can significantly impact the pharmacokinetics and pharmacodynamics of ART, leading to fluctuating drug levels in circulation and increasing the risk of treatment failure. In a study by Kabarambi et al. (2022) conducted on youth aged 10 to 24 years in Cape Town (South Africa), it was found that the risk of changing the ART regimen increased with the severity of the disease at the start of ART, as evidenced by the increase in WHO clinical stage or the decrease in CD4 count at inclusion. The main reasons for these substitutions were side effects (20.0%), virological failure (17.9%), and drug formulation changes (27.8%). Other reasons such as pregnancy, hepatitis B, tuberculosis, and psychosis were also mentioned (Kabarambi et al., 2022).

The emergence of drug resistance is one of the main reasons for ART substitutions, as mutations in HIV can compromise the efficacy of specific ART regimens. These mutations generally result from prolonged exposure to ineffective treatment regimens, incomplete viral suppression, or intermittent adherence to ART (Assefa & Hussein, 2014; Woldemedhin & Wabe, 2012; Mutwa et al., 2014; Rugemalila et al., 2023). Consequently, patients may need to switch to a more potent or alternative regimen, which may not always be well-tolerated or readily available, especially in resource-limited settings. Furthermore, erratic adherence to ART, due to socio-economic constraints, pill burden, psychosocial barriers, or stigma, often leads to fluctuating drug concentrations, which can promote viral replication and resistance. When patients experience side effects, ranging from mild symptoms to severe toxicities, clinicians may opt for treatment modifications to improve patient comfort and adherence (Rugemalila et al., 2023).

Given the potential impact of drug substitutions on treatment outcomes, it is essential that healthcare workers implement rigorous therapeutic monitoring strategies. These strategies

should include regular VL tests, resistance profiling, and continuous adherence education. Such approaches will help minimize unnecessary regimen changes and optimize the long-term effectiveness of ART (WHO, 2016). Furthermore, further research is needed to assess the long-term impact of drug substitutions on virological suppression and ART durability, to guide policy recommendations and improve therapeutic practices for CALHIV. Rigorous clinical follow-up is critical to identify the underlying factors driving these treatment changes, ensuring both efficacy and long-term treatment adherence.

2.4.2.11. Impact of ART duration on virological suppression in children and adolescents living with HIV

The duration of ART is a critical factor in achieving viral suppression among CALHIV. The results of this meta-analysis support earlier research (Tsikhutsu et al., 2022; Munyayi & van Wyk, 2022) showing that an ART duration of less than 24 months is strongly linked to a higher risk of USVL. These findings underscore the susceptibility of patients in the initial phases of treatment, underscoring the importance of vigilant monitoring and personalized interventions to enhance treatment outcomes.

The initial phase of ART is a critical period characterized by active viral suppression and the beginning of immune restoration. However, this phase is also marked by physiological and psychosocial challenges that may affect treatment adherence and, consequently, its overall effectiveness. Several factors, including medication side effects, regimen complexity, and psychosocial barriers such as stigma and concerns related to status disclosure, can compromise adherence (Chinyandura et al., 2022). Without adequate support mechanisms, these challenges may lead to inconsistent ART intake, increasing the risk of incomplete viral suppression and the potential development of drug resistance.

Moreover, ART pharmacokinetics vary among individuals, and achieving optimal therapeutic levels may take time, especially in pediatric and adolescent populations. Weight-based dose adjustments, crucial in these growing populations, add complexity to treatment management and can impact drug exposure stability and virological outcomes. Additionally, the initial months of ART frequently involve addressing opportunistic infections and pre-existing comorbidities, which may impede immune recovery and viral suppression efforts.

Adolescents with longer ART experience generally benefit from improved status disclosure management, reduced psychosocial barriers (such as stigma), and greater self-efficacy and competence in adhering to treatment (Munyayi & van Wyk, 2022; Cherutich et al., 2016; Jobanputra et al., 2015). These factors play a crucial role in enhancing viral suppression rates, highlighting the significance of integrated and sustained care strategies to guarantee long-term treatment stability.

Given these complexities, targeted interventions during the first two years of ART initiation are essential to enhance sustained viral suppression. These interventions should include intensified adherence counseling, continuous caregiver education, frequent viral load monitoring, and proactive management of ART-related side effects. Additionally, integrating psychosocial support and mental health services into pediatric and adolescent HIV care could further improve retention in treatment and adherence, ultimately leading to better virological outcomes.

Available data suggest that the early phase of ART represents a critical window during which enhanced clinical and psychosocial support is necessary to reduce the risk of unsuppressed viral load (Tsikhutsu et al., 2022; Munyayi & van Wyk, 2022; Cherutich et al., 2016). Optimized management during this period can have lasting benefits, ensuring

that CALHIV transition successfully to long-term treatment stability and achieve optimal HIV care outcomes.

2.4.2.12. Association between Nevirapine-based regimens and unsuppressed viral load in children and adolescents living with HIV

A growing body of evidence indicates that the use of nevirapine-based antiretroviral regimens is significantly associated with inadequate virologic suppression in children and adolescents living with HIV. Consistent with the findings of this meta-analysis, several studies conducted in sub-Saharan Africa (Shiferaw et al., 2019; Muri et al., 2019; Bitwale et al., 2021; Mchomvu et al., 2022; Tweya et al., 2020; Isaac et al., 2020; Chouraya et al., 2019; Afrane et al., 2021; Machila et al., 2023; Zenebe et al., 2021) have consistently demonstrated that patients on nevirapine-based ART are at a higher risk of virologic failure compared to those receiving other therapeutic regimens. This increased risk is attributed to multiple factors, including the pharmacokinetic limitations of nevirapine, its low genetic barrier to resistance, and age-related differences in immune system development (Makadzange et al., 2015; Gopalan et al., 2017). Duong et al. (2014) conducted a study in the UK that revealed maternal exposure to antiretroviral therapy during the perinatal period increased the risk of virologic failure in children. Specifically, exposure to nevirapine-based ART in the mother was associated with a higher likelihood of treatment failure in the child. Mendes-Ferreira et al. (2024) also emphasize that maternal exposure to certain antiretrovirals, such as nevirapine or efavirenz, before birth increases the risk of resistance in children.

Despite its widespread use, particularly in resource-limited settings, nevirapine presents several limitations that compromise its virologic efficacy. One of the key challenges is its low genetic barrier to resistance, meaning that a single viral mutation can result in

significant resistance, leading to rapid virologic failure (Makadzange et al., 2015; Gopalan et al., 2017). Moreover, nevirapine is associated with considerable interindividual variability in metabolism, especially in children and adolescents, where dose adjustments based on weight are necessary. This variability can lead to inconsistent plasma drug concentrations, thereby increasing the risk of incomplete viral suppression. Furthermore, hepatic toxicity and hypersensitivity reactions associated with nevirapine often require treatment interruptions, complicating long-term adherence and therapeutic efficacy.

In response to these challenges, many HIV treatment programs have gradually incorporated more effective therapeutic regimens, such as those based on dolutegravir. Recent studies (Kim et al., 2024; Deng et al., 2024; Gebremedhin et al., 2024; White et al., 2025; Dou et al., 2024; Skrivankova et al., 2025) show that dolutegravir-based regimens offer superior virologic suppression rates, largely due to their higher genetic barrier to resistance, favorable pharmacokinetic profile, and better tolerability. The widespread adoption of dolutegravir in many low- and middle-income countries represents a major shift in pediatric and adolescent HIV treatment strategies. However, as this transition occurred after the completion of many studies included in this meta-analysis, further longitudinal research is needed to assess the long-term impact of dolutegravir on virologic suppression rates in diverse populations.

Additionally, the association between nevirapine-based regimens and inadequate viral suppression may also contribute to the heterogeneity observed between studies, due to variations in age groups, geographical regions, and methodologies employed. Factors such as healthcare infrastructure, access to regular viral load monitoring, and the availability of adherence support programs may influence treatment outcomes and explain some of the observed disparities. While many countries are gradually phasing out nevirapine in favor

of more potent treatments, it is essential that future research evaluates the actual effectiveness of these transitions and their impact on virologic suppression.

The WHO recommends dolutegravir as first- and second-line antiretroviral therapy for all populations, due to its superior efficacy, ease of administration, and favorable side-effect profile compared to alternative treatments (WHO, 2021, 2022). While nevirapine has played a key role in ART programs, its limitations in achieving durable virologic suppression, particularly in children and adolescents living with HIV, highlight the need to shift to more effective alternatives such as dolutegravir. The WHO therefore encourages a transition to dolutegravir-based regimens while emphasizing the need for continued research to assess its long-term effectiveness and ensure equitable access to these optimized therapeutic options in diverse healthcare settings (WHO, 2021; 2022).

These findings provide crucial insights for the development of targeted interventions aimed at improving ART outcomes in vulnerable populations, particularly in SSA, where the burden of HIV remains disproportionately high. Despite global efforts, such as the UNAIDS 95% VLS target (UNAIDS, 2014) and renewed commitments to eradicating AIDS among pediatric and adolescent groups (Govender & Bekker, 2021), achieving these ambitious goals requires more than just widespread implementation of ART. It demands focused attention on specific subgroups, including younger children, rural residents, orphans, and CALHIV with advanced WHO clinical stages or OIs.

For instance, CALHIV, particularly those in resource-limited settings, face unique challenges, such as insufficient access to healthcare services, poor adherence to ART, and delayed diagnosis due to a lack of early screening programs. Rural populations often experience barriers to healthcare access, including long distances to clinics, limited availability of trained healthcare providers, and insufficient infrastructure for continuous

viral load monitoring. Orphans, who may lack the support systems that help ensure treatment adherence, are particularly vulnerable to interruptions in care. Moreover, CALHIV with advanced WHO clinical stages or OIs require specialized treatment and management, as their compromised immune systems often make them more susceptible to ART failure and complications.

Addressing these disparities requires the integration of community-based interventions, the implementation of more comprehensive health systems strengthening, and the adoption of innovative approaches to healthcare delivery, such as mobile health technologies and decentralized care models. Additionally, there is a need to tailor ART regimens, such as dolutegravir-based treatments, to meet the specific needs of these vulnerable populations. This includes considering pharmacokinetic factors, managing co-morbidities, and ensuring that families and caregivers are equipped with the knowledge and resources needed to support adherence, particularly in regions where healthcare literacy may be low. Furthermore, policy makers and global health organizations must continue to prioritize equitable access to care, ensuring that marginalized groups are not left behind in the fight to end the HIV epidemic.

2.4.3. Limitations

This systematic review and meta-analysis have several limitations that need to be considered when interpreting the findings. We focused exclusively on studies that utilized the WHO-defined threshold for VLS (< 1,000 copies/mL) (WHO, 2023) to ensure consistency across the studies. This exclusion of studies using alternative VL thresholds (such as ≥ 80, ≥ 400, or ≥ 5,000 copies/mL) ensures that we did not underestimate VLS rates by combining different thresholds. However, we recognize that this approach may limit the generalizability of our findings. Many of the included studies were cross-sectional,

which limits the ability to establish causal relationships between the identified factors and USVL. Longitudinal studies would provide more robust evidence on the temporal relationship between these factors and VL outcomes. Additionally, this review did not account for the varying USVL rates in very young children or the impact of horizontal versus vertical transmission on VLS. These factors may contribute to differential VLS rates that were not fully captured in our analysis. Moreover, we observed unrealistically large OR estimates (e.g., 154.50; 209.42) and confidence limits (e.g., 575.51; 716.10) in some included studies, which suggest sparse-data bias. This bias may have carried over into the combined estimates and should be considered an important limitation of the study. The small number of studies included in some of the meta-analyses of risk factors may have led to inaccurate estimation of between-study heterogeneity. Although we used the Hartung-Knapp-Sidik-Jonkman approach and its modification for random-effects meta-analysis, which aims to provide more accurate estimates in the presence of few studies, this remains a limitation of our study. Despite our efforts to adjust for the confounders reported in the individual studies, unmeasured confounding factors may still be present and could potentially influence the results. Finally, we did not apply inverse probability weighting using population weights for the combined proportion, which could have enhanced the precision and generalizability of the estimates. This should also be considered an important limitation of the study. Despite these limitations, this review provides valuable insights into the magnitude and factors associated with USVL among CALHIV on ART in SSA. It offers a foundation for guiding future research and intervention strategies.

2.5. Conclusions

Despite significant advancements in ART, a substantial proportion of CALHIV in SSA fail to achieve VLS. This poses a significant challenge to individual health outcomes and broader public health goals.

Key factors contributing to USVL include under-5 years, male sex, rural residence, orphan status, to attend a level 1 or 2 healthcare facility, HIV status not disclosed, poor ART-adherence, advanced WHO clinical stage, low CD4+ T-cell counts, history of OIs, nevirapine-based regimen, drug substitution history, and not receive cotrimoxazole prophylaxis. These insights highlight the necessity for targeted strategies to enhance adherence, optimize ART-regimens, and provide comprehensive support to vulnerable groups, particularly in rural areas and among orphans.

Addressing these factors through targeted interventions and informed policy-making is essential to enhance treatment outcomes and progress towards the UNAIDS 95 – 95 – 95 targets. Policymakers, healthcare practitioners, and implementers must leverage these findings to inform resource allocation and develop effective public health interventions.

CHAPTER THREE

METHODOLOGY

This chapter outlines the methodological framework adopted for the present research, which aimed to assess both the clinical determinants and the lived experiences influencing VLS among CALHIV in Lubumbashi, DRC. In line with Creswell and Plano Clark (2018), the chapter is organized to ensure clarity, coherence, and transparency in describing the underlying paradigm, research design, study procedures, populations, tools, and ethical safeguards.

The study was grounded in a pragmatist paradigm, which recognizes that no single methodological approach can adequately capture the complexity of real-world public health phenomena (Morgan, 2014). Pragmatism prioritizes the research question over methodological purity and supports the integration of quantitative and qualitative evidence to provide a more complete and actionable understanding of the problem under investigation. This paradigm was particularly relevant for the present study, given the multifactorial nature of VLS and the need to combine measurable clinical outcomes with nuanced contextual insights from lived experiences.

Consistent with this paradigm, the research employed a convergent mixed-methods design. This approach involves the concurrent collection and analysis of quantitative and qualitative data, followed by the integration of findings to draw meta-inferences (Creswell & Plano Clark, 2018; Fetters et al., 2013). The rationale for adopting this design was threefold:

1° Complementarity – Quantitative data were used to identify statistical associations between clinical and sociodemographic variables and USVL, while qualitative

narratives provided an in-depth understanding of the barriers and facilitators to VLS.

2° Triangulation – The integration of both datasets allowed for the cross-validation of findings, increasing the credibility and robustness of conclusions (Denzin, 2012).

3° Practical utility – In the context of the DRC, where evidence for policy must address both epidemiological trends and socio-cultural realities, this design enabled the development of recommendations that are both evidence-based and contextually grounded.

The quantitative component adopted a retrospective cross-sectional design, focusing on routinely collected clinical data to identify determinants of USVL among CALHIV on ART within a pragmatist paradigm (Morgan, 2014), which guided the integration of complementary quantitative and qualitative approaches to address the multifactorial nature of VLS in CALHIV. The qualitative component explored barriers and facilitators to VLS from the perspectives of adolescents and their caregivers, guided by the socioecological model developed by Galea et al. (2018), which situates individual behavior within broader interpersonal, community, and structural influences and was further enriched by social constructionist theory (Segre, 2016), which emphasizes how meanings and experiences around HIV are shaped through social interactions. The theoretical positioning was not limited to the qualitative strand; instead, both the socioecological model and social constructionist theory provided a unifying conceptual lens across the entire study, shaping research questions, informing a convergent mixed-methods design (Creswell & Plano Clark, 2018), and guiding the integration of findings. This design allowed the quantitative strand—using multiple logistic regression—to statistically identify determinants across individual, familial, and structural domains, while the qualitative strand deepened the understanding of how these factors operate in lived contexts.

While this methodological choice offered significant strengths—namely, the breadth and depth of analysis—it also required rigorous integration procedures. In line with best practices in mixed-methods research, integration of datasets was conducted using joint displays and side-by-side comparisons (Guetterman et al., 2015) to ensure theoretical coherence between statistical determinants and contextual narratives. This approach enabled qualitative insights to inform the interpretation of quantitative patterns and vice versa, revealing multi-layered barriers—such as stigma, ART side effects, and economic constraints—and facilitators, including family support, peer clubs, psychosocial follow-up, and positive healthcare relationships, consistent with socioecological and social constructionist perspectives.

This chapter is structured as follows:

- Section 3.1 presents the quantitative study, beginning with the study design, setting, and population (3.1.1–3.1.3), followed by a description of the viral load testing process in HIV clinics (3.1.4). It then details the data collection methods and quality control procedures (3.1.5), the study variables and operational definitions (3.1.6), the statistical analysis plan (3.1.7), and the related ethical considerations (3.1.8).
- Section 3.2 presents the qualitative study, starting with the study design and setting (3.2.1), population (3.2.2), and the theoretical framework underpinning the analysis (3.2.3). It continues with the data collection process (3.2.4), data processing and analysis (3.2.5), and ends with ethical considerations specific to this component (3.2.6).

Overall, the convergent mixed-methods design allowed for a holistic understanding of the multifactorial determinants of VLS among CALHIV in Lubumbashi. The concurrent analysis of complementary datasets generated a richer and more actionable evidence base

than either approach could have produced in isolation—thereby enhancing the relevance of the findings for both clinical practice and health policy in resource-limited settings.

3.1. Quantitative study: A retrospective analysis of unsuppressed HIV viral load in CALHIV on ART in Lubumbashi, DRC

3.1.1. Study design, period, and contextual setting

A hospital-based cross-sectional study was conducted across 21 randomly selected HIV care clinics from the eleven health zones of Lubumbashi city, which are distributed across the seven municipal communes of the city (Figure 3.1). These clinics were chosen from a comprehensive list of facilities providing services to CALHIV, ensuring representativeness across the zones; only clinics actively managing children and adolescents living with HIV were included in the study to ensure relevance and data quality. No external influence (e.g., from authorities) affected the selection process.

The study covered a five-year period, from January 2018 to December 2023, with data collection taking place from July to September 2024.

Lubumbashi, the second-largest city in the DRC, is situated in the southeastern region of the country. In 2024, the city has an estimated population of around 2,933,962, distributed across 747 km², leading to a population density of over 3,927 inhabitants per km² (Mukuku et al., 2024).

Administratively, Lubumbashi is divided into eleven health zones, each with its healthcare infrastructure. With the exception of one, all health zones have a General Referral Hospital, which acts as the main referral facility within their respective areas. On average, each health zone consists of approximately 15 health centers, resulting in a total of over

350 healthcare facilities, including hospitals, polyclinics, and health centers throughout the city. Significantly, 70% of these healthcare facilities are located in the densely populated urban core.

The private sector dominates the healthcare landscape, accounting for more than 60% of the total healthcare facilities. Among the existing health structures, approximately 50 facilities offer HIV care services. These HIV care clinics provide a range of services, including HIV testing, ART initiation and follow-up, VL monitoring, prevention of mother-to-child transmission (PMTCT), and psychosocial support for CALHIV and their caregivers. HIV services in Lubumbashi are primarily funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), with coordination overseen by the National HIV/AIDS Programme (PNLS). However, recent shifts in PEPFAR's strategic priorities—including an increased focus on local ownership, health system strengthening, and sustainability—may influence the future delivery and organization of these services in the region (Balakrishnan, 2025). This restricted definition excludes several vulnerable groups—including children and adolescents—from benefiting from expanded prevention and support packages, such as access to pre-exposure prophylaxis (PrEP), comprehensive sexual and reproductive health services, mental health and psychosocial support, and targeted interventions for key populations (Balakrishnan, 2025). PEPFAR plays a crucial role in achieving UNAIDS' 95–95–95 targets by 2030, while the PNLS ensures the implementation of national guidelines and treatment protocols. In the DRC, PEPFAR collaborates with PNLS, the Ministry of Health, and other international and local partners to expand access to ART, VL monitoring, PMTCT, and strengthen healthcare facilities. As the lead entity in the national HIV response, PNLS also oversees treatment implementation, WHO standards compliance, and program evaluation to measure the impact of funded interventions.

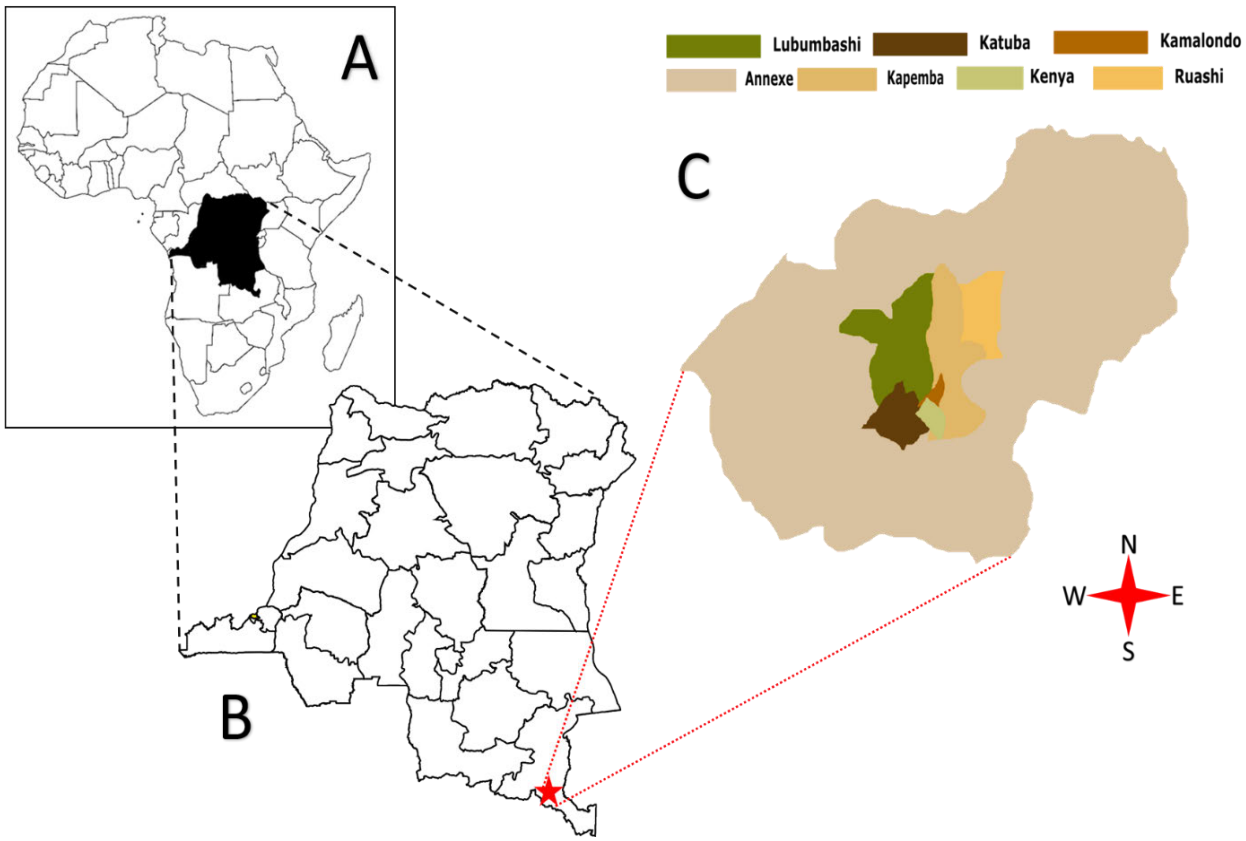

Figure 3.1 Maps of Africa (A), the Republic Democratic of the Congo (B), and Lubumbashi city (C). The star represents Lubumbashi city.

3.1.2. Operational procedures for viral load testing in Lubumbashi HIV clinics

In Lubumbashi, VL testing for people living with HIV follows a structured and well-coordinated process designed to ensure timely, equitable, and free access to this essential service. This process involves several key steps, from test prescription to result delivery, allowing for effective monitoring of adherence to ART and treatment success.

3.1.2.1. Prescription and sample collection

In HIV care clinics across Lubumbashi, VL testing is prescribed by healthcare workers following national HIV care guidelines. The decision to conduct a VL test is based on established clinical protocols, taking into account factors such as the duration of ART, previous VL test results, and the patient's health status.

Blood samples for VL testing are collected in EDTA tubes at the same HIV care clinic where the patient receives antiretroviral therapy. Trained healthcare workers ensure proper identification of the patient before packaging the samples for transport. Following strict protocols to maintain accuracy and prevent contamination, the samples undergo specialized processing and are rapidly transported to the University Clinics of Lubumbashi for viral load measurement.

3.1.2.2. Sample transport and processing

After collection, the samples are systematically transported to the University Clinics of Lubumbashi, which serves as the central testing laboratory for the entire Haut-Katanga province. This centralized approach helps standardize testing procedures, improve efficiency, and ensure quality control in result processing.

The transport of samples is managed by a structured logistics system coordinated by the health authorities, with external technical and financial support from partners such as the U.S. President's Emergency Plan for AIDS Relief and the Global Fund to fight AIDS, Tuberculosis and Malaria. This support ensures that the service remains free of charge for all patients. HIV care clinics in Lubumbashi operate within a well-organized sample transport network, enabling regular and timely shipment of specimens to avoid delays in processing.

3.1.2.3. Analysis and quality of viral load results

At the University Clinics of Lubumbashi, VLsamples undergo processing following rigorous molecular biology protocols to precisely quantify the VL. The techniques employed include real-time polymerase chain reaction (qPCR), which gauges the viral RNA levels in the bloodstream. Initially, each sample is registered in a laboratory

management system for comprehensive traceability. Subsequently, a sample preparation procedure ensues, involving viral RNA extraction. The quantification is carried out by juxtaposing the outcomes with a standard curve, guaranteeing a high level of accuracy in the measurements.

Viral load results (HIV RNA) are expressed in log10/mL or copies/mL, measured using the COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test by Roche (Roche Molecular Systems, Inc., Branchburg, New Jersey, USA), with a detection range of 48 to 10,000,000 copies/mL. To ensure result reliability, a quality assurance system is implemented, comprising routine internal and external controls. Laboratory technicians adhere to standardized protocols, and equipment undergoes regular calibration. Subsequently, biologists validate the results before transmission to the clinics, guaranteeing optimal care for PLHIV.

3.1.2.4. Transmission and use of viral load results

Once the VL tests are completed, the results are transmitted back to the healthcare facilities, either electronically through a medical data management system or in paper format. Healthcare providers then review these results and discuss them with patients during their follow-up appointments, ensuring that the information is communicated clearly and understood.

3.1.2.5. Clinical decision-making

The viral load results play a pivotal role in evaluating the efficacy of ART. In instances of VLS, patients are advised to maintain their treatment with the same degree of adherence. If a high VL is identified, immediate clinical interventions are implemented. This may

entail offering adherence assistance, or modifying the treatment plan in accordance with national guidelines to tackle potential concerns like drug resistance.

This well-structured process ensures optimal follow-up for PLHIV in Lubumbashi, while also ensuring financially accessible and equitable access to VL testing, contributing to improved health outcomes and enhanced treatment success (Figure 3.2).

Figure 3.2 Key steps in the viral load testing process at HIV clinics in Lubumbashi

3.1.3. Population and eligibility criteria

The study included CALHIV aged 0 to 19 years who were receiving ART in 21 selected HIV care clinics, with a minimum follow-up period of six months and at least one available VL result at the clinic (Figure 3.2).

The following participants were excluded from the study: those whose records were inaccessible or had incomplete data; those who were lost to follow-up; those not receiving ART; those with a follow-up period of less than six months; and those with missing VL results during the study period.

The study involved a review of all medical records of the study population. We utilized a simple random sampling technique to select participants.

The sample size was calculated using the following formula:

$$n = \frac{z^2.\,\mathrm{p}(1-\mathrm{p})}{e^2}$$

Where: *n* represents the minimum sample size, *z* is the confidence intervals (1.96), *p* was set at 0.5 (due to unknown prevalence of USVL in CALHIV in the DRC), and *e* represents the margin error (0.05). Using this calculation, we determined a minimum sample size of 382 participants. To account for potential missing data in medical records, an additional 10% was added, resulting in a total study sample size of 420 participants.

The study involved a review of all medical records of CALHIV who met the inclusion criteria (utilizing the census method), which were sourced from the VL registration books of the HIV care clinics. To ensure the presence of all required data for the study, all medical records were thoroughly examined.

In our study, a total of 847 participants met the inclusion criteria during the recruitment process, as detailed in Figure 3.3. This sample is considered representative of the broader

population, as it includes patients from 21 different health facilities, ensuring a diverse and comprehensive representation.

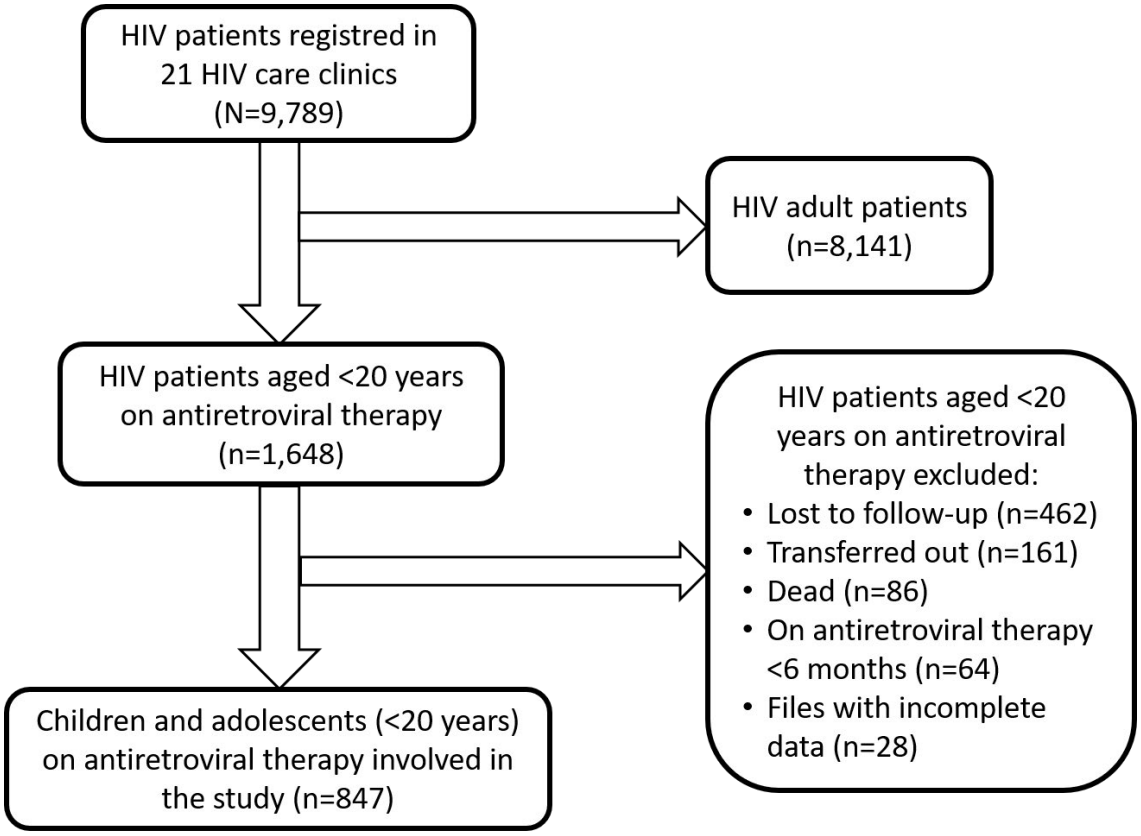

Figure 3.3 Flow chart showing a selection of HIV-positive children and adolescents on ART in 21 HIV care clinics in Lubumbashi, DRC.

3.1.4. Data collection and quality control

Data collection for this study was carried out in 21 HIV care clinics located in the 11 health zones of Lubumbashi. Standardized clinical files and registers were used to maintain consistency and accuracy in patient record-keeping. The selection of these clinics was based on a list provided by the Provincial Health Division of Haut-Katanga. Strict inclusion criteria were followed, including maintaining a cohort of CALHIV under ART since at least 2022, adherence to nationally standardized HIV care protocols and viral load testing procedures, systematic documentation and reporting of patient data, and

management by government, private, or faith-based organizations supported by implementing partners of the national HIV/AIDS program. The selected clinics included University Clinics of Lubumbashi, Jason Sendwe Provincial General Reference Hospital, SNCC Hospital, Radem Hospital, Tshamilemba Center for STI/HIV Screening and Treatment, Katuba Center for STI/HIV Screening and Treatment, La Promesse Health Center, Lumière Health Center, Bakhita 2 Health Center, Jenovic Health Center, Franciphar Health Center, Bethsaida Health Center, Amani Health Center, Maman Elisabeth Medical Center, Mapendano Health Center, Famika Health Center, Laïs Health Center, Saint Sauveur Health Center, Jemima Health Center, La Foi Health Center, and M-Soma Health Center. These clinics followed national standardized clinical protocols, ensuring consistency and reliability across all sites.

After obtaining authorization from the Haut-Katanga Provincial Ministry of Public Health, the governing body responsible for approving data collection at all healthcare facilities in Lubumbashi, I was able to proceed with data collection at the selected clinics without requiring additional permissions. Once the clinics were identified, I reached out to their administrators to outline the study's goals, data needs, and consent procedures. With approval from the clinic managers, healthcare providers caring for PLHIV were involved to assist in accessing the necessary clinical documentation.

Given the geographical distribution of the selected clinics, a team of 21 qualified healthcare workers, specifically ART providers, was designated as data collectors. Each individual was assigned to work in their respective clinic to ensure local familiarity with the clinic's protocols and patient population. To ensure consistency and accuracy in data collection, these healthcare providers underwent a rigorous three-day training program. The training emphasized the study's objectives, correct usage of institutional recording forms, and the

process of accurately completing the data extraction tool in Microsoft Excel. This approach was designed to ensure standardized data collection practices across all healthcare facilities.

The data collection period spanned from August to November 2024, during which all essential materials, including data extraction forms and training resources, were deployed to ensure alignment with ethical and professional standards. Time management was carefully considered to guarantee an efficient data collection process, focusing on the accuracy and validity of the data.

All data were treated with the utmost care and in strict adherence to ethical guidelines and data management protocols to safeguard participant confidentiality, privacy, and security. Initially, all data were de-identified to remove personally identifiable information, ensuring the anonymity of participants. Following de-identification, the data were securely stored on password-protected electronic devices and in locked cabinets or secure facilities, with access restricted to authorized personnel involved in data analysis and oversight. Upon the expiration of the data retention period, as per the research protocol or institutional policies, the data were irreversibly destroyed using secure methods, such as shredding physical documents or employing data-wiping software for electronic files. Throughout the disposal process, comprehensive documentation was maintained to record the date, method, and responsible individuals involved, ensuring full compliance with data protection regulations and ethical standards.

To maintain the highest standards of data integrity, I conducted regular site visits throughout the data collection period. These visits offered real-time oversight, on-site guidance, and immediate resolution of any emerging issues. Data quality was closely monitored, with any errors or inconsistencies being corrected on-site.

A crucial aspect of the data collection process involved utilizing a pre-tested checklist (APPENDIX C) to systematically record all necessary variables. The data collection was predominantly conducted by ART providers and myself, working in conjunction to extract information from diverse sources such as ART patient intake forms, ART monitoring record books, follow-up charts, and registers. This process encompassed a retrospective examination of viral load data, along with regularly gathered HIV-related details like patient demographics and treatment adherence records.

Before data collection began, all data collectors underwent a comprehensive training session to ensure their understanding of the protocols, the variables to be collected, and the correct utilization of institutional recording forms. In order to uphold patient confidentiality, a unique study identification number was allocated to each participant, reducing biases and guaranteeing anonymity.

Before inputting the collected data into the Microsoft Excel sheet, a thorough review was conducted to ensure completeness, consistency, and the absence of duplicates. Any missing variables were promptly addressed. The finalized data were then entered into the Excel sheet, which served as the primary tool for data analysis and reporting. Rigorous quality control measures were followed throughout the entire data entry process to ensure the accuracy and reliability of the data for subsequent analysis.

3.1.5. Study variables and operational definitions

The final dataset comprised de-identified information for each participant, which included data on VL tests and results, as well as sociodemographic factors, living conditions of children and adolescents, caregiver demographics and health characteristics, clinical and immunological aspects, and medication-related factors. The primary outcome variable,

viral load suppression, was categorized into two groups: suppressed and non-suppressed status. VLS was defined according to the DRC National HIV/AIDS Programme (PNLS, 2021) and WHO (2023) guidelines (Moudachirou et al., 2020), where a VL of less than 1,000 copies/mL was considered suppressed. Per the DRC guidelines, the first VL test is recommended to take place six months after the initiation of ART. VLS serves as a crucial marker for monitoring global HIV treatment goals and evaluating the effectiveness of HIV prevention and treatment strategies in the ongoing fight against AIDS (WHO, 2023).

The independent variables were:

3.1.5.1. Child or adolescent demographic and living conditions

1° Age was defined as the time span from a child's date of birth to the date of data collection, expressed in years. The age categories are as follows: <5 years, 5-9 years, 10-14 years, and 15-19 years.

2° Sex was categorized as either male or female.

3° Educational level was categorized to reflect the highest level of formal education completed or currently attended by the individual. Categories are as follows:

- Never been to school: No formal education.
- Primary: completed or attending primary school.
- Secondary: completed or attending secondary school.
- Higher/University: completed or attending post-secondary education.

4° Currently living with/in: refers to the household or living arrangement of a child or adolescent. It categorizes the individual based on the primary caregiver or living environment, which includes:

- At least one biological parent: living with at least one biological parent.

- A non-parent family member: living with a non-parent relative (e.g., grandparent, aunt/uncle).
- Adoptive parents: living with adoptive parents.
- Group housing: living in institutional or group settings (e.g., orphanage).

5° Orphan status: refers to the parental survival status of a child or adolescent. It is categorized as:

- Non-orphan: both biological parents are alive.
- At least one biological parent died: one biological parent is deceased.
- Double orphan: both biological parents are deceased.

3.1.5.2. Caregiver demographic and health characteristics

1° Age of caregiver: refers to the age of the primary individual responsible for the care of the child or adolescent. It was categorized as: <40 years and ≥40 years.

2° Caregiver's sex: refers to the sex of the primary caregiver responsible for the child or adolescent living with HIV, categorized as male or female.

3° Caregiver's occupation: refers to the employment status of the primary caregiver responsible for the child or adolescent living with HIV. It was categorized as follows:

- Unemployed: the caregiver does not have any formal or informal employment.
- Employed: the caregiver is engaged in any form of paid work, including formal employment, self-employment, or informal labor.

4° Caregiver's HIV status refers to whether the primary caregiver has been diagnosed with HIV. It is categorized as follows:

- Positive: the caregiver has tested HIV-positive.
- Negative: the caregiver has tested HIV-negative.
- Unknown: the caregiver's HIV status is not known or has not been disclosed.

5° Caregiver's alcohol use refers to whether the caregiver self-reported alcohol consumption during clinical visits. It is categorized as follows:

- No: the caregiver does not consume alcohol.
- Yes: the caregiver consumes alcohol.

6° Caregiver's marital status refers to the current marital status of the caregiver. It is categorized as follows:

- Married: The caregiver is legally or traditionally married.
- Single/Divorced/Widowed: The caregiver is either single (never married), divorced (previously married but legally separated), or widowed (lost their spouse).

3.1.5.3. Clinical and immunological characteristics

1° HIV transmission route refers to the mode through which a child or adolescent acquired HIV. It is categorized as follows:

- Perinatal (vertical transmission): HIV was acquired from the mother during pregnancy, childbirth, or breastfeeding.
- Transfusion: HIV was acquired through a blood transfusion.
- Sexual: HIV was acquired through sexual contact.
- Unknown: the route of HIV infection is not known.

2° HIV status disclosure to CALHIV: refers to the process by which a child or adolescent living with HIV is informed about their HIV-positive status. Disclosure is a crucial step in ensuring adherence to ART, promoting psychological well-being, and empowering children and adolescents to take responsibility for their health.

- Before 12 years: the child or adolescent was informed about their HIV status before reaching the age of 12.

- At 12 years: the child or adolescent was informed about their HIV status at the age of 12.
- No disclosure: the child has not been informed about their HIV status.

According to Law No. 18-012 of July 9, 2018, which amends and supplements Law No. 08-011 of July 14, 2008, regarding the protection of the rights of people living with HIV/AIDS and affected individuals (J.O.RDC., July 23, 2018, Special Issue, Col. 9), the disclosure of HIV status to a minor must be based on their age and level of understanding. This implies that while the generally recommended age for full disclosure is 12 years, the disclosure process should be tailored to the child's cognitive and emotional maturity. The lack of clear standards and guidelines in this area has led to delayed disclosure of HIV status to children, which can affect the trust placed in adults. Furthermore, it appears that there are no specific laws or guidelines in the Democratic Republic of the Congo regarding the disclosure of HIV status to minors, particularly in terms of a specific age for disclosure as is the case in other countries, whether they were infected in vertical transmission or later through blood transfusion or sexual transmission.

In practice, certain circumstances may necessitate earlier disclosure. For instance, children who frequently fall ill, require strict adherence support, or express persistent curiosity about their medical condition may benefit from gradual and age-appropriate disclosure before the age of 12. Healthcare providers and caregivers play a critical role in facilitating this process, ensuring that the child receives adequate psychological support to cope with their diagnosis.

3° HIV status disclosure to others refers to whether a child or adolescent has had their HIV status shared with individuals beyond healthcare workers. This disclosure may involve family members, teachers, close friends, or other trusted individuals.

- Yes: the child's or adolescent's HIV status has been disclosed to others, such as family members, guardians, or individuals in their social or educational environment. Disclosure may be intentional (by the caregiver or child) or unintentional (due to medical visits, medication visibility, or external assumptions).
- No: the child's or adolescent's HIV status has not been disclosed to others.

4° WHO clinical stage: The WHO clinical stage system is a classification used to describe the progression of HIV infection, based on clinical manifestations. This system helps healthcare providers assess the severity of HIV-related illnesses and guide treatment and care decisions. It categorizes CALHIV into four stages (1–4) based on the symptoms and conditions observed (WHO, 2016).

- Stage 1: Asymptomatic or mild HIV-related conditions (persistent generalized lymphadenopathy).
- Stage 2: Moderate HIV-related conditions, such as mild mucocutaneous manifestations.
- Stage 3: Severe HIV-related conditions, including chronic symptoms like weight loss.
- Stage 4: AIDS-related conditions, including opportunistic infections.

5° Nutritional status refers to the overall health related to a person's diet and nutrition, assessed using indicators such as weight-for-height z-score or body mass index. It is categorized into three levels: normal or well-nourished child, moderate malnutrition (for children under the age of 5, moderate malnutrition is defined by a weight-for-height z-score less than -2 or a mid-upper arm circumference between 115 mm and 125 mm), and severe malnutrition (for children under the age of 5, severe malnutrition is indicated by a weight-for-height z-score less than -3, a mid-upper arm circumference

less than 115 mm, or the presence of oedema (swelling caused by fluid retention)) (WHO, 2016).

6° History of tuberculosis (TB) in the last six months indicates whether an individual has been diagnosed with TB during this period. It was categorized into two groups: "Yes" for CALHIV diagnosed with TB in the past six months and "No" for those not diagnosed with TB during this time.

3.1.5.4. Medication-related characteristics

1° Cotrimoxazole prophylaxis involves the use of the combination antibiotic cotrimoxazole (trimethoprim-sulfamethoxazole) to prevent opportunistic infections in PLHIV.

It is recommended for children, adolescents, and adults with HIV, particularly in regions with a high burden of bacterial infections, malaria, and other opportunistic diseases (WHO, 2016). It is categorized as follows: "yes" if the child or adolescent has received cotrimoxazole prophylaxis, or "no" if the child or adolescent has not received cotrimoxazole prophylaxis.

Cotrimoxazole prophylaxis is a key recommendation for infants, children, and adolescents living with HIV, regardless of their clinical condition or immune status. It is especially critical for children under 5 years old, irrespective of their CD4 count or clinical stage, as well as for those with severe or advanced HIV disease (classified as WHO clinical stage 3 or 4) or those with a CD4 count ≤350 cells/mm3. These children are at greater risk of infections and benefit most from the protective effects of cotrimoxazole (WHO, 2016). In areas where malaria or severe bacterial infections are common (like the DRC), cotrimoxazole prophylaxis should be continued until adulthood, even if the individual is

on ART. This recommendation is based on moderate-quality evidence, as these infections remain a serious risk (WHO, 2016). On the other hand, in regions where malaria and bacterial infections are less prevalent, cotrimoxazole prophylaxis may be stopped for children aged 5 years or older who are clinically stable, have been virally suppressed on ART for at least 6 months, and have a CD4 count >350 cells/mm3. This decision is based on very low-quality evidence, as long-term benefits in such low-risk environments are less clear (WHO, 2016). Cotrimoxazole prophylaxis plays a vital role in preventing infections in children with HIV, especially in regions with high rates of opportunistic infections, and the decision to continue or discontinue its use is based on both local epidemiology and the child's health status (WHO, 2016).

2° Isoniazid prophylaxis involves the use of the antibiotic isoniazid to prevent TB in individuals, particularly in those living with HIV, who are at higher risk of contracting TB due to their compromised immune system. It is categorized as follows: "yes" if the child or adolescent has received isoniazid prophylaxis, or "no" if the child or adolescent has not received isoniazid prophylaxis.

Isoniazid preventive therapy is recommended for adults, adolescents, and children living with HIV to prevent TB, particularly in settings where TB is prevalent. For adults and adolescents without symptoms of active TB (such as cough, fever, weight loss, or night sweats), isoniazid preventive therapy should be given for at least 6 months. Those with a positive tuberculin skin test or a history of TB contact should also receive isoniazid preventive therapy, regardless of their immune status or ART use (WHO, 2016). In children living with HIV, those over 12 months of age, who do not show symptoms and have no contact with a TB case, should receive 6 months of isoniazid preventive therapy. However, children under 12 months should only receive isoniazid preventive therapy if

they have had TB exposure and have been evaluated and cleared of active TB (WHO, 2016). All children who have completed TB treatment should also receive isoniazid preventive therapy for an additional 6 months as part of their HIV care. This strategy helps reduce the risk of TB in CALHIV, especially those without active TB symptoms but at high risk of latent TB (WHO, 2016).

3° History of ART interruption since ART initiation: refers to whether there has been any pause or discontinuation in the prescribed ART regimen since the initiation of treatment.

ART is generally recommended to be continued without interruption to maintain VLS and prevent the development of drug resistance. Treatment interruptions may occur for various reasons, such as side effects, access issues, or personal choice. It is categorized as follows: "yes" if the ART regimen has been interrupted at any time since initiation, or "no" if the ART regimen has not been interrupted. Clients who have missed an appointment for ART refill within the recommended time frame, specifically when the gap exceeds 28 days from the last appointment date are considered to have experienced an ART interruption (Ayana et al., 2024). Missing a refill appointment can lead to a disruption in the continuity of ART treatment, which may affect VLS and increase the risk of drug resistance. Continuous adherence to ART is critical for the effective management of HIV and the prevention of drug resistance (WHO, 2016).

4° ART-induced side effects refer to any negative symptoms or reactions arising after the initiation of ART.

These effects can be directly related to the ART or may reflect immune reactivation, where previously suppressed infections become clinically apparent. According to the WHO

(2016), side effects encompass any harmful or unintended responses, such as gastrointestinal issues, skin reactions, liver abnormalities, or other adverse conditions resulting from ART. ART side effects refer to any adverse effects that occur when medications are taken at standard doses intended for humans. In assessing side effects caused by ART, it is important to differentiate between reactions directly related to the treatment and new symptoms arising from other health conditions (Ayana et al.; 2024; WHO, 2002; WHO, 2016). It was categorized into two groups: "Yes" if the ART regimen has caused side effects, "No" if the ART regimen has not caused side effects.

5° Adherence to ART was assessed by calculating the percentage of pills taken in the previous month compared to the prescribed quantity, in accordance with the WHO guidelines outlined in the follow-up chart. Adherence to ART was assessed based on the percentage of pills reportedly taken over the preceding month compared to the prescribed amount, following WHO criteria, as recorded in the patients' medical files. All adherence information was extracted retrospectively from clinical records. For adolescents, these records were primarily based on self-reported adherence documented during clinical visits, whereas for younger children, adherence was reported by caregivers and noted by the healthcare provider. CALHIV were categorized according to their adherence to ART:

- Good adherence: >95% of prescribed doses taken (≤2 doses missed out of 30).
- Fair adherence: 85-95% of prescribed doses taken (3–5 doses missed out of 30).
- Poor adherence: <85% of prescribed doses taken (≥6 doses missed out of 30).

CALHIV were categorized as poor or fair adherents if they reported taking less than 95% of their prescribed ART doses, while those who reported taking more than 95% of the

prescribed doses were classified as good adherents (Ayana et al., 2024; Emagnu et al., 2020).

6° Current ART regimen type refers to the specific combination of antiretroviral medications a patient is currently prescribed for their HIV treatment. This can include different types of regimens based on the medication class used. A Dolutegravir-based regimen uses dolutegravir as the core drug, a Nevirapine-based regimen centers around nevirapine, and an Efavirenz-based regimen relies on efavirenz.

7° ART duration refers to the length of time a CALHIV has been on antiretroviral therapy and is categorized into three groups: 6-24 months, 25-48 months, and >48 months.

Regimen change refers to any alteration made to the originally prescribed antiretroviral therapy regimen, whether it involves switching, adding, or discontinuing specific medications, as part of the patient's ongoing treatment management (Moudachirou et al., 2020). Patients were classified as lost to follow-up if they had not been referred to another healthcare facility, had not passed away, or had not returned to the HIV care clinic for a period of at least three months after their last missed appointment (Gebremichael et al., 2021; Moudachirou et al., 2020). These operational definitions are crucial for systematically categorizing and measuring each variable, offering a structured framework that ensures consistency and clarity in data collection and analysis. This approach is especially important in epidemiological studies, as it enhances the accuracy and reliability of results, facilitates comparisons across different studies, and supports the interpretation of findings.

3.1.6. Statistical analysis

3.1.6.1. Data management and preliminary analysis

The data were carefully cleaned, coded, and meticulously reviewed for completeness after the data collection phase. This step ensured that missing values and inconsistencies were identified and addressed before statistical analysis. The cleaned dataset was initially inputted into Microsoft Excel version 2019 for preliminary verification and subsequently exported to Stata software version 16 for further analysis (StataCorp, 2019).

A descriptive analysis was performed to provide a comprehensive overview of the demographic and living conditions of children or adolescents, the demographic and health characteristics of their caregivers, clinical and immunological aspects, and medication-related factors. The mean age and standard deviation of both children/adolescents and caregivers were calculated to assess their age distribution in the study population. The proportion of USVL was defined as the percentage of CALHIV whose VL exceeded 1000 copies/mL among those tested. To further explore the prevalence of USVL, the analysis was stratified by various independent variables. These included sociodemographic factors, such as age, gender, and socioeconomic status, as well as clinical aspects, including WHO clinical stage, nutritional status, and a history of comorbidities like tuberculosis. Therapeutic variables, such as the type of ART regimen, levels of adherence, and history of treatment interruptions, were also assessed. This thorough approach enabled a deeper understanding of the factors that influence viral load suppression in this population.

3.1.6.2. Definition and classification of unsuppressed viral load

The VL results were classified into two categories:

- Suppressed VL: < 1,000 copies/mL

- Unsuppressed VL: ≥ 1,000 copies/mL

This threshold is based on WHO guidelines, which define "unsuppressed VL" (or virological failure) as a VL ≥ 1,000 copies/mL after at least six months of ART (WHO, 2023).

3.1.6.3. Bivariate analysis

A bivariate analysis was conducted to explore potential associations between various independent variables and USVL. This analysis involved calculating crude odds ratios (cOR) along with their corresponding 95 % confidence intervals (95 % CI) for each independent variable, providing a measure of the strength and direction of the associations. The chi-square test (or Fisher's exact test, when appropriate) was used to assess the statistical significance of these associations, helping to identify variables with potential links to USVL. Any variables that yielded a p-value <0.20 in the bivariate analysis were considered for inclusion in the subsequent multivariable logistic regression model. This threshold was chosen to capture variables that, while not immediately statistically significant, might still be important confounders influencing the outcome when adjusted for other factors. This method is supported by literature such as Bursac et al. (2008), who advocate for purposeful variable selection strategies that begin with a more inclusive p-value cutoff (e.g., <0.20 or <0.25) to improve model robustness and interpretability in real-world data settings. This step ensures a comprehensive examination of all relevant variables and helps control for confounding influences.

3.1.6.4. Multivariate analysis

The final multivariable analysis aimed to identify the most significant predictors of USVL by employing a multiple logistic regression model. This model adjusted for potential

confounders, providing a more robust and reliable understanding of the factors independently associated with USVL in CALHIV. In this analysis, the dependent variable (Y) was binary (with '0' representing suppressed viral load and '1' indicating unsuppressed viral load) and a function of several independent variables ($x_1, \ldots, x_n$). The model assessed the relationship between virological non-suppression and the independent variables using the following logistic regression equation (Szklo & Nieto, 2014):

$$\text{logit}\,(p) = \ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_n x_n$$

where:

- p represents the probability of USVL,
- β_0 is the intercept,
- $\beta_1, \beta_2, \ldots, \beta_n$ are the regression coefficients,
- $x_1, x_2, \ldots, x_n$ are the independent variables.

After fitting the multivariable logistic regression model, I computed adjusted odds ratios (aOR) along with their corresponding 95% confidence intervals (CI) to assess the strength and direction of associations between independent variables and virological non-suppression. Statistical significance was determined using a threshold of $p < 0.05$, indicating that only variables meeting this criterion were deemed significant in the final analysis.

3.1.6.5. Model performance and evaluation

3.1.6.5.1.1. Sensitivity and specificity calculation

The sensitivity (true positive rate) and specificity (true negative rate) of the logistic regression model were evaluated using a confusion matrix derived from the model's

predictions. Sensitivity quantifies the model's ability to correctly identify individuals experiencing virological non-suppression (unsuppressed VL), ensuring that true positive cases are accurately detected. Conversely, specificity assesses the model's accuracy in correctly classifying individuals with virological suppression (suppressed VL), minimizing false positives. These two metrics are crucial for evaluating the model's overall performance in distinguishing between suppressed and unsuppressed viral loads. Sensitivity and specificity were calculated as follows (Szklo & Nieto, 2014; Florkowski, 2008):

$$Sensitivity = \frac{True\ positives\ (TP)}{True\ positives\ (TP) + False\ negatives\ (FN)}$$

$$Specificity = \frac{True\ negatives\ (TN)}{True\ negatives\ (TN) + False\ positives\ (FP)}$$

A high sensitivity indicates that the model effectively detects the majority of CALHIV experiencing virological non-suppression, minimizing false negatives. Conversely, a high specificity demonstrates that the model accurately classifies CALHIV with suppressed VL, reducing the likelihood of false positives. These metrics offer a thorough evaluation of the model's performance in distinguishing between suppressed and unsuppressed viral loads.

To comprehensively evaluate the classification performance of the logistic regression model, I employed the "*estat classification*" command in Stata to compute the sensitivity and specificity. This enabled us to measure the model's accuracy in distinguishing CALHIV with virological non-suppression and suppression. Additionally, I created a sensitivity and specificity plot using the "*lsens*" command. This visual representation not only offers a more in-depth view of the balance between sensitivity and specificity but also allows us to analyze how these metrics vary at different classification thresholds.

3.1.6.5.1.2. Receiver Operating Characteristic (ROC) curve

To evaluate the discriminatory power of the logistic regression model, I employed the Receiver Operating Characteristic (ROC) curve and computed the Area Under the Curve (AUC). The ROC curve visually depicts sensitivity (true positive rate) against 1-specificity (false positive rate), offering valuable insights into the model's effectiveness in discriminating between CALHIV with unsuppressed VL and those with suppressed VL. The AUC serves as a quantitative measure of the model's predictive performance (Mahdizadeh, & Zamanzade, 2022; Nahm, 2022; Mukuku et al., 2019; Hoo et al., 2017; Kumar & Indrayan, 2011).

- AUC = 0.5 indicates no discrimination, meaning the model performs no better than random chance,
- $0.5 \leq AUC < 0.6$ suggests failed discrimination,
- $0.6 \leq AUC < 0.7$ suggests poor discrimination,
- $0.7 \leq AUC < 0.8$ suggests fair discrimination,
- $0.8 \leq AUC < 0.9$ reflects good discrimination,
- $0.9 \leq AUC$ reflects excellent discrimination, demonstrating a strong ability to differentiate between suppressed and unsuppressed viral loads.

A model with an AUC close to 1 is considered highly predictive, whereas an AUC approaching 0.5 suggests poor discrimination. The ROC curve was generated using the "*lroc*" command in Stata, which provides a visual assessment of the model's classification performance.

3.1.6.5.1.3. Hosmer-Lemeshow goodness-of-fit test

To evaluate the overall fit of the logistic regression model, I conducted the Hosmer-Lemeshow goodness-of-fit test, which is a widely recognized method for determining how well the predicted probabilities align with the observed outcomes in the dataset. This test operates by grouping the observations into deciles of predicted probabilities, allowing us to compare the expected frequencies of events (i.e., virological suppression or non-suppression) to the observed frequencies within each decile. The Hosmer-Lemeshow test statistic is calculated with the following formula (Hosmer Jr et al., 2013; Lemeshow & Hosmer Jr, 1982; Archer et al., 2004):

$$HL = \sum_{g=1}^{G} \frac{(O_g - E_g)^2}{E_g(1 - E_g)}$$

where:

- HL is the Hosmer-Lemeshow test statistic,
- g is the index of summation,
- O_g and E_g are the observed and expected values in each group g,
- G is the number of groups (commonly 10 deciles),
- Σ = summation notation.

The test then calculates a p-value; a value greater than 0.05 indicates that the model fits the data well, suggesting that the predicted probabilities are a good reflection of the actual observations. Conversely, a p-value less than 0.05 would imply that the model does not adequately fit the data (Hosmer Jr et al., 2013; Lemeshow & Hosmer Jr, 1982; Archer et al., 2004).

To conduct this test, I employed the "*estat gof, group(10)*" command in Stata, which executes the Hosmer-Lemeshow test by partitioning the data into 10 groups according to predicted probabilities and then contrasting the expected and observed outcomes for each group. For a model to be deemed well-fitting, it should ideally exhibit a non-significant Hosmer-Lemeshow test ($p > 0.05$), a robust area under the curve (AUC) exceeding 0.7, and satisfactory sensitivity and specificity values.

To evaluate the model's specification, I performed a Linktest in Stata using the command *"linktest"*. This test assesses whether the model is correctly specified by regressing the dependent variable on the predicted values (_hat) and their squared term (_hatsq). A well-specified model should have a significant coefficient for _hat ($p < 0.05$) and a non-significant coefficient for _hatsq ($p > 0.05$), indicating no omitted nonlinearity. I then used the command *"bootstrap, reps(1000): logit y x1 x2"* followed by *"estat bootstrap, percentile*" to enhance result stability through resampling. The bootstrapped estimates aligned with the original model, affirming its reliability (Chong & Choo, 2011; Beran, 2008; Hesterberg, 2011).

By employing this comprehensive approach, I ensure a robust and reliable evaluation of the logistic regression model. The results from the Hosmer-Lemeshow test, combined with other performance metrics such as the AUC, sensitivity, and specificity, provide a more nuanced understanding of the model's accuracy and predictive power. This process enhances the clinical relevance and interpretability of the findings, supporting their application in real-world settings and guiding decision-making.

3.1.7. Ethical statements

For this study, I used data from medical records available in HIV care clinics caring for CALHIV. I complied with the guidelines for the ethical review of research involving human subjects in the Democratic Republic of the Congo (MSP, 2023) as well as the 1964 Declaration of Helsinki and its later amendments (World Medical Association, 2001). These recommendations state that research involving human beings must prioritize the protection of life, health, privacy, and the dignity of research participants, take greater precautions to protect participants from harm, and conduct the research because the purpose of the study is more important than any potential risks, either now or in the future.

The study was approved by the Medical Ethics Committee of the University of Lubumbashi (N° approval: UNILU/CEM/036/2023) (see APPENDIX I) and the Humanities & Social Sciences Research Ethics Committee of the University of KwaZulu Natal (N° HSSREC/00006817/2024) (see APPENDIX G). I obtained authorizations to conduct the study and to access the data from the Haut-Katanga provincial Ministry of Public Health (N° 10.8/001257/CAB/MIN.PROV/SANTE&C.O.NU/HKAT/2023 and N°10.8/002725/CAB/MIN.PROV/SANTE&C.O.NU/HKAT/2024) (see APPENDIX H).

To ensure confidentiality, I used a password-protected computer for data management and analysis. The data extraction process excluded any unique identifiers, such as address, file number, identity number, surname and first name, to ensure anonymity and the protection of personal information. We, the study team and I as the principal investigator, recognize the sensitive nature of the study and that the data pertains to a vulnerable group.

According to the Guidelines for the Ethical Review of Research Involving Human Subjects in the DRC (MSP, 2023), since the study involves retrospective secondary analysis of

existing data collected as part of routine care and there was no contact with patients, individual informed consent was not required. Moreover, to protect the anonymity and confidentiality of all participants, no patient identifiers were collected.

Prior to data collection, I arranged a meeting with the managers of the HIV care clinics involved in the study to present the research and address any concerns they may have. This meeting helped them comprehend the research and provide the necessary authorization letter from the Haut-Katanga Provincial Ministry of Public Health and ethical approval letter from the Medical Ethics Committee of the University of Lubumbashi. The letters of approval were presented to the heads of the HIV care clinics, who each signed a letter of authorization granting me access to the registers and medical files. With all these letters of approval, I was able to access the data collection files.

During data collection, together with data collectors, we reviewed medical records and extract the necessary data for the study as indicated on the data extraction form (APPENDIX C). The data extraction form did not include any identifiable client information, but only used codes to identify individual patients. Data collection took place on site and the medical records did not leave the HIV clinic. After using the medical records, I returned them to their manager to be stored in locked cabinets as usual. The completed data were be kept on my computer in a Microsoft Excel sheet.

At the end of the data collection in each HIV care clinic, I organized a brief meeting with the clinic manager to report on what I have done and the data collected. The data on my computer were password-protected, and a copy was saved on a password-protected external hard drive kept in my office. Additionally, I ensured that appropriate safeguards are in place to prevent accidental disclosure of sensitive data relating to study participants.

Upon completion of the study and approval of my thesis, written feedback on the study results will be provided to the various HIV care clinics, along with suggestions for

improving services for better outcomes. Additionally, a summary of the results will be shared with regional stakeholders, accompanied by recommendations and suggestions for improvement based on existing evidence in other countries.

3.2. Qualitative study: Barriers and facilitators to viral load suppression among adolescents living with HIV in Lubumbashi, Democratic Republic of the Congo

3.2.1. Study design and setting

This qualitative study was conducted at four HIV care clinics in Lubumbashi, in the DRC, from June to July 2024. Lubumbashi, the second-largest city in the DRC, is located in the southeastern part of the country. The city has an estimated population of over 2,933,962 in 2024, covering an area of 747 km² and resulting in a population density of approximately 3,927 inhabitants per km² (Mukuku et al., 2024). Healthcare facilities were selected based on their capacity to provide HIV care specifically for adolescents living with HIV, with no consideration given to the number of PLHIV, facility type (public or private), or ownership, as all selected facilities receive similar support through the Haut-Katanga provincial health authority, the U.S President's Emergency Plan for AIDS Relief (PEPFAR) funding, and coordination by the DRC National HIV/AIDS Programme.

3.2.2. Study population and sampling

The study triangulated data from different sources, including ALHIV (aged 13–19 years) (n = 39) and their caregivers through in-depth interviews (IDIs) (n = 14), and healthcare workers (HCWs) through focus group discussions (FGDs) (n = 16). This population was selected because it reflects the key stakeholders directly experiencing, influencing, or facilitating VLS among adolescents. ALHIV represented the primary unit of analysis for

understanding personal and contextual barriers or facilitators to adherence, caregivers offered perspectives on family and community-level influences, while HCWs provided insights into structural and health-system-level challenges.

A purposive sampling approach was employed to recruit participants meeting predefined inclusion criteria. This strategy targeted information-rich individuals capable of offering varied perspectives on VLS. Sampling choices were informed by the study's research questions, grounded in the socio-ecological theoretical framework, and supported by evidence from prior studies conducted in comparable settings. Initially, ALHIV were identified from the clinical records and registers at the HIV care clinics in Lubumbashi, with permission obtained from the relevant ethical committees and health facilities to access and review these records. This process allowed us to ensure that only those who met the inclusion criteria were selected.

To be eligible for inclusion in the study, adolescents had to meet the following criteria: (1) being HIV-positive, (2) currently receiving ART for a minimum of 6 months, (3) residing in Lubumbashi city, (4) aware of his/her HIV status, and (5) having undergone VL testing, with classification as either virally suppressed (VL < 1,000 copies/mL) or unsuppressed (VL ≥ 1,000 copies/mL) in line with the DRC National HIV/AIDS Programme and WHO guidelines. Additionally, participants needed to provide informed consent or assent to join in the study. Adolescents not on ART or who had not initiated treatment yet, as well as those on ART for less than six months, were excluded from the study.

We systematically selected participants who met these criteria and ensured that we also included caregivers of the ALHIV. The goal was to achieve a balanced and comprehensive understanding of the barriers and facilitators to ART adherence and to achieve VLS among this group.

Given that younger adolescents rely on their parents or guardians for ART adherence and treatment decisions, we also purposively sampled adult parents or guardians who agreed to participate and provided written informed consent. Parents or guardians of ALHIV who were severely ill and in need of immediate care at the time of the study were excluded.

Additionally, healthcare workers, including doctors, nurses, and pharmacists involved in the care of ALHIV in the health facilities selected for the study were purposively selected to participate in FGDs. These HCWs were chosen to participate in FGDs because of their expertise in managing ALHIV via ART and their understanding of the challenges related to ART adherence and the specific care needs of this population. We included those with one or more years of experience in the care of ALHIV, excluding those who had been newly transferred to the study site for less than six months. A purposive sampling technique was used to select participants based on characteristics or traits that would allow for a detailed understanding of the subject. Selection decisions were based on research questions, theoretical perspectives, and evidence informing the study.

In our study, PLHIV were primarily cared for through the HIV care clinics in Lubumbashi, where they received ART and ongoing health support. PLHIV, including the ALHIV, were part of routine care provided by HCWs such as doctors, nurses, and pharmacists at these clinics. The care provided to PLHIV included regular ART follow-ups, VL testing, and psychosocial support to help manage both the physical and emotional aspects of living with HIV. HCWs were trained and experienced in managing the healthcare needs of ALHIV, with a particular focus on ART adherence and VLS. This healthcare support was part of the broader HIV care services facilitated through national and international programs such as PEPFAR. In this study, ALHIV and their caregivers, were involved through their participation in interviews. This provided insights into the specific challenges they faced in

managing HIV, particularly regarding ART adherence, psychosocial barriers, and support systems. Their involvement in the study did not interfere with their ongoing care (without disrupting their regular care routines), and all interviews were conducted in a manner that respected their confidentiality and well-being.

3.2.3. Conceptualization and theoretical framework

Our study utilizes the socioecological model to examine the barriers and facilitators barriers and facilitators to ART adherence and VLS among adolescents living with HIV on ART. The socio-ecological model was developed by Urie Bronfenbrenner in the 1970s as a conceptual framework for comprehending human development, later evolving into a formal theory in the 1980s (Bronfenbrenner, 1977; 1986; 1989; Kilanowski, 2017). This model is based on the notion that an individual's development is shaped by a system of interconnected elements that interact dynamically. Bronfenbrenner outlined five levels of influence: the microsystem (direct interactions with family, friends, school, community); the mesosystem (connections among these different components); the exosystem (external factors that indirectly affect the individual, such as educational policies); the macrosystem (cultural values, economic contexts); and the chronosystem (impacts of time and contextual changes) (Bronfenbrenner, 2005). Represented by concentric circles with the individual at the core, this model emphasizes the intricate interactions among individual, community, and environmental factors. When applied to health, it provides a comprehensive approach to understanding health behaviors and crafting interventions that are tailored to social and structural realities (Kilanowski, 2017).

In the context of adherence to antiretroviral therapy and achieving VLS, the socio-ecological model allows for an in-depth analysis of barriers and facilitators at different levels of influence. It highlights how individual behaviors result from complex interactions

between personal characteristics and social systems, ranging from the individual (intrapersonal) level to community and structural influences.

At the individual level, factors such as knowledge, attitudes, self-efficacy, and internalized stigma play a crucial role in adherence to treatment and achieving VLS. Common barriers include forgetfulness, depression, HIV-related stigma, and side effects of antiretroviral therapy, which can impair adherence and lead to discontinuation of care (Mukumbang et al., 2017; Shubber et al., 2016). Internalized stigma, for example, can affect self-image and reduce motivation to continue treatment (Helms et al., 2017). However, targeted interventions, such as cognitive behavioural therapy and psychoeducation, can boost self-efficacy and improve treatment adherence (Tsai et al., 2017). Self-efficacy, in particular, is a key predictor of good adherence to ART (Turan et al., 2016) and indirectly to achieving VLS. Moreover, these individual factors are often modifiable, which opens up avenues for the development of adapted interventions to improve adherence to ART and achieve viral load suppression (Dilorio et al., 2009).

The interpersonal level encompasses interpersonal processes that influence social identity and roles, such as those of a partner, friends, and family. An individual's social environment continually shapes their behavior. Family and peer support can yield beneficial effects on behavioral, psychological, and physical health, while their absence can exacerbate problematic behaviors and impede the adoption of a healthy lifestyle (Hagell et al., 2018). Support from family, friends, and peers plays a pivotal role in treatment adherence, fostering self-esteem, alleviating disease stress, fostering optimism, and enhancing treatment adherence (Shumaker & Hill, 1991), thereby contributing to achieving viral load suppression. Conversely, the lack of social support and the presence of stigma, including the internalization of HIV-related stigma, are linked to isolation,

loneliness, and suboptimal adherence to treatment (Takada et al., 2014; Turan et al., 2016). Peer support groups, particularly among adolescents, are instrumental in reducing stigma, fostering acceptance, and thereby enhancing disease management and promoting positive health behaviors (Mburu et al., 2014; Cohen, 2004; Umberson et al., 2010).

At the health service level, the availability and accessibility of care are key factors influencing adherence to antiretroviral therapy. Easier access to medicines, adapted infrastructure and well-organised healthcare services promote better adherence to treatment (WHO, 2016). In addition, a benevolent welcome in health facilities and a relationship of trust with health care staff strengthen the commitment of adolescents living with HIV in their care pathway (Strother et al., 2022; Ahmed et al., 2023; Ammon et al., 2018; Audi et al., 2021; MacPherson et al., 2015; Balejo et al., 2023). Health education, by providing clear and tailored information, allows patients to better understand the importance of treatment and adopt health-promoting behaviors (Zhou et al., 2018).

At the community level, the social environment significantly influences adherence to ART. Cultural norms, societal values, and economic precariousness play a crucial role (Sallis & Owen, 2002). In SSA, HIV stigma persists, leading to social exclusion and discrimination (Wadley et al., 2019). This marginalization can lead to low self-esteem and psychological disorders, hindering adherence to treatment (Zeng et al., 2018). Community-based initiatives to reduce stigma and improve access to care are key to building adherence (Pantelic et al., 2020; Turan et al., 2019; Logie et al., 2018) and achieve VLS. Moreover, economic challenges like poverty and food insecurity represent significant barriers to ART adherence, necessitating targeted socioeconomic interventions (Yakob & Ncama, 2016).

Adherence to ART is a critical factor in achieving VLS, thereby reducing the risk of HIV transmission and enhancing the health of individuals living with the virus. The principle

"Undetectable = Untransmittable" (U=U) demonstrates the direct impact of strict treatment adherence, underscoring the necessity of a comprehensive and coordinated approach (Thomford et al., 2020). To enhance adherence and achieve VLS, it is crucial to engage all stakeholders: adolescents living with HIV, their families, healthcare professionals, and community entities. An integrated strategy, considering individual, interpersonal, healthcare-related services, and community factors, not only diminishes barriers to adherence like stigma, psychological distress, or care accessibility challenges but also bolsters facilitating factors like social support, educational interventions, and psychosocial support.

While the socioecological model provides a structured, multilevel framework to examine the factors influencing ART adherence and viral load suppression, our study is grounded within a social constructionist epistemology. Social constructionism, broadly understood as the view that knowledge and meaning are constructed through social interactions and contexts rather than existing objectively, guides our interpretation of participants' experiences (Burr & Dick, 2017). This approach contrasts with more deductive frameworks by emphasizing the co-construction of reality between researcher and participants, allowing for rich, contextualized understanding of adherence behaviors as socially and culturally situated phenomena.

The terms social constructionist and social constructionism reflect both the philosophical stance underpinning our qualitative methodology and the analytical lens through which we interpret data. While the socioecological model outlines the multiple levels influencing adherence, the social constructionist perspective enables an inductive exploration of how adolescents and their communities interpret and give meaning to these influences in their lived realities.

Thus, rather than a purely deductive application of the socioecological model, our study integrates it within a constructionist framework, allowing flexibility and responsiveness to emergent themes from participants' narratives. This dual positioning helps bridge structural determinants and subjective experiences, ensuring a comprehensive understanding of ART adherence and viral suppression among adolescents living with HIV.

Data analysis in this study is informed by the socioecological model as a conceptual framework to identify multilevel factors shaping behavior, while simultaneously adopting a social constructionist approach to interpret how participants construct meanings around ART adherence and VLS in their social contexts (Galea et al., 2018; Izudi et al., 2024). Intrapersonal factors encompass age, gender, education, knowledge, and attitudes; interpersonal factors revolve around close relationships (family, friends, peers); health service factors encompass accessibility and quality of care (Galea et al., 2018; Izudi et al., 2024); and community factors involve stigma and cultural norms, which can either impede or facilitate ART adherence and viral suppression (Izudi et al., 2024; Izudi et al., 2024).

3.2.4. Data collection process

The IDIs and FGDs were conducted using interview guides customized for each participant group, featuring open-ended questions (APPENDIX D), and conducted in either French or Swahili based on the participants' language preference. The interview guides used for both the IDIs and FGDs were designed based on the socioecological model, which served as the theoretical framework for our study. This model helped structure the questions to explore the various factors influencing ART adherence and VLS among ALHIV. The questions were developed to capture perspectives at multiple levels, including individual, interpersonal, health service-related, and community factors. Additionally, the guides incorporated insights from the literature on HIV care, ART

adherence, and the psychosocial challenges faced by ALHIV. The sessions were recorded and subsequently translated into English for analysis.

Thirty-nine ALHIV who met the inclusion criteria were identified from the clinical records of HIV care clinics. The inclusion criteria for ALHIV were based on a voluntary participation process and aimed at selecting eligible participants who could meaningfully contribute to the study. Adolescents had to:

- Be aged between 13 and 19 years.
- Have a confirmed HIV-positive status.
- Be on ART at the time of the study and have been on treatment for at least six months to one year, irrespective of their virological status (both those who had achieved viral suppression and those who had not).
- Be in generally good health to participate in the study.
- Be able to communicate in French or Swahili.
- Be available for interviews and willing to engage in the study.
- Provide informed consent, with parental or legal guardian consent required for minors.
- Be a resident of Lubumbashi.

These criteria aimed to ensure that participants met the study's objectives and could provide relevant information for analysis. The study did not include non-disclosed adolescents; all interview participants were adolescents who were already disclosed, thus avoiding adverse events related to disclosure. However, to mitigate any potential psychological distress, two clinical psychologists supported the data collection process. These psychologists, with over seven years of experience in caring for PLHIV, closely collaborated with the psychologists working in the HIV care clinics. Therefore, all

participants had free access to psychological care in case of any adverse events. No adverse events were recorded during the study.

The study utilized a triangulated data collection approach, integrating various sources to guarantee a thorough comprehension of the factors impacting USVL among ALHIV on ART. A total of 39 ALHIV underwent individual IDIs, out of the 42 initially approached. Three ALHIV opted out of participation, citing time constraints. Furthermore, 18 caregivers were invited to partake in IDIs, with 14 consenting and the remaining four declining due to time constraints.

Furthermore, FGDs were conducted with 16 HCWs from the selected HIV care clinics, with each FGD comprising four participants: a doctor, two nurses, and a pharmacist. To ensure optimal participation, HCWs were contacted in advance, and discussions were scheduled at convenient times to minimize disruptions to their clinical responsibilities. Notably, all invited HCWs accepted to participate.

Each ALHIV was interviewed individually in a private and quiet room within the HIV care clinics where they received care, ensuring a confidential and comfortable environment for open discussions. The interviews were conducted on weekdays, from June to July 2024, between 9:00 a.m. and 4:00 p.m., with each session lasting approximately 25–30 minutes.

To streamline scheduling and optimize engagement, HCWs from the chosen clinics reached out to ALHIV and their caregivers beforehand to set up appointments. An initial phone call was placed at least a week prior to the scheduled interview date to verify availability, enabling participants to choose a time slot that aligned with their timetable. A follow-up reminder was dispatched at least two days before the interview to reaffirm attendance. The specified liaison within each HIV care clinic played a pivotal role in

harmonizing these schedules, guaranteeing that appointments did not overlap with regular medical check-ups or other commitments.

This structured scheduling approach provided participants with flexibility while minimizing disruptions to their daily activities. The use of dedicated interview rooms further reinforced confidentiality and encouraged open, honest discussions between the participants and interviewers.

The selection of the four HIV care clinics—Tshamilemba Center for STI/HIV Screening and Treatment, Katuba Center for STI/HIV Screening and Treatment, University Clinics of Lubumbashi, and Jason Sendwe Provincial General Reference Hospital—was based on findings from a preceding quantitative study that mapped and categorized healthcare facilities providing services to ALHIV in Lubumbashi. These clinics were chosen according to predefined inclusion criteria to ensure they were the most suitable settings for conducting the study.

The selection criteria included:

- A high number of ALHIV receiving care at these clinics compared to others ensured a representative sample.
- The permanent availability of a clinical psychologist to provide psychosocial support tailored to ALHIV.
- The provision of a dedicated office space for confidential IDIs ensured that all data protection and confidentiality requirements were strictly adhered to, safeguarding the privacy of study participants.

- An organized care pathway for ALHIV and their caregivers was formulated to enable researchers to systematically evaluate service delivery and patient experiences.

In this qualitative study on the barriers and facilitators of VLS among ALHIV in Lubumbashi, a structured pathway was established to ensure comprehensive follow-up for all participants. This process was designed to provide tailored support for each ALHIV while maintaining confidentiality and facilitating data collection. Two distinct pathways were developed: one for ALHIV and another for their caregivers, with a distinction between those HIV-positive and those whose HIV-negative or unknown.

The ALHIV's pathway begins at the reception, where the receptionist verifies the ALHIV's identity, explains the study's objectives, data collection methods, risks, and participants' rights, and obtains informed consent. Subsequently, they are registered and referred to a clinical psychologist.

The process commences with an interview with the clinical psychologist to assess the adolescent's psychological state and address treatment adherence and stigma. This is followed by a medical consultation where a general examination is conducted, treatment adherence is evaluated, and viral load results are reviewed. The doctor also identifies any potential morbidities or ART side effects.

Following this, a second session with the psychologist allows for an IDI with a deeper discussion of the factors facilitating or hindering ART adherence and achieving VLS. Next, the ALHIV proceeds to the pharmacy, where they obtain their medications and receive guidance on strict adherence and side effects management.

Subsequently, they revisit the reception to validate completion of all steps and arrange a follow-up appointment. This systematic approach guarantees a well-organized and ongoing care pathway (Figure 3.4).

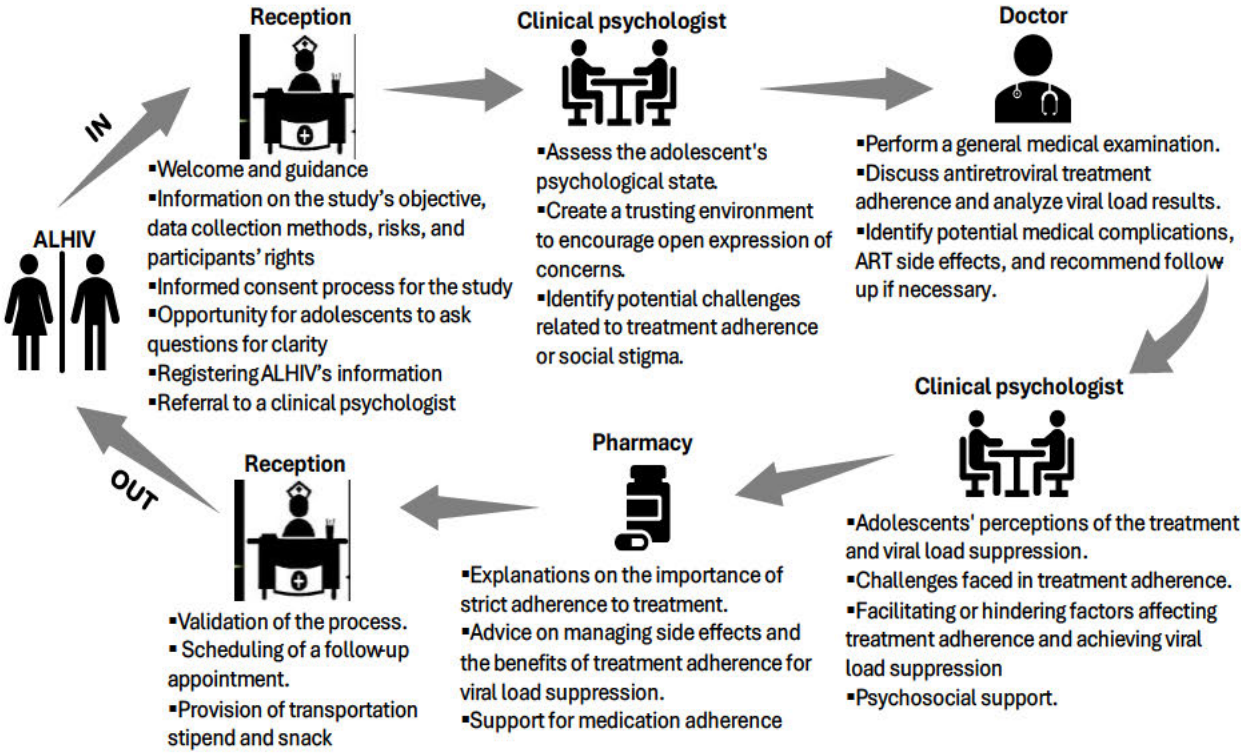

Figure 3.4 Flowchart of the care pathway and in-depth interview process for adolescents living with HIV: Overview of the ALHIV circuit in the study

A parallel pathway was established for the ALHIV's caregivers, considering their serological status, to offer them personalized support (Figure 3.5). Upon arrival, HIV-positive parents or guardians (identified during the appointment scheduling process and based on their medical records) were greeted, briefed on the study's objectives and significance, and their consent was obtained. They were also provided with information regarding their rights, such as the right to withdraw at any time, before being enrolled. Subsequently, they were given the chance to ask any questions to address any concerns.

Next, they were referred to a clinical psychologist for an in-depth interview. This interview focused on their personal experience with HIV, the challenges they faced as parents of an ALHIV, and the strategies they had implemented to support their ALHIV's adherence to ART. The psychologist also addressed the barriers and facilitators to ART adherence and viral load suppression. This session was an opportunity to identify the challenges they faced as parents of an ALHIV, assess existing strategies, and suggest personalized solutions to improve treatment follow-up. Emphasis was placed on the psychosocial aspects of their parental role and ways to enhance support for their ALHIV. Tailored advice was given to help strengthen their ability to encourage treatment adherence while preserving their own well-being.

After the interview, parents were referred to a doctor who assessed their general health and provided follow-up for their treatment, if needed. This medical follow-up helped identify any healthcare needs and ensure they received appropriate medical support. Parents on ART could also collect their medications at the pharmacy at the same time as their ALHIV's, ensuring better treatment coordination and aligning treatment schedules to simplify adherence. They received targeted advice on managing both their own treatment and their ALHIV's, and were encouraged to create a positive, supportive home environment.

Before leaving, parents passed through reception where it was confirmed that all steps had been completed and follow-up was scheduled to ensure continuity of care, including arranging a follow-up appointment. Transport and a snack were also provided.

Parents or guardians whose serological status was negative or unknown followed a similar pathway, but tailored to their specific needs. After registration, they were referred to a clinical psychologist for an initial interview to assess their understanding of HIV, discuss

the challenges of supporting an ALHIV, and provide tools for supporting their ALHIV without stigma. This exchange allowed them to ask questions and address their concerns. A specific educational session was then organized to strengthen their knowledge of HIV, antiretroviral treatment, and the importance of adherence. They were informed about the barriers and facilitators to ART adherence and viral load suppression, and the challenges they faced as parents of an ALHIV were identified. This session also aimed to assess existing strategies and offer personalized solutions to improve treatment follow-up and strengthen their psychosocial support to better manage their own health while supporting their ALHIV.

Following this session, they proceeded to the pharmacy where they were counseled on the significance of ART for their ALHIV and were equipped with methods to bolster treatment adherence while combatting stigma. Subsequently, prior to departure, their progression through the program was confirmed, and a follow-up plan was devised with suggestions to guarantee optimal care for the ALHIV and foster a supportive family setting that encourages treatment adherence. Additionally, transportation and a snack were offered.

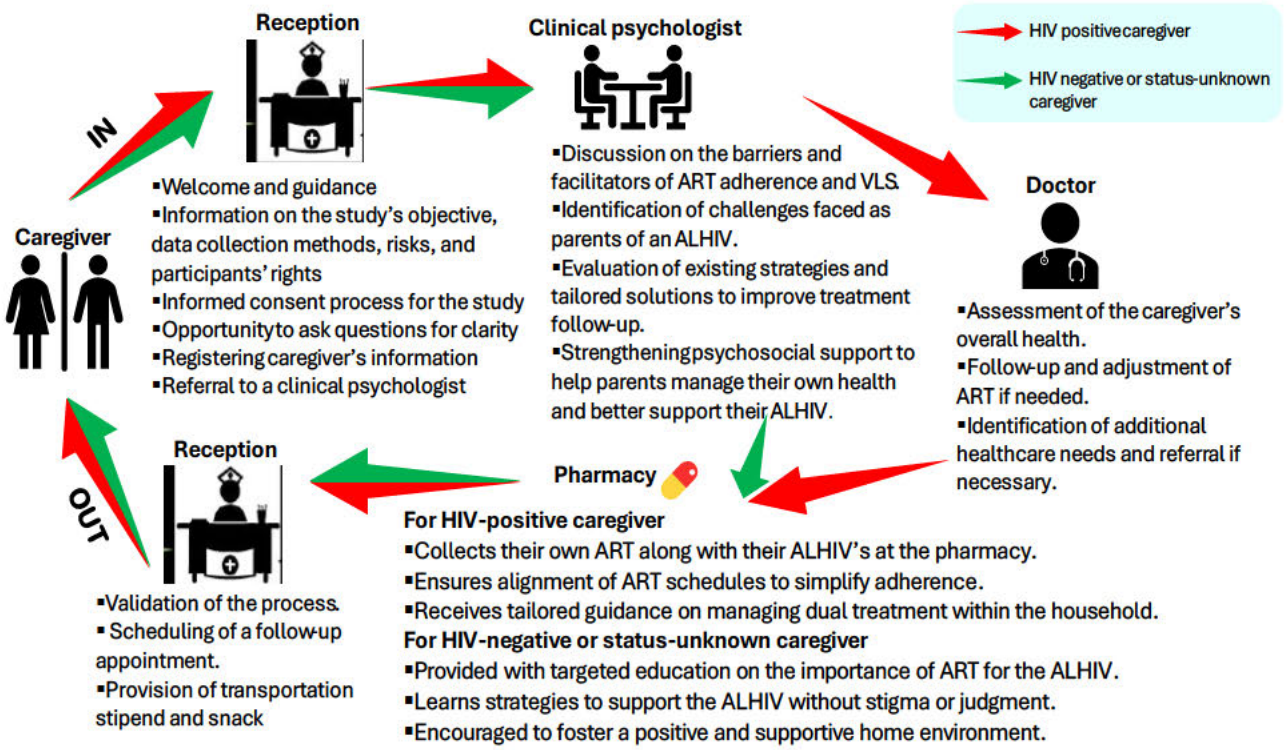

Figure 3.5 Flowchart of the care pathway and in-depth interview process for caregivers: Overview of the caregiver circuit in the study

During data collection, I was supported by two clinical psychologists with over seven years of experience in caring for PLHIV. These psychologists underwent recruitment and training on various topics, including the study's objectives, qualitative research techniques, participant recruitment, data management, research ethics, and quality assurance. They also received specific training on interview approaches with vulnerable populations, particularly ALHIV. The IDIs utilized a semi-structured guide with open-ended questions and suggested prompts covering broad topics such as knowledge about HIV, treatment, factors influencing VLS and ART adherence, psychosocial support, personal perspectives on medication, and barriers and facilitators of achieving VLS and ART adherence for ALHIV.

3.2.5. Data processing and analysis

Audio recordings from the FGDs with HCWs and IDIs with ALHIV and their caregivers were transcribed verbatim and imported into NVivo 14 for qualitative analysis. To ensure a comprehensive understanding of the dataset, the research team, including the co-investigator and myself, reviewed the transcripts in their entirety before developing preliminary coding frameworks. Distinct coding frameworks were constructed for the ALHIV and caregiver interviews, and for the HCW FGDs, to account for differences in participant characteristics and data collection methods.

The discussion topics were organized in line with the socio-ecological model, which conceptualizes individual behavior as shaped by multiple interacting levels: individual, interpersonal (caregivers, family, friends, relatives), healthcare services, and community (Figure 3.6).

Thematic analysis was applied to identify, analyze, and interpret recurrent patterns within the qualitative data. Following Braun and Clarke's six-phase framework (2006), the analysis involved: (1) familiarization with the data; (2) generation of initial codes; (3) searching for themes; (4) reviewing themes; (5) defining and naming themes; and (6) producing the final report. This systematic approach enabled an in-depth exploration of the multifaceted factors influencing antiretroviral therapy (ART) adherence and viral load suppression among ALHIV, providing nuanced insights into the interplay of personal, social, and structural determinants.

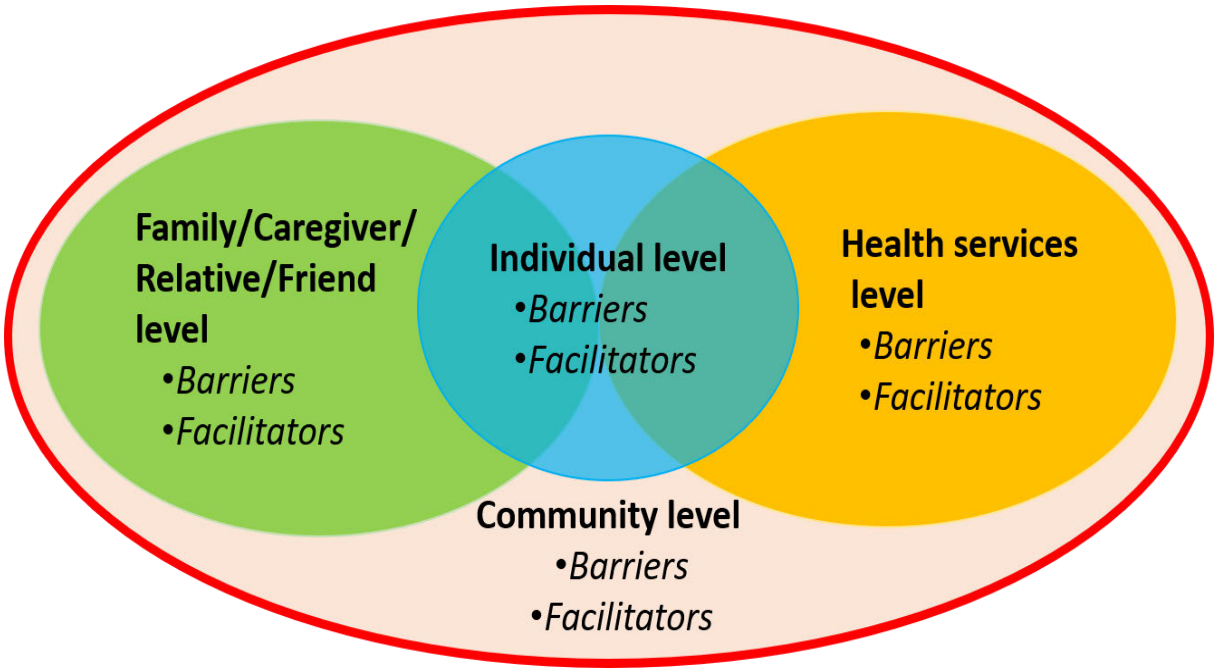

Figure 3.6 Socioecological model used to identify the barriers to and facilitators of HIV viral load suppression among ALHIV receiving ART in Lubumbashi, DRC.

Next, we conducted a detailed comparative content analysis in which each transcript was re-examined, and codes were assigned to similar thematic sections. Some codes were predetermined, whereas others emerged as new themes. The text was then structured based on these codes and organized into matrices to identify recurring issues and differences in the narratives. During the analysis, we engaged in discussions to address and resolve any disagreements in coding.

To ensure data saturation and capture emerging or divergent themes, the data were reviewed periodically throughout the study. After the initial interviews and FGDs, the data were revisited regularly to identify new themes as they emerged, allowing for an iterative approach to analysis.

Additionally, field notes were used during data collection. The clinical psychologists who assisted with data collection and I took detailed field notes during the IDIs and FGDs.

These notes captured contextual information, non-verbal cues, and reflections on the interactions during the interviews. The field notes were reviewed in conjunction with the transcriptions to enhance the analysis and provide a more comprehensive understanding of the findings.

The conceptualization and analysis of the data were further informed by the socioecological model, which helped in understanding the dynamic interactions between ALHIV and their environment. Once the data were organized into matrices and consolidated into broad themes, those specifically related to ART adherence were aligned with an ecological systems model to better represent the findings.

3.2.6. Ethical statements

The study received approval from several key bodies: the Medical Ethics Committee of the University of Lubumbashi (N° UNILU/CEM/036/2023) (see APPENDIX I), the Humanities & Social Sciences Research Ethics Committee of the University of KwaZulu Natal (N° HSSREC/00006817/2024) (see APPENDIX G), the Haut-Katanga Provincial Ministry of Public Health (N° 10.8/001257/CAB/MIN.PROV/SANTE& C.O.NU/HKAT/2023 and N°10.8/002725/CAB/MIN.PROV/SANTE& C.O.NU/HKAT/2024) (see APPENDIX H), and the managers of HIV care clinics. These entities thoroughly reviewed and approved the study protocol, research instruments, and procedural methods before fieldwork commenced. The study adhered to the ethical standards for research involving human subjects as defined by the DRC (MSP, 2023) and the 1964 Declaration of Helsinki, including its subsequent amendments (World Medical Association, 2001).

I placed a high priority on protecting the privacy, confidentiality, and safety of all participants. All study members were trained in human subject research and good clinical practices.

Participants were recruited based on the scientific goals of the study, without discrimination based on vulnerability, privilege, or other unrelated factors. Before the start of each IDI or FGD, participants were provided with a permission script in French (APPENDIX A), which will describe the study and provide all necessary information regarding their rights as research participants. Participants had the opportunity to ask questions before agreeing to participate. For adolescents under 18 years of age, parents or guardians signed the informed consent form, while those aged 18 and over signed their own informed consent in accordance with the laws of the DRC.

For adolescents between the ages of 13 and 17, I obtained the informed consent from parents or guardians and also obtain the adolescent's assent to participate (APPENDIX B) in following guideline 27 for the ethical review of research involving children and adolescents in the DRC (MSP, 2023). This guideline recommends that adolescents should be involved in the decision to participate in research, according to their capacity for physical, psychological, and social development, once they have reached the minimum age of 13 years. Parental informed consent must be followed by an adolescent's assent before enrolling them in a study (MSP, 2023).

HCWs provided their agreement individually. Once all participants have signed the consent forms, they received a copy of the informed consent script, which included my telephone number to call if they have any questions or concerns.

It is up to potential participants to decide whether or not they wish to continue taking part in research. This is accomplished through an informed consent process in which participants (Figure 3.7):

- Understanding the details of the research: Participants were thoroughly informed about the research objectives, methodologies, potential risks, anticipated benefits, and available alternatives. This comprehensive overview ensured that they had a clear understanding of the study's scope and relevance, as well as its possible impact on their lives or the lives of those they care for.
- Making an informed decision: Equipped with all necessary information, participants were able to make a conscious choice about their involvement in the study. They were given ample opportunity to consider the implications of their participation, including any potential personal and clinical effects, before deciding whether or not to take part.
- Relating the information to their personal situation: Participants were encouraged to reflect on how the details of the research pertained specifically to their own clinical circumstances or personal interests. This step allowed them to assess how participation aligned with their values, priorities, and personal well-being. By doing so, they were able to make a well-considered and meaningful decision regarding their involvement in the research.

This process ensured that participants had not only the information needed but also the support and autonomy to make decisions that were well-aligned with their individual needs and circumstances.

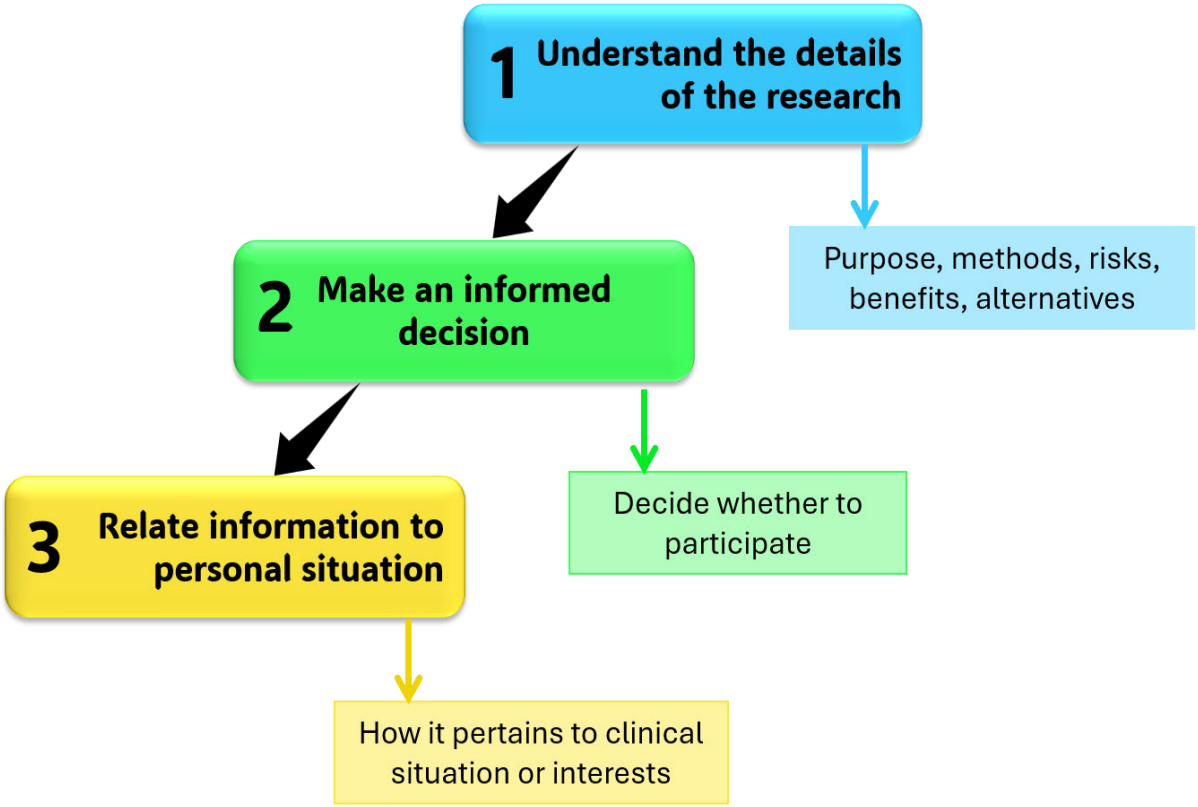

Figure 3.7 Informed consent process for study participation

Ensuring the safety, confidentiality, and anonymity of all participants were crucial to facilitating data analysis, discussion, and dissemination of findings. The participant recruitment process for this study did not use coercive methods. Participants were treated with respect from the time they were approached for possible participation, throughout their participation, and after their participation ends, even if they refuse enrollment in the study. The study team did not influence disclosure or non-disclosure in any manner due to the potential risks associated with HIV-related disclosure. Participants were informed that their decision to participate in the study was not affect their care.

For children living in group homes or who were orphans, specific provisions were made to protect their rights and interests. In these cases, the study sought consent from the legal guardians or authorities responsible for these children, such as the directors of group homes or social workers assigned to them. Additionally, the assent of the children themselves was

obtained to ensure they understood the study and agreed to participate. This dual consent process safeguarded the children's rights, ensuring they were fully informed about their involvement in the study.

The study adhered to ethical guidelines and legal requirements to protect these vulnerable participants, ensuring that their participation was both voluntary and informed. Onsite, participants had access to comprehensive psychosocial services. Formal agreements had been established with the HIV care clinics where the study took place. These agreements, documented in letters of support, guaranteed that clinical psychologists and social workers were available to provide ongoing psychosocial support and further management for all participants. These measures were implemented to ensure that participants received the necessary support throughout the study.

This qualitative study did not include non-disclosed adolescents; all interview participants were adolescents who had already been disclosed, thereby avoiding such adverse events. Additionally, I worked alongside two clinical psychologists to conduct these interviews. They collaborated closely with the psychologists in the HIV care clinics where these interviews were held, ensuring that all participants had free access to psychological care in the event of an adverse event.

ALHIV and their caregivers received a snack and transportation stipends of $5 USD each. The transportation stipend was provided to cover travel expenses, while the snack was offered as a gesture of appreciation for their time and participation. Both the stipend and the snack were intended to support participants in their involvement in the study and were not intended to influence their decision to participate. HCWs were compensated for their time and contributions to the study.

The IDIs and FGDs took place in places where the conversation could not be heard or seen, and where interruptions were kept to a minimum. All transcripts were kept anonymous.

CHAPTER FOUR

RESULTS

4.1. Quantitative study

Figure 3.2 shows the selection process of CALHIV on ART across 21 HIV care clinics in Lubumbashi, in the DRC. Out of 9,789 HIV-positive patients enrolled in these clinics, 1,648 were under the age of 20. Among them, 847 CALHIV were included in the study, while 801 were excluded for the following reasons: 86 had died, 462 were lost to follow-up, 161 were transferred to other facilities, 28 had incomplete data, and 64 had been on ART for less than 6 months.

4.1.1. Description of the study population

Table 4.1 presents the demographic characteristics of the study population, with a total of 847 participants. The mean age of the CALHIV is approximately 11.6 years, with a standard deviation of 5.0 years (range: 2 and 19 years). The age distribution shows that the majority of participants are adolescents, with the largest group being those aged 15 – 19 years (35.1%). The next largest groups are children aged 5 – 9 years (28.8 %) and 10-14 years (27.4%), while 8.7% of the participants are under 5 years old. In terms of sex, the study population consists of 59.7% females (n = 506) and 40.3% males (n = 341), indicating a higher representation of females in the sample. Regarding educational level, the majority of participants have attended primary school (46.7%), followed by those who have completed secondary school (33.8%). A smaller proportion of participants have never been to school (15.0 %), and only 4.5% have reached higher or university-level education.

Table 4.1 Sociodemographic characteristics of the 847 children and adolescents living with HIV

Variable	Total (N=847), *n (%)*
Age	
< 5 years	74 (8.7)
5 – 9 years	244 (28.8)
10 – 14 years	232 (27.4)
15 – 19 years	297 (35.1)
Sex	
Male	341 (40.3)
Female	506 (59.7)
Educational level	
Never been to school	127 (15.0)
Primary	396 (46.7)
Secondary	286 (33.8)
Higher / University	38 (4.5)
Currently living with/in	
At least one biological parent	592 (69.9)
A non-parent family member	191 (22.6)
Adoptive parents	50 (5.9)
Group housing	14 (1.6)
Orphan status	
Non-orphan	390 (46.0)
At least one biological parent died	330 (39.0)
Double orphan	127 (15.0)

When considering the living situation, most participants (69.9%) currently live with at least one biological parent, while 22.6% live with a non-parent family member, and 5.9% are in the care of adoptive parents. A small proportion (1.6%) lives in group housing. In terms of orphan status, nearly half of the participants (46.0%) are non-orphans. However, a

significant portion (39.0 %) has lost at least one biological parent, and 15.0 % are double orphans, having lost both parents.

Table 4.2 provides an overview of the caregiver characteristics for the study population. the mean age of the caregivers is approximately 39.0 years, with a standard deviation of 9.9 years (range: 20 and 75 years). In terms of age, 53.6% of caregivers are under 40 years old (n = 454), while 46.4% are 40 years or older (n = 393). The sex of the caregivers shows a strong female predominance, with 81.4% of caregivers being female (n = 689) and 18.6% male (n = 158).

Regarding employment status, slightly more than half of the caregivers (51.4%) are unemployed (n = 435), while 48.6% are employed (n = 412), indicating a relatively high rate of unemployment among caregivers in this sample. In terms of HIV status, the majority of caregivers are HIV-positive (58.7%, n = 497), while 24.7% are HIV-negative (n = 209). A significant portion (16.7%, n = 141) have an unknown HIV status. Regarding alcohol use, 52.1% of caregivers reported using alcohol (n = 441), while 47.9 % did not (n = 406), indicating a slight majority of caregivers with alcohol use. Finally, in terms of marital status, 60.7% of caregivers are married (n = 514), while 39.3% are single, divorced, or widowed (n = 333), highlighting that the majority of caregivers are in a marital relationship.

Table 4.2 Sociodemographic and clinical characteristics of the 847 children and adolescents living with HIV's caregivers

Variable	Total (N=847), *n (%)*
Age of caregiver	
< 40 years	454 (53.6)
≥ 40 years	393 (46.4)
Caregiver's sex	
Male	158 (18.6)
Female	689 (81.4)
Caregiver's occupation	
Unemployed	435 (51.4)
Employed	412 (48.6)
Caregiver HIV status	
Positive	497 (58.7)
Negative	209 (24.7)
Unknown	141 (16.7)
Caregiver alcohol use	
No	406 (47.9)
Yes	441 (52.1)
Caregiver marital status	
Married	514 (60.7)
Single / Divorced / Widowed	333 (39.3)

Table 4.3 presents key clinical and HIV-related characteristics among the 847 CALHIV. The majority of participants acquired HIV through perinatal transmission (69.5%, n = 589), while 22.3% (n = 189) contracted HIV via blood transfusion. A smaller proportion (3.1%, n = 26) acquired HIV through sexual transmission, and for 5.1% (n = 43), the mode of transmission remains unknown. Regarding disclosure of HIV status to CALHIV, 35.3

% (n = 299) were informed at the age of 12, while only 2.7 % (n = 23) learned about their status before this age. However, a significant proportion (62.0%, n = 525) had not been informed of their HIV status at the time of the study. In terms of disclosure to others, 75.8% (n = 642) of participants had disclosed their HIV status to someone, while 24. % (n = 205) had not. The majority of participants were classified under WHO clinical stage 1 (62.0 %, n = 525), indicating asymptomatic or mild disease. Another 25.2% (n = 213) were in stage 2, while 11.5% (n = 97) had reached stage 3. Only 1.4% (n = 12) were classified in stage 4. In terms of nutritional status, 89.9% (n = 761) of participants had a normal nutritional status. Moderate malnutrition was observed in 8.7 % (n = 74), while severe malnutrition was reported in 1.4% (n = 12). A history of TB within the last six months was reported in 15.2% (n = 129) of participants, while 84.8% (n = 718) had no recent TB history.

Table 4.3 Clinical and HIV-related characteristics of the 847 children and adolescents living with HIV

Variable	Total (N=847), *n (%)*
HIV transmission route	
Perinatal (vertical)	589 (69.5)
Transfusion	189 (22.3)
Sexual	26 (3.1)
Unknown	43 (5.1)
HIV status disclosure to CALHIV	
Before 12 years	23 (2.7)
At 12 years	299 (35.3)
No	525 (62.0)
HIV status disclosure to others	
Yes	642 (75.8)
No	205 (24.2)
WHO clinical stage	
1	525 (62.0)
2	213 (25.2)
3	97 (11.5)
4	12 (1.4)
Nutritional status	
Normal	761 (89.9)
Moderate malnutrition	74 (8.7)
Severe malnutrition	12 (1.4)
History of TB in the last 6 months	
Yes	129 (15.2)
No	718 (84.8)

Table 4.4 presents key aspects of ART use, adherence to ART, and prophylaxis among the 847 children and adolescents living with HIV. Cotrimoxazole prophylaxis was widely administered, with 99.4 % (n = 842) of participants receiving it. Similarly, 92.9% (n = 787)

were on isoniazid prophylaxis for tuberculosis prevention, while 7.1% (n = 60) had not received it. Since ART initiation, 16.1% (n = 136) of participants had experienced at least one treatment interruption, while the majority (83.9%, n = 711) reported continuous ART use. ART-induced side effects were reported by 26.9% (n = 228) of participants, whereas 73.1% (n = 619) did not report any adverse effects. Regarding adherence to ART, 72.4% (n = 613) of participants demonstrated good adherence, while 27.6 % (n = 234) had poor or fair adherence. The majority of participants (93.9%, n = 795) were on a dolutegravir-based regimen, which is recommended for its high efficacy and tolerability. A small proportion was on nevirapine-based (2.5%, n = 21) and efavirenz-based (3.7%, n = 31) regimens. Most participants had been on ART for more than 48 months (60.2%, n = 510), indicating long-term engagement in treatment. Others had been on ART for 25 – 48 months (19.0%, n = 161) or between 6 – 24 months (20.8%, n = 176).

Table 4.4 Antiretroviral therapy and prophylaxis-related characteristics of the 847 children and adolescents living with HIV

Variable	Total (N=847), *n (%)*
Cotrimoxazole prophylaxis	
Yes	842 (99.4)
No	5 (0.6)
Isoniazid prophylaxis	
Yes	787 (92.9)
No	60 (7.1)
History of ART interruption since ART initiation	
Yes	136 (16.1)
No	711 (83.9)
ART-induced side effects	
Yes	228 (26.9)
No	619 (73.1)
ART adherence	
Good	613 (72.4)
Poor / Fair	234 (27.6)
Current ART regimen	
Dolutegravir based regimen	795 (93.9)
Nevirapine based regimen	21 (2.5)
Efanvirenz based regimen	31 (3.7)
ART duration	
6 – 24 months	176 (20.8)
25 – 48 months	161 (19.0)
> 48 months	510 (60.2)

4.1.2. Prevalence of unsuppressed viral load among children and adolescents living with HIV on antiretroviral therapy

In this study, the prevalence of USVL was 24.7% (209 out of 847 CALHIV; 95 % CI: 21.9% – 27.7%) (Figure 4.1). This suggests that almost a quarter of the CALHIV in the sample did not reach VLS.

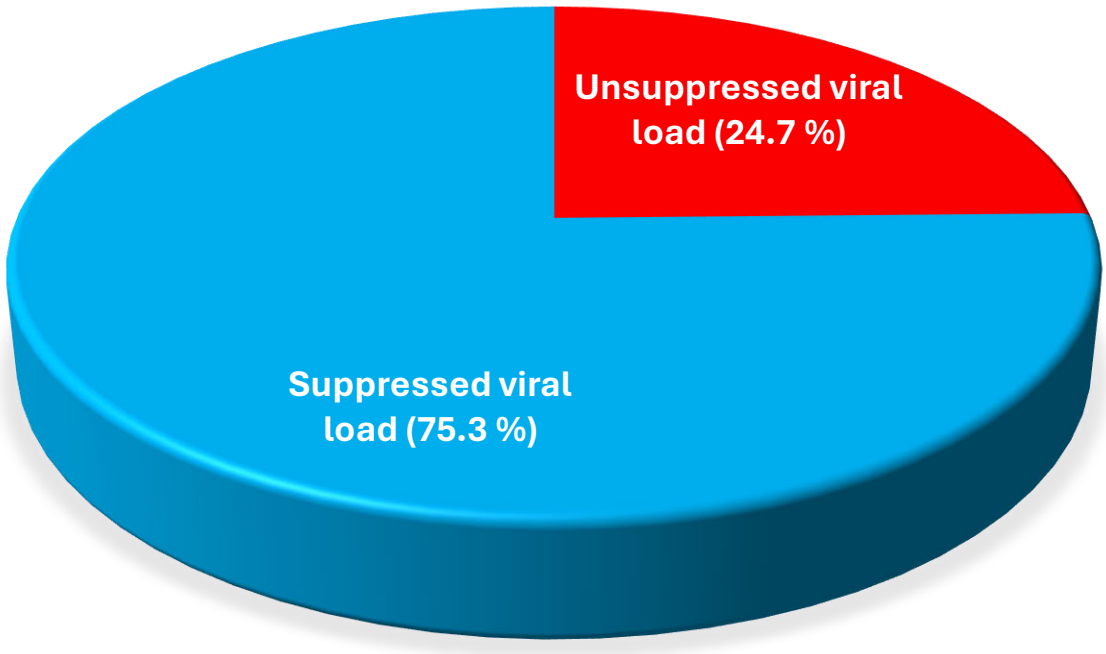

Figure 4.1 Prevalence of unsuppressed viral load among the 847 children and adolescents living with HIV on antiretroviral therapy in Lubumbashi, DRC.

4.1.3. Sociodemographic characteristics of children and adolescents living with HIV on antiretroviral therapy and their caregivers attending HIV care clinics in Lubumbashi categorized by viral load suppression status

Table 4.5 presents sociodemographic characteristics of CALHIV on ART and their caregivers attending HIV care clinics in Lubumbashi, categorized by VLS status (suppressed vs. unsuppressed). It is observed that older age groups, particularly 10-14 years

(cOR = 3.9; 95% CI: 1.6 – 9.4; p = 0.001) and 15-19 years (cOR = 6.0; 95% CI: 2.5 – 14.3; p < 0.0001), have higher odds of USVL compared to those under 5 years, with significant p-values indicating a strong association between age and VLS status. Moreover, when considering gender, there is no significant difference in VLS between males and females (cOR = 1.0; 95% CI: 0.7 – 1.4; p = 0.853). In terms of education, it is noteworthy that higher educational levels are associated with lower rates of VLS. Specifically, those with secondary (cOR = 2.9; 95% CI: 1.6 – 5.1; p < 0.001) or higher/university education (cOR = 3.8; 95% CI: 1.6 – 8.7; p = 0.001) have significantly higher odds of having an USVL compared to those who have never attended school. Furthermore, CALHIV living with non-parent family members (cOR = 1.7; 95% CI: 1.2 – 2.5; p = 0.002) or in group housing (cOR = 3.6; 95% CI: 1.2 – 10.5; p = 0.011) have higher odds of being unsuppressed compared to those living with at least one biological parent. Double orphans have significantly higher odds of USVL compared to non-orphans (cOR = 2.0; 95% CI: 1.3 – 3.0; p = 0.003).

Additionally, caregivers aged 40 or above are associated with higher odds of CALHIV having USVL compared to younger caregivers (cOR = 1.5; 95% CI: 1.1 – 2.1; p = 0.006). Moreover, CALHIV with male caregivers face a higher risk of not achieving VLS compared to those with female caregivers (cOR = 1.7; 95% CI: 1.2 – 2.5; p=0.004). Furthermore, CALHIV with caregivers who are HIV-negative have significantly higher odds of being unsuppressed compared to those with HIV-positive caregivers (cOR = 1.9; 95% CI: 1.3 – 2.7; p < 0.001). In addition, married caregivers are associated with higher odds of USVL in CALHIV compared to those with single, divorced, or widowed caregivers (cOR = 1.4; 95% CI: 1.0 – 1.9; p = 0.047). On the other hand, no statistically significant association was noted between the caregiver's alcohol use (p = 0.408) or the caregiver's occupation (p = 0.071) and the VLS status of CALHIV.

Table 4.5 Sociodemographic characteristics of children and adolescents living with HIV on antiretroviral therapy and their caregivers attending HIV care clinics in Lubumbashi, by viral load suppression status

Variable	Total (N=847), *n (%)*	HIV viral load		cOR [95% CI]	aOR [95% CI]	p-value
		Unsuppressed (n=209), *n (%)*	Suppressed (n=638), *n (%)*			
CALHIV's age*						
<5 years	74 (8.7)	6 (8.1)	68 (91.9)	Reference	Reference	
5-9 years	244 (28.8)	41 (16.8)	203 (83.2)	2.3 [0.9-5.6]	0.6 [0.1-4.1]	0.614
10-14 years	232 (27.4)	59 (25.4)	173 (74.6)	3.9 [1.6-9.4]	0.8 [0.1-6.2]	0.862
15-19 years	297 (35.1)	103 (34.7)	194 (65.3)	6.0 [2.5-14.3]	0.7 [0.1-6.1]	0.783
CALHIV's sex						
Male	341 (40.3)	83 (24.3)	258 (75.7)	Reference		
Female	506 (59.7)	126 (24.9)	380 (75.0)	1.0 [0.7-1.4]		
CALHIV's educational level*						
Never been to school	127 (15.0)	17 (13.4)	110 (86.6)	Reference	Reference	
Primary	396 (46.7)	90 (22.7)	306 (77.3)	1.9 [1.1-3.3]	4.0 [0.9-14.4]	0.055
Secondary	286 (33.8)	88 (30.8)	198 (69.2)	2.9 [1.6-5.1]	2.6 [0.7-9.7]	0.162
Higher/University	38 (4.5)	14 (36.8)	24 (63.2)	3.8 [1.6-8.7]	1.0 [0.1-7.9]	0.971
Currently living with/in*						
At least one biological parent	592 (69.9)	128 (21.6)	464 (78.4)	Reference	Reference	
A non-parent family member	191 (22.6)	62 (32.5)	129 (67.5)	1.7 [1.2-2.5]	2.1 [0.7-6.3]	0.187
Adoptive parents	50 (5.9)	12 (24.0)	38 (76.0)	1.1 [0.6-2.3]	0.5 [0.1-3.3]	0.473
Group housing	14 (1.6)	7 (50.0)	7 (50.0)	3.6 [1.2-10.5]	1.7 [0.1-31.4]	0.735
Orphan status*						
Non-orphan	390 (46.0)	81 (20.8)	309 (79.2)	Reference	Reference	
At least one biological parent died	330 (39.0)	85 (25.8)	245 (74.2)	1.3 [0.9-1.9]	0.7 [0.3-1.5]	0.376
Double orphan	127 (15.0)	43 (33.9)	84 (66.1)	2.0 [1.3-3.0]	0.6 [0.1-2.4]	0.449
Caregiver's age						
<40 years	454 (53.6)	95 (20.9)	359 (79.1)	Reference	Reference	

≥40 years	393 (46.4)	114 (29.0)	279 (71.0)	1.5 [1.1-2.1]	0.7 [0.3-1.5]	0.327
Caregiver's sex						
Male	158 (18.6)	53 (33.5)	105 (66.5)	1.7 [1.2-2.5]	2.0 [0.8-4.9]	0.132
Female	689 (81.4)	156 (22.6)	533 (77.4)	Reference	Reference	
Caregiver's occupation						
Unemployed	435 (51.4)	96 (22.1)	339 (77.9)	Reference		
Employed	412 (48.6)	113 (27.4)	299 (72.6)	1.3 [0.9-1.8]		
Caregiver's HIV status*						
Positive	497 (58.7)	102 (20.5)	395 (79.5)	Reference	Reference	
Negative	209 (24.7)	68 (32.5)	141 (67.5)	1.9 [1.3-2.7]	0.6 [0.2-1.9]	0.403
Unknown	141 (16.7)	39 (27.7)	102 (72.3)	1.5 [0.9-2.3]	0.9 [0.3-3.0]	0.900
Caregiver alcohol use						
No	406 (47.9)	95 (23.4)	311 (76.6)	Reference		
Yes	441 (52.1)	114 (25.9)	327 (74.1)	1.1 [0.8-1.6]		
Caregiver's marital status						
Married	514 (60.7)	139 (27.0)	375 (73.0)	1.4 [1.0-1.9]	2.4 [1.2-5.0]	0.019
Single/Divorced/Widowed	333 (39.3)	70 (21.0)	263 (79.0)	Reference	Reference	

95% CI: 95% confidence interval; %: percentage; aOR: adjusted odds ratio; ART: antiretroviral therapy; CALHIV: children and adolescents living with HIV; cOR: crude odds ratio; n: number; TB: tuberculosis; WHO: World Health Organization

** Overall p-value <0.2 for categorical variables with more than two modalities*

Note: *Variables with an overall p-value of less than 0.2 in the bivariable chi-square analysis were included in the multivariable logistic regression model. Based on this criterion, CALHIV's sex, cotrimoxazole prophylaxis, caregiver's occupation, and caregiver alcohol use were excluded from the multivariable logistic regression model.*

4.1.4. Clinical and treatment information for children and adolescents living with HIV on antiretroviral therapy at HIV care clinics in Lubumbashi categorized by viral load suppression status

Table 4.6 presents clinical information for CALHIV on ART at HIV care clinics in Lubumbashi, categorized by VLS status. The odds of USVL are significantly higher for those infected through horizontal route (cOR = 2.1; 95% CI: 1.5 – 2.9; p < 0.001) compared to vertical route.

Disclosure of HIV status (cOR = 1.8; 95% CI: 1.3 – 2.4; p < 0.001) was associated with higher odds of USVL compared to non-disclosure.

Advanced WHO clinical stages (3-4) (cOR = 21.4; 95% CI: 12.8 – 35.7; p < 0.0001) were strongly linked to USVL compared to stages 1-2.

Additionally, moderate and severe malnutrition significantly elevate the risk of USVL (cOR = 14.3; 95% CI: 8.4-24.3; p < 0.0001) compared to normal nutritional status. A history of TB in the last 6 months is strongly linked to an USVL (cOR = 17.3; 95% CI: 11.0 – 27.1; p < 0.0001).

The absence of isoniazid prophylaxis increases the likelihood of USVL (cOR = 4.6; 95% CI: 2.7 – 7.8; p < 0.0001), while cotrimoxazole prophylaxis shows no significant effect (cOR = 2.0; 95% CI: 0.2 – 18.0; p = 0.602). Interruptions in ART significantly raise the odds of USVL (cOR = 2.5; 95% CI: 1.7 – 3.6; p < 0.0001), as do ART induced side effects (cOR = 16.3; 95% CI: 11.2 – 23.8; p < 0.0001). Poor/fair adherence to ART is highly associated with an USVL (cOR = 135.0; 95 % CI: 76.9 – 236.9; p < 0.0001), emphasizing the importance of consistent treatment. CALHIV on Nevirapine (cOR = 4.4; 95% CI: 1.8 – 10.7; p < 0.001) or Efavirenz-based regimens (cOR = 2.4; 95% CI: 1.2 – 5.0; p = 0.016)

are more likely to experience USVL compared to those on Dolutegravir-based regimens. Additionally, shorter ART durations [6 – 24 months (cOR = 1.4; 95% CI: 0.9 – 2.1; p = 0.073] or 25 – 48 months (cOR = 1.5; 95% CI: 1.0 – 2.3; p = 0.036)] are linked to higher odds of USVL compared to longer treatment periods (> 48 months).

Table 4.6 Clinical and treatment features of children and adolescents living with HIV on antiretroviral therapy attending HIV care clinics in Lubumbashi, by viral load suppression status

Variable	Total (N=847), *n (%)*	HIV viral load		cOR [95% CI]	aOR [95% CI]	p-value
		Unsuppressed (n=209), *n (%)*	Suppressed (n=638), *n (%)*			
HIV infection route						
Vertical (perinatal)	589 (69.5)	120 (20.4)	469 (79.6)	Reference	Reference	
Horizontal (transfusion, sexual, unknown)	258 (30.5)	89 (34.5)	169 (65.5)	2.1 [1.5-2.9]	2.3 [1.0-5.2]	0.042
HIV status disclosure to CALHIV						
Yes	322 (38.0)	101 (31.4)	221 (68.6)	1.8 [1.3-2.4]	1.4 [0.6-3.4]	0.446
No	525 (62.0)	108 (20.6)	417 (79.4)	Reference	Reference	
HIV status disclosure to others						
Yes	642 (75.8)	151 (23.5)	491 (76.5)	Reference	Reference	
No	205 (24.2)	58 (28.3)	147 (71.7)	1.3 [0.9-1.8]	1.3 [0.6-2.8]	0.466
WHO clinical stage						
1-2	738 (87.1)	121 (16.4)	617 (83.6)	Reference	Reference	
3-4	109 (12.9)	88 (80.7)	21 (19.3)	21.4 [12.8-35.7]	3.5 [1.0-13.7]	0.048
Nutritional status						
Normal	761 (89.9)	143 (18.8)	618 (81.2)	Reference	Reference	
Moderate/ Severe malnutrition	86 (10.2)	66 (76.7)	20 (23.3)	14.3 [8.4-24.3]	2.0 [0.7-6.1]	0.202
History of TB in the last 6 months						
Yes	129 (15.2)	98 (76.0)	31 (24.0)	17.3 [11.0-27.1]	0.9 [0.3-2.8]	0.819
No	718 (84.8)	111 (15.5)	607 (84.5)	Reference	Reference	
Cotrimoxazole prophylaxis						
Yes	842 (99.4)	207 (24.6)	635 (75.4)	Reference		
No	5 (0.6)	2 (40.0)	3 (60.0)	2.0 [0.2-18.0]		

Isoniazid prophylaxis						
Yes	787 (92.9)	175 (22.2)	612 (77.8)	Reference	Reference	
No	60 (7.1)	34 (56.7)	26 (43.3)	4.6 [2.7-7.8]	1.8 [0.6-5.8]	0.290
History of ART interruption since ART initiation						
Yes	136 (16.1)	55 (40.4)	81 (59.6)	2.5 [1.7-3.6]	1.3 [0.6-3.0]	0.551
No	711 (83.9)	154 (21.7)	557 (78.3)	Reference		
ART-induced side effects						
Yes	228 (26.9)	147 (64.5)	81 (35.5)	16.3 [11.2-23.8]	3.8 [1.9-7.9]	<0.001
No	619 (73.1)	62 (10.0)	557 (90.0)	Reference	Reference	
ART adherence						
Good	613 (72.4)	19 (3.1)	594 (96.9)	Reference	Reference	
Poor/Fair	234 (27.6)	190 (81.2)	44 (18.8)	135.0 [76.9-236.9]	107.8 [50.3-231.1]	<0.001
Current ART regimen*						
Dolutegravir-based regimen	795 (93.9)	184 (23.1)	611 (76.9)	Reference	Reference	
Nevirapine-based regimen	21 (2.5)	12 (57.1)	9 (42.9)	4.4 [1.8-10.7]	1.2 [0.2-5.9]	0.833
Efavirenz-based regimen	31 (3.7)	13 (41.9)	18 (58.1)	2.4 [1.2-5.0]	0.4 [0.1-1.3]	0.116
ART duration*						
6-24 months	176 (20.8)	50 (28.4)	126 (71.6)	1.4 [0.9-2.1]	2.0 [0.8-4.8]	0.132
25-48 months	161 (19.0)	48 (29.8)	113 (70.2)	1.5 [1.0-2.3]	2.3 [0.9-5.5]	0.059
>48 months	510 (60.2)	111 (21.8)	399 (78.2)	Reference	Reference	

95% CI: 95% confidence interval; %: percentage; aOR: adjusted odds ratio; ART: antiretroviral therapy; CALHIV: children and adolescents living with HIV; cOR: crude odds ratio; n: number; TB: tuberculosis; WHO: World Health Organization

** Overall p-value <0.2 for categorical variables with more than two modalities*

Note: *Variables with an overall p-value of less than 0.2 in the bivariable chi-square analysis were included in the multivariable logistic regression model. Based on this criterion, CALHIV's sex, cotrimoxazole prophylaxis, caregiver's occupation, and caregiver alcohol use were excluded from the multivariable logistic regression model.*

4.1.5. Multiple logistic regression analysis of factors associated with unsuppressed viral load among children and adolescents living with HIV in Lubumbashi

The multiple logistic regression analysis identified several significant factors associated with USVL among CALHIV. Specifically, CALHIV whose caregivers are married are almost three times more likely to have an USVL compared to those whose caregivers are single, divorced, or widowed (aOR=2.4; 95%CI: 1.2–5.0; p=0.019).

CALHIV infected through horizontal transmission (e.g., transfusion, sexual contact, or unknown route) are more than twice as likely to have USVL compared to those infected perinatally (aOR=2.3; 95%CI: 1.0–5.2; p=0.042). Those in WHO clinical stages 3 or 4 are 3.5 times more likely to have USVL compared to those in stages 1 or 2 (aOR=3.5; 95%CI: 1.0–13.7; p=0.048).

CALHIV who experience ART-induced side effects are nearly four times more likely to have USVL compared to those not reporting such side effects (aOR=3.8; 95%CI: 1.9–7.9; p<0.001).

Finally, poor or fair ART adherence is the strongest predictor of USVL. CALHIV with poor/fair adherence are more than 100 times more likely to have USVL compared to those with good adherence (aOR=107.8; 95%CI: 50.3–231.1; p<0.001) (Tables 4.5 and 4.6).

The Linktest results indicate that the model is well-specified. The coefficient for *_hat*, representing the predicted values, is statistically significant ($p < 0.0001$), suggesting that the model effectively predicts the unsuppressed viral load in our population study. On the other hand, the coefficient for *_hatsq*, the squared predicted values, is not significant (p =

0.900), implying no major specification errors or omitted nonlinearity. These findings confirm that the model does not suffer from specification issues (Table 4.7).

Table 4.7 Linktest results for model specification

Unsuppressed viral load	Coefficient	Standard error	z	P>z	[95% confidence interval]	
_hat	1.01	0.09	11.69	< 0.0001	0.84	1.18
_hatsq	0.00	0.03	0.13	0.900	-0.06	0.07
_cons	-0.02	0.21	-0.09	0.928	-0.44	0.40

Furthermore, bootstrapping with 1,000 replications confirmed the robustness of the model's coefficients, as the confidence intervals remained consistent with those obtained through conventional standard error estimation. These findings reinforce the reliability of our logistic regression model.

The assessment of the model's fit using the Hosmer-Lemeshow test shows a good fit for the data. The chi-square statistic is 4.0 with 6 degrees of freedom and a p-value of 0.6747, well above the threshold of 0.05. This indicates that the observed and expected values do not differ significantly, suggesting a satisfactory fit of the logistic model to the data.

The classification matrix analysis shows that the model performs well overall, with a correct classification rate of 92.1 %. Sensitivity, which measures the model's ability to correctly identify CALHIV with unsuppressed viral load, is 85.2 %, indicating that the model correctly identifies the majority of affected individuals. Specificity is also high (94.4 %), demonstrating good ability to recognize CALHIV with suppressed viral load.

The predictive values are also robust: the positive predictive value (83.2 %) means that, among individuals classified as CALHIV with unsuppressed viral load, 83.2 % are indeed positive. Similarly, the negative predictive value (95.1 %) suggests that the model correctly classifies a large proportion of CALHIV with suppressed viral load. However, the false negative rate of 14.8 % indicates that a number of CALHIV with unsuppressed viral load are not identified by the model, which could be problematic if the main objective is to maximize the detection of CALHIV with unsuppressed viral load. These results suggest that the logistic regression model used performs well with excellent specificity and a good fit to the data. The evaluation of the logistic model's performance using the ROC curve demonstrates excellent discriminative ability, as evidenced by an area under the curve (AUC) of 0.9581 (Figure 4.2).

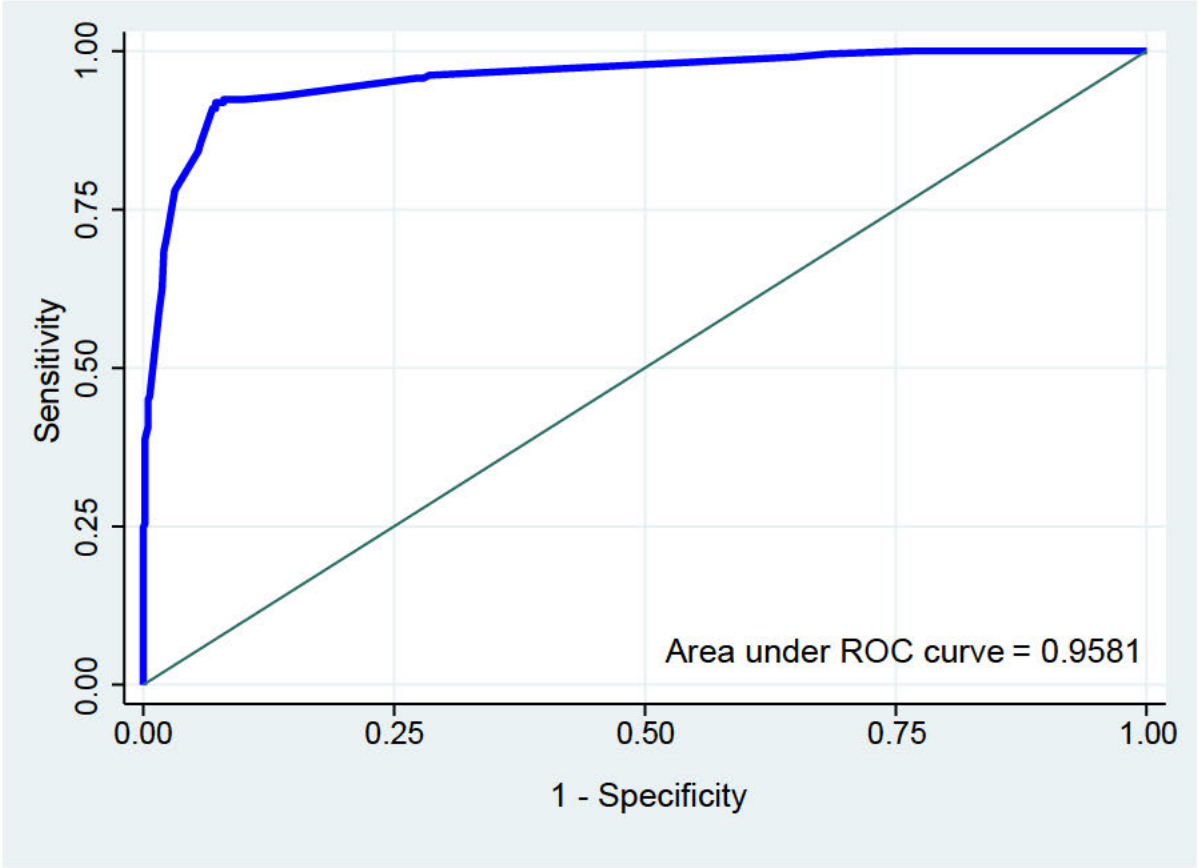

Figure 4.2 Evaluation of logistic model performance using ROC curve

A value close to 1 signifies the model's effectiveness in distinguishing between CALHIV with unsuppressed viral load and those with suppressed viral load. With a correct classification rate of 92.1 %, sensitivity of 85.2 %, and specificity of 94.4 %, the model's performance is further supported (Figure 4.3). Nevertheless, improving the false negative rate (14.8 %) could enhance its precision in identifying CALHIV with USVL.

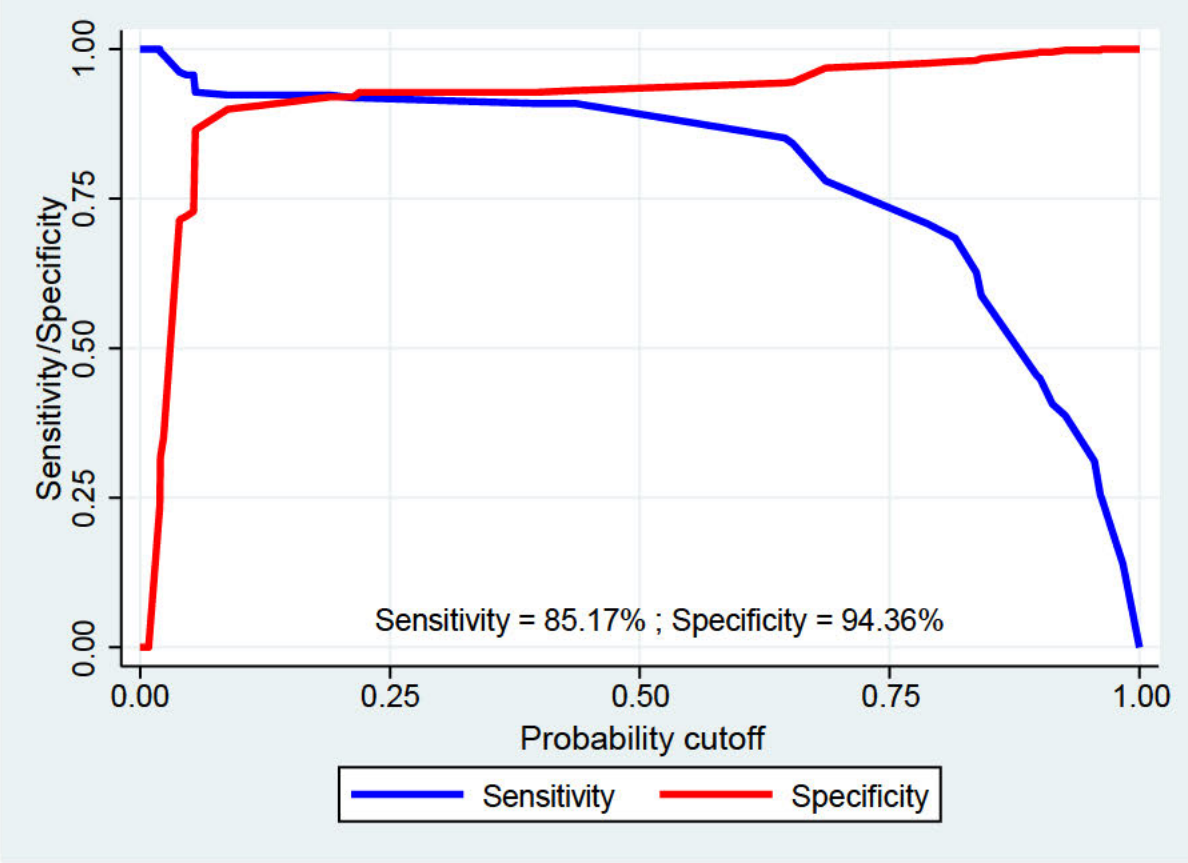

Figure 4.3 Model performance metrics for distinguishing children and adolescents living with HIV with suppressed and unsuppressed viral load

The results of the linear regression indicate that the model is globally significant ($p < 0.0001$), suggesting that the independent variables account for a substantial amount of the variance in USVL ($R^2 = 0.6871$). This implies that 68.7 % of the variability in USVL can be explained by the variables incorporated in the model.

The regression model equation is as follows:

Unsuppressed viral load in CALHIV = − 4.8 + (1.6 × Advanced WHO clinical stage) + (4.5 × Poor/Fair ART-adherence) + (0.9 × ART-induced side effects) + (0.9 × Horizontal HIV transmission) + (1.0 × Married caregivers).

This equation illustrates the impact of each variable on the unsuppressed viral load in CALHIV, highlighting the significant influence of poor/fair adherence and advanced WHO clinical stage (3 or 4).

4.2. Qualitative study

4.2.1. Characteristics of the study participants

Table 4.8 presents the characteristics of the ALHIV, their parents/guardians and the HCWs involved in the study. The majority of ALHIV were aged between 16 and 19 years (35/39) and the majority were female (22/39).

The majority of ALHIV (33/39) had a suppressed VL and were in secondary school (35/39). In terms of living arrangements, more than half of the adolescents lived with at least one biological parent (20/39), whereas 28.2 % lived with non-parental family members.

The caregivers were mainly aged between 40 and 59 years (6/14) and were mostly women (9/14). The HIV status of these caregivers varied: just over one-third were HIV-positive (5/14), whereas 42.9 % (6/14) did not know their HIV status. Most of the HCW were women (10/16), and most were aged 40 years or over (9/16). The group comprised 4 doctors, 8 nurses, and 4 pharmacists.

Table 4.8 Characteristics of the study participants

ADOLESCENTS	**N = 39**
Age	
13 - 15 years	4 (10.3%)
16 - 19 years	35 (89.7%)
Mean ± standard deviation	*17.14 ± 1.06*
Sex	
Female	22 (56.4%)
Male	17 (43.6%)
HIV viral load status	
Suppressed	33 (84.6%)
Non-suppressed	6 (15.4%)
Educational level	
Secondary	35 (89.7%)
Higher	4 (10.3%)
Occupation	
Student	34 (87.2%)
Self-employed	5 (12.8%)
Currently living with/in	
At least one biological parent	20 (51.3%)
A non-parent family member	11 (28.2%)
A non-family member	5 (12.8%)
Group housing	3 (7.7%)
Current ART regimen	
Dolutegravir based regimen	36 (92.3%)
Efavirenz based regimen	3 (7.7%)
CAREGIVERS	**N = 14**
Age	
20-39 years	4 (28.6%)
40-59 years	6 (42.8%)
≥60 years	4 (28.6%)
Mean ± standard deviation	*47.21 ± 12.26*
Sex	
Female	9 (64.3%)
Male	5 (35.7%)
HIV status	
Positive	5 (35.7%)
Negative	3 (21.4%)
Unknown	6 (42.9%)
HEALTHCARE WORKERS	**N = 16**
Age	
20-39 years	7 (43.8%)
≥40 years	9 (56.2%)
Mean ± standard deviation	*41.75 ± 13.17*
Sex	
Female	10 (62.5%)
Male	6 (37.5%)
Medical title	
Doctor	4 (25.0%)
Nurse	8 (50.0%)
Pharmacist	4 (25.0%)

4.2.2. Barriers to and facilitators of viral load suppression in adolescents living with HIV according to the socioecological model

Table 4.9 below summarizes the barriers and facilitators to achieve VLS among ALHIV aged 13-19 years receiving ART in Lubumbashi (in the DRC), based on the domains of the socioecological model.

Table 4.9 Summary of barriers and facilitators to viral load suppression in adolescents living with HIV according to the socioecological model

Level	Barriers	Facilitators
Individual	• ART side effects • Forgetting to take medication • Lack of food • Being too busy • Feeling healthy and not perceiving the necessity of ART • Being away from home	• Confidence in the effectiveness of ART • Awareness of the importance of ART adherence • Having a structured routine • Use of reminder tools • Ability to manage side effects of ART
Interpersonal	• Undisclosed HIV-positive status	• Staying healthy for his/her loved ones • Peer support clubs
Family	• Broken families and loss of parents • Lack of assistance in taking ART • Stigma and discrimination	• Support from family and friends in initiating and adhering to ART
Health-related services	-	• Positive and open relations with nursing staff • Mental health support
Community	• Stigma and discrimination	-

4.2.3. Facilitators of viral load suppression

4.2.3.1. Individual facilitators

4.2.3.1.1. Confidence in the effectiveness of antiretroviral therapy

ALHIV and their caregivers expressed increasing confidence in the effectiveness of ART, which promotes strict adherence to treatment. This trust in the benefits of ART enhances their dedication to consistent medication intake, along with the support provided by caregivers throughout the process.

> *"Since I have been taking my ART daily, my life has completely changed. My condition has stabilized, my VL is undetectable, and I can live a full life despite my HIV status."* (Adolescent 32, female, 16 years)

> *"My two children and I are HIV-positive. I always take my ART at the same time as my children to stay healthy and live a long life."* (Caregiver 13, mother, HIV-positive)

4.2.3.1.2. Awareness of the importance of antiretroviral therapy adherence

Understanding the critical role of adherence to ART has empowered ALHIV and caregivers to prioritize treatment. This awareness often stems from personal experiences and psychological support, reinforcing the necessity of consistent adherence.

> *"When my daughter learned her medication was for HIV, she stopped taking it. I sought advice from psychologists and constantly reminded her about the risks. Now, she takes it on her own and keeps her VL under control."* (Caregiver 04, father, HIV-positive)

> *"I thought I could manage without ART, but my health worsened drastically. From that moment, I vowed to follow my treatment rigorously."* (Adolescent 34, female, 19 years)

4.2.3.1.3. Importance of a structured routine

A structured daily routine emerged as a crucial factor for maintaining ART adherence and achieving VLS. Participants emphasized the role of discipline and consistency in promoting successful health management.

> *"Since I was young, I've taken my medicine at 8:30 p.m. without reminders. Even when traveling, I never miss it."* (Adolescent 05, male, 19 years)

> *"My daughter and I are both HIV-positive. We remind each other to take our medication daily, even from a distance."* (Caregiver 11, mother, HIV-positive)

4.2.3.1.4. Use of reminder tools

Reminder tools such as alarms, diaries, and mobile phones have significantly reduced forgetfulness and enhanced adherence to ART. Family support also plays a vital role, particularly when an adult ensures medication intake.

> *"I bought a small phone for a 16-year-old girl in my care. The alarm reminds her to take her medication, even during challenging times like funerals."* (Caregiver 05, non-family member, HIV unknown status)

4.2.3.1.5. Managing antiretroviral therapy-related side effects

Building resilience to manage ART side effects is crucial for adherence and achieving VLS. Caregivers and HCWs offer counseling to empower ALHIV and their families to overcome challenges caused by nausea, fatigue, and other side effects.

> *"Despite experiencing nausea and fatigue, I remind myself of the significance of maintaining my health. As advised by medical professionals, I make sure to have a meal before my medication."* (Adolescent 24, female, 17 years)

> *"Since transitioning to TLD [Tenofovir + Lamivudine + Dolutegravir], we've observed fewer ART side effects compared to previous regimens."* (FGD 01, HCW 04, male, doctor)

4.2.3.2. Interpersonal facilitators

4.2.3.2.1. Staying healthy for their loved ones

Emotional connections with loved ones are a powerful motivator for ART adherence and achieving VLS among ALHIV. Support from family and significant others fosters a sense of responsibility and encourages ALHIV to remain committed to their treatment, even during challenging times.

> *"Since I started dating my girlfriend, my commitment to ART has grown. Even when discouraged, her encouragement and my mother's reminders help me stay determined."* (Adolescent 19, male, 18 years)

These relationships are crucial, underscoring how family and close connections significantly influence treatment outcomes.

4.2.3.2.2. Peer support clubs

Peer support clubs, especially those on platforms like WhatsApp, significantly improve ART adherence among ALHIV. These groups foster a sense of community and mutual accountability, inspiring members to adhere to their medication schedules and exchange coping strategies.

> *"Someone in our JADO WhatsApp group asks if everyone has taken their medication. This reminder helps me stay on track."* (Adolescent 34, female, 19 years)

Peer support is particularly transformative for younger adolescents struggling with their diagnosis:

> *"My 12-year-old niece struggled with her diagnosis. After joining a support group, she became more consistent with her ART and successfully suppressed her VL."* (Caregiver 10, maternal uncle, HIV unknown status)

HCWs highlight the importance of peer educators in facilitating these groups:

> *"Peer educators help ALHIV participate in support groups, where they exchange experiences and encourage each other to improve ART adherence and to achieve VLS. Some have created WhatsApp groups to further this support."* (FGD 02, HCW 03, male, pharmacist)

These clubs foster resilience, normalize challenges, and create a positive environment that reinforces adherence.

4.2.3.3. Family facilitators: Support from family and friends in initiating and adhering to ART

Family and friend support is crucial for achieving VLS among ALHIV. This support provides emotional encouragement and practical assistance, including reminders to take medication and attend medical appointments. Caregivers play a significant role in assisting adolescents in navigating the emotional challenges of an HIV diagnosis. Often, ALHIV may experience denial or despair initially, which can hinder adherence. Therefore, ongoing support from caregivers is essential in fostering commitment to treatment.

> *"I used to consider giving up, but my mother and aunt motivate me daily. Their support helps me stay disciplined with my medication, knowing I'm important to them and they prioritize my well-being."* (Adolescent 28, female, 19 years)

Shared family routines can reinforce adherence.

> *"My 18-year-old daughter and I are both HIV-positive. We take our medication together at 8 p.m. each night, ensuring one of us remembers if the other forgets."* (Caregiver 09, mother, HIV-positive status)

A caregiver involvement in healthcare appointments also enhances adherence:

> *"My 16-year-old daughter refused her medication and appointments. However, since I started accompanying her, she now consistently attends appointments, and we take our medication together."* (Caregiver 12, mother, HIV-positive status)

4.2.3.4. Health service facilitators

4.2.3.4.1. Positive and friendly relationships with HCWs

In the global response to HIV, constructive and supportive relationships with HCWs play a critical role in achieving VLS among ALHIV. These interactions help adolescents understand their condition and the importance of ART adherence, thereby reducing the risk of treatment interruption and unsuppressed VL. Positive relationships foster open communication, enabling ALHIV to seek guidance and address challenges effectively.

> *"I have a very good relationship with my doctor; he advises and encourages me to take my medication... When I meet with him, he listens to my concerns, discusses various topics, and provides valuable feedback on my health. I truly feel cared for."* (Adolescent 39, female, 17 years)

4.2.3.4.2. Psychological support

ALHIV often face stigma and discrimination, which can lead to significant psychological distress, undermining ART adherence and VLS achievement. Health services stress the importance of psychological support from families, friends, and professionals to assist adolescents in coping with stigma-related stress and depression.

> *"Most ALHIV struggle to accept their status after prolonged medication use without disclosure. When they learn their HIV-positive status, many experience despair and psychological issues, leading to missed medical appointments. To address this, we collaborate with clinical psychologists to provide HIV education and mental support. This helps them adhere to ART and regain emotional stability."* (FGD 03, HCW 05, female, nurse)

4.2.4. Barriers to viral load suppression

4.2.4.1. Individual level barriers

4.2.4.1.1. Antiretroviral therapy-related side effects

ART side effects, such as nausea, headaches, and fatigue, are significant barriers to ART adherence and achieving VLS among ALHIV. These discomforts often deter consistent treatment, despite the efforts of caregivers to provide support.

> *"Before starting treatment, I felt fine and didn't even know I was HIV-positive. However, since I started treatment, I have been constantly suffering from nausea, headaches, and fatigue, which makes it difficult to follow the treatment rigorously and keep my VL under control. Sometimes these side effects discourage me and seem insurmountable."* (Adolescent 35, male, 18 years)

4.2.4.1.2. Forgetting to take medication

Forgetting to take medication is a common issue. Life occupations/distractions such as school, social activities, or work can interfere with adherence, impacting VLS.

> *"Sometimes I'm in a hurry to get to mass as a singer in the choir, and since the church is quite far away, I go home exhausted and forget to take my medicine."* (Adolescent 02, female, 16 years)

> *"... on several occasions I've gone to parties and had beer. When I got home, I forgot to take my medication because I was so drunk."* (Adolescent 35, male, 18 years)

4.2.4.1.3. Lack of food

A lack of food is a significant barrier to ART adherence for some ALHIV, particularly those living in precarious situations, such as orphans with limited financial resources. This

scarcity of food can make it challenging to adhere to medication, impact its efficacy, and jeopardize achieving VLS. Several participants shared their experiences, illustrating how the inadequate availability of food affects their ability to adhere to their treatment regimen.

> *"I often take my medication without food, which weakens my body. I was once hospitalized because of this."* (Adolescent 04, male, 17 years)

> *"Sometimes, I have to take my medication when there's no food available, so I have to take it on an empty stomach."* (Adolescent 02, female, 16 years)

4.2.4.1.4. Busy schedules

During the interviews, some ALHIV mentioned that their busy schedules, combining studies and income-generating activities, created constraints that made it difficult for them to take their medication regularly. These additional responsibilities can sometimes interfere with ART adherence to treatment schedules, as described by one ALHIV:

> *"I often have to decorate for parties, and these tasks sometimes take longer than expected. This prevents me from getting home in time to take my medication."* (Adolescent 23, boy, 16 years)

4.2.4.1.5. Feeling healthy and not perceiving the necessity of antiretroviral therapy

Like many chronic diseases, HIV can remain asymptomatic for a long period. Consequently, some PLHIV may feel well for months or even years without experiencing any immediate symptoms of their HIV status. This false sense of good health can cause them to underestimate the significance of ART. A member of the nursing staff exemplified this occurrence:

> *"Some ALHIV, feeling healthy after taking medication for a while stop taking their treatment. This may be due to several factors: some do not understand that HIV / AIDS*

> *is a chronic disease, whereas others, despite knowing their status, do not see the need to continue ART. However, this decision can have serious and unbearable long-term consequences for many patients."* (FGD 04, HCW 02, female, doctor)

4.2.4.1.6. Distance from home

Adolescents' daily journeys, often far from home, complicate their medication routine, potentially compromising the effectiveness of ART and the achievement of VLS. Being away from home without their medications at hand can lead them to overlook the significance of consistent treatment.

> *"On Sundays, I'm often very busy with lots of things to do. Sometimes I don't get home until 8:00' p.m., and as I don't take my medication with me when I go to Mass, I end up forgetting to take it."* (Adolescent 39, female, 17 years).

> *"... when I went on holiday to stay with my uncle in Mbuji-Mayi, I stopped taking my medication…"* (Adolescent 25, male, 16 years)

4.2.4.2. Interpersonal barriers: undisclosed HIV status

Many ALHIV choose to keep their HIV status hidden from peers, sharing it only with their guardians and HCWs. This lack of disclosure creates challenges in adhering to ART, as it often leads to secrecy and stigma.

> *"I hide my medication from everyone except my aunt, as I don't want others to know I'm sick."* (Adolescent 22, female, 18 years).

Caregivers also emphasized this challenge as a significant barrier to adherence to ART, underscoring the importance of ALHIV disclosure of their status for effective management.

> *"Many caregivers are reluctant to openly address an adolescent's HIV-positive status, often disguising the medication as treatment for a cough, a nutritional supplement like vitamins, or for another unrelated condition. However, upon discovering the truth,*

> *adolescents may react by resisting medication intake, thereby heightening their susceptibility to opportunistic infections from not achieving VLS."* (FGD 02, HCW 07, female, nurse)

4.2.4.3. Barriers at the family level

4.2.4.3.1. Broken families and parental loss

The family is central to an individual's development; however, many ALHIV in this study reported challenges arising from parental loss, living with guardians, or broken families. These circumstances impede their ability to adhere to ART and achieve VLS.

> *"Becoming an orphan at the age of 12, I moved in with my grandmother, who, due to her age, finds it challenging to take care of us. The loss of my parents, coupled with the enduring emotional distress, impacts my ability to adhere to my medication regimen consistently."* (Adolescent 04, male, 17 years)

> *"Since my parents passed away, my family stopped caring for me, except for my grandmother, which sometimes leads me to skip my medication."* (Adolescent 26, male, 17 years)

4.2.4.3.2. Lack of assistance in taking antiretroviral therapy

HCWs emphasized that the lack of assistance in ensuring ALHIV take their medication is a significant barrier to ART adherence and achieving VLS. Some caregivers administer medications without verifying whether the adolescent actually consumes them, resulting in missed doses.

> *"I've always advised ALHIV's caregivers to be cautious, as some adolescents may deceive them by pretending to take their medication, holding it in their mouths, and then*

> *discarding it. I even witnessed the tragic outcome of a girl who deceived her grandmother by pretending to adhere to her medication, only to dispose of it when unsupervised. Owing to her irregular medication intake, the girl failed to achieve VLS despite multiple medical assessments, ultimately resulting in her untimely death."* (FGD 02, HCW 03, male, pharmacist)

4.2.4.3.3. Stigma and discrimination within the family

Family stigma and discrimination significantly impact ART adherence. ALHIV frequently face isolation and marginalization within their own homes, potentially resulting in treatment abandonment.

> *"After my mother's death, I faced discrimination at my aunt's house. I was given separate dishes and cups, and no one would share with me. This mistreatment led me to stop taking my medication for two years."* (Adolescent 04, male, 17 years)

4.4.4. Barriers at the community level: stigma and discrimination

Participants did not identify any community-level facilitators for achieving VLS but emphasized stigma and discrimination as major barriers to ART adherence and to achieve VLS. Within communities, social discrimination is widespread, especially towards young individuals with chronic illnesses such as HIV, often coming from peers or classmates. All ALHIV in this study mentioned hiding their HIV status to prevent stigmatization.

> *"When my son's father left me because of my HIV status, it discouraged me from continuing my medication. He claimed that if he hadn't been infected yet, it was by chance, and he preferred to separate to avoid the HIV acquisition risk."* (Adolescent 34, female, 19 years)

"At home, I take my medication secretly. No one, including my friends at school, knows my status. This has caused major difficulties, like when I confided in a boy about my status and he left me." (Adolescent 37, female, 18 years)

CHAPTER FIVE

DISCUSSION

5.1. Prevalence of unsuppressed viral load among children and adolescents living with HIV on antiretroviral therapy

This study provides critical insights into the prevalence of unsuppressed viral load among children and adolescents living with HIV in Lubumbashi, DRC. Despite significant progress in expanding antiretroviral therapy coverage and intensified global efforts to achieve the UNAIDS 95 – 95 – 95 targets, our study found that 24.7 % of CALHIV failed to achieve VLS, meaning that approximately one in four individuals on ART continues to face challenges in reaching optimal treatment outcomes. This underscores persistent gaps in treatment effectiveness and highlights the need for targeted interventions to improve treatment outcomes in this vulnerable population. While ART has significantly improved the prognosis of CALHIV, the high prevalence of USVL in Lubumbashi reflects ongoing barriers to optimal adherence to ART and treatment success.

These challenges are not unique to the DRC but are widely observed across many SSA countries. This mirrors trends observed in other regions of SSA, where achieving sustained VLS remains significant. When compared to other studies across sub-Saharan Africa (SSA), the prevalence rates of USVL vary considerably from one region to another, from one country to another, and even within the same country, from one city to another.

In Eastern Africa, Sibhat et al. (2020) reported a prevalence of 23.76% in Tigray, Ethiopia, while Abera et al. (2023) found a lower prevalence of 17.28 % in the Oromia Region of Ethiopia. In Kenya, Tsikhutsu et al. (2022) reported a prevalence of 19.79% in the South

Rift Valley and Kisumu, whereas Onyango et al. (2023) observed a much lower prevalence of 14.07% across 34 counties. Kabogo et al. (2017) noted a significantly higher prevalence of 43.83% in Nairobi, highlighting regional disparities within the same country. Tanzania presents a unique case with varying prevalence across different regions: Khamadi et al. (2023) reported the lowest prevalence of 15.84% in the Southern Highland Zone, while Mchomvu et al. (2022) observed a significantly higher rate of 32.80% in the Tabora region; similarly, Bitwale et al. (2021) noted a prevalence of 34.00% in Dodoma Municipality, and Muri et al. (2017) found a prevalence of 25.35% in the Kilombero District. These findings illustrate the heterogeneity of USVL prevalence within a single country, potentially reflecting differences in ART program implementation, healthcare access, and patient adherence.

In Southern Africa, studies have shown similarly variable USVL rates. Tweya et al. (2020) reported the lowest prevalence of 15.85% among CALHIV in Lilongwe, Malawi. In Zimbabwe, Makadzange et al. (2015) observed a prevalence of 30.55% in Harare, while Jackson et al. (2022) found a prevalence of 36.19% in both Harare and Blantyre, Malawi. Additionally, Bacha et al. (2022) conducted a multi-country study in Botswana, Eswatini, Lesotho, Malawi, Tanzania, and Uganda, reporting an average prevalence of 25.36%. Lorenzetti et al. (2024) identified a prevalence of 27.29% in Mozambique, covering multiple cities including Inhambane, Maputo City, Tete, and Nampula.

In Central Africa, USVL rates appear to be among the highest recorded. Soudebto et al. (2024) found a prevalence of 45.59% in Yaoundé, Cameroon, while Mbébi-Enoné et al. (2023) reported a slightly lower prevalence of 29.83% in the Littoral region of Cameroon. These figures emphasize the substantial burden of USVL in this sub-region, potentially linked to barriers in ART access, adherence challenges, and systemic healthcare issues.

Western Africa also exhibits high USVL rates among CALHIV. In Nigeria, Isaac et al. (2020) reported a staggering prevalence of 51.28% in the northern region, which is the highest among the studies reviewed. This highlights the pressing need for targeted interventions to enhance ART adherence and viral suppression outcomes in this context.

A statistical comparison between the prevalence reported in this study (209 out of 847, or 24.7%) and that reported in the systematic review and meta-analysis in Chapter Two (44,408 out of 169,949, or 26.1%) revealed that these two prevalences are comparable. The Chi-square test showed no statistically significant difference (X^2=0.85; p=0.3564).

Our findings, alongside evidence from other SSA countries, underscore the pressing need for reinforced interventions to reduce USVL among CALHIV. While significant progress has been made in expanding ART coverage and improving adherence programs, the persistent burden of USVL highlights critical gaps in treatment effectiveness. Socio-economic challenges, stigma, healthcare accessibility issues, and systemic inefficiencies continue to pose formidable barriers to achieving sustained viral suppression (Nasuuna et al., 2019; Bermudez et al., 2018; Jimu et al., 2021; Mavhu et al., 2013). Addressing these challenges demands a comprehensive, multi-pronged approach that strengthens healthcare infrastructure, enhances adherence support systems, and promotes community-driven initiatives to combat stigma and discrimination.

The urgency of addressing USVL among CALHIV cannot be overstated, as inadequate viral suppression not only compromises individual health outcomes but also increases the risk of HIV transmission within communities. Achieving sustainable VLS requires more than just ART availability—it necessitates an in-depth understanding of the socio-economic, cultural, and structural obstacles that impede treatment success. Without

decisive action to bridge the gap between ART accessibility and effective utilization, many CALHIV will continue to grapple with unsuppressed viral load.

While healthcare policies must prioritize evidence-based, context-specific strategies to enhance treatment efficacy. Strengthening the integration of psychosocial support (Mavhu et al., 2013), improving patient-centered care models, and ensuring equitable access to high-quality ART services will be key to achieving long-term viral suppression among CALHIV in SSA.

5.2. Determinants of unsuppressed viral load in children and adolescents living with HIV on antiretroviral therapy

The multivariate logistic regression analysis revealed five key factors significantly associated with unsuppressed viral load. These factors included the caregiver's marital status, HIV acquisition through horizontal transmission, advanced WHO clinical stage, poor adherence to antiretroviral therapy, and adverse side effects related to ART. Together, these elements underscore the complex interplay of social, clinical, and behavioral determinants that influence treatment outcomes among children and adolescents living with HIV.

5.2.1. Caregiver marital status as an independent factor associated with unsuppressed viral load among children and adolescents living with HIV

Adherence to ART is crucial for achieving viral load suppression and ensuring long-term treatment success among CALHIV. In early childhood, caregivers play a fundamental role in ensuring adherence by administering medications consistently and monitoring treatment responses (Beals et al., 2006). As the child grows older, their autonomy increases, and direct caregiver involvement may decrease. However, ongoing caregiver

support remains essential throughout childhood and adolescence, as adherence challenges can persist due to developmental, psychological, and social factors (Haberer & Mellins, 2009).

One significant determinant of ART adherence and VLS is the marital status of the caregiver. Our study findings suggest that CALHIV with married caregivers are more likely to achieve VLS (aOR = 2.8; 95 % CI: 1.5 – 5.2) compared to those with single, divorced, or widowed caregivers. This association might seem counterintuitive at first, given that a two-caregiver household theoretically provides more support for ART adherence. However, a possible explanation is that in dual-caregiver households, responsibilities may be divided, leading to situations where one caregiver assumes that the other is managing the child's medication schedule. This dynamic can result in miscommunication and lapses in adherence. Additionally, married households may face increased stress from marital conflicts, financial burdens, and the responsibility of managing multiple children, all of which can reduce their ability to focus on strict ART adherence (Lowenthal et al., 2014).

Interestingly, our findings contrast with those of Mena et al. (2023), who reported a higher risk of ART failure among children with single or widowed caregivers. Similarly, they differ from those of Eticha and Berhane (2014), who found better adherence among children with unmarried or married caregivers compared to those with divorced or separated caregivers. This discrepancy underscores the complexity of family dynamics, their varying impacts on treatment outcomes, and the role of family support in providing care for their children. In some contexts, single caregivers may develop highly structured adherence routines out of necessity, ensuring that the child receives consistent care. In contrast, in two-parent households, there may be an implicit assumption that adherence is a shared responsibility, potentially leading to inconsistencies. This highlights the

importance of clearly defining medication-related responsibilities among family members, as emphasized by Martin et al. (2007), to ensure consistent support and adherence to treatment. Moreover, the level of social support available to caregivers, regardless of their marital status, plays a critical role in ART adherence. Caregivers who benefit from extended family support, community networks, or healthcare assistance may be better equipped to manage the challenges associated with ART (Ferrand et al., 2017). This social factor highlights the need for holistic interventions that address not only medical adherence but also the broader social determinants of health. To improve adherence outcomes, healthcare programs should consider providing targeted support for caregivers, regardless of marital status. This support could include adherence counseling, mental health services, and community-based interventions designed to strengthen caregiver-child communication and medication management strategies (Dow et al., 2016; Ferrand et al., 2017). Addressing this factor is essential to ensuring long-term ART success and improving health outcomes for CALHIV.

5.2.2. Impact of transmission route on viral load suppression among children and adolescents living with HIV

The observed association between horizontal transmission and unsuppressed viral load among CALHIV, compared to those infected vertically, raises important questions regarding care dynamics, social challenges, and healthcare access. Studies have highlighted significant disparities in viral suppression between these two groups, which can be attributed to a complex interplay of clinical, psychosocial, and systemic factors influencing adherence to antiretroviral therapy and overall health management (Haghighat et al., 2021; Low et al., 2021). Consistent with our findings, population-based HIV impact assessment surveys conducted in Malawi, Eswatini, Zimbabwe, Zambia, and Lesotho between 2015

and 2017 reported that adolescents with vertically acquired HIV had significantly higher rates of virological suppression compared to those with behaviorally acquired infection (53.2 % vs. 30.8 %) (Low et al., 2021). Similarly, a study of 1,058 HIV-positive adolescents from the Eastern Cape, South Africa, found that vertically infected adolescents were more likely to adhere to ART, remain engaged in healthcare, and receive better treatment from clinic staff. In contrast, those with horizontally acquired HIV were more likely to experience depression, anxiety, internalized stigma, suicidal ideation, and excessive substance use (Sherr et al., 2018).

A major factor contributing to unsuppressed viral load among CALHIV infected through horizontal transmission (via transfusion, sexual contact, or unknown routes) is the delay in diagnosis and treatment initiation (Myburgh et al., 2020; Low et al., 2021). Compared to vertical infections, horizontally acquired infections are often diagnosed later in life, meaning that individuals may experience prolonged periods of untreated infection. This lack of timely intervention allows disease progression, often resulting in a higher viral load at the time of diagnosis, making viral suppression more challenging. Myburgh et al. (2020) highlight that in numerous cases, HIV diagnosis occurs after the age of six, with the majority of children presenting at an advanced stage of the disease. At this point, severe immunosuppression, HIV-related comorbidities, and recurrent hospitalizations are common. Starting ART at such a late stage, when both clinical and immunological deterioration have already set in, significantly reduces treatment efficacy and makes achieving viral suppression even more challenging. This delay in diagnosing horizontally acquired infections is particularly problematic in settings where access to healthcare is limited or where awareness of the importance of early HIV testing is low (Ugwu & Eneh, 2014; Low et al., 2021). Prolonged untreated HIV infection significantly increases the risk

of complications, including the development of drug resistance and irreversible damage to vital organs, further complicating long-term disease management and treatment success.

Another significant factor contributing to the differences in viral load suppression among CALHIV infected through horizontal and vertical transmission is the increased prevalence of comorbidities and related complications associated with horizontal transmission routes. Adolescents who contract HIV through sexual transmission often encounter more intricate health issues, including co-infections with other sexually transmitted infections (STIs) and participation in high-risk behaviors that elevate the chances of treatment failure. These challenges are especially common among individuals infected horizontally, given their usual late diagnosis and extended periods without antiretroviral therapy.

Moreover, effectively managing these comorbidities necessitates specialized medical care, which many adolescents find difficult to access due to financial constraints, geographic barriers, and social stigmatization. These obstacles further impede treatment adherence and the attainment of sustained viral suppression, worsening health disparities among CALHIV.

The diagnostic delay factor is further exacerbated by the stigma surrounding horizontal transmission, especially sexual transmission. CALHIV, particularly those infected through sexual transmission, may experience feelings of shame or guilt related to their HIV status, leading them to delay or avoid HIV testing (Martinez et al., 2014). Consequently, stigma becomes a significant barrier to the early identification of infection and timely initiation of treatment. This HIV-related stigma distinguishes CALHIV infected through horizontal transmission from those infected vertically. Youth infected horizontally with HIV have historically faced rejection, violence, and discrimination upon disclosing their status, reflecting the pervasive societal stigma associated with individuals perceived to have

acquired HIV through risky behavior (Martinez et al., 2014; Sherr et al., 2018). CALHIV infected through sexual transmission or blood transfusion often bear a heavy social and psychological burden, as these transmission modes are frequently linked to behaviors considered shameful or immoral, such as sexual activities or risky practices. The resulting stigma can significantly impact adherence to antiretroviral treatment, as CALHIV may fear being identified and judged by their community or family (Martinez et al., 2014; Sherr et al., 2018). This fear of stigma not only hinders CALHIV from seeking healthcare but can also lead to avoidance behaviors, where they may choose not to take their medication regularly due to concerns about social exclusion or discrimination.

Studies on stigma have shown that young people living with HIV, particularly those who acquired the virus through horizontal transmission, are more likely to experience depression, anxiety, and other psychosocial disorders that compromise their ability to adhere consistently to antiretroviral therapy (Martinez et al., 2014; Sherr et al., 2018; Cluver et al., 2016; Operario et al., 2007). Moreover, social isolation and family tensions caused by stigma can create an environment where adherence to ART becomes particularly challenging, and viral load suppression appears nearly unattainable. Stigma can also reduce access to regular healthcare. CALHIV infected through horizontal transmission may avoid medical consultations for fear of being identified and judged by healthcare providers (Sherr et al., 2018). However, when youth report high levels of satisfaction with healthcare providers, it can mitigate the negative impact of stigma on adherence to treatment (Martinez et al., 2012). As a result, these CALHIV are less likely to receive adequate follow-up care, benefit from education about the importance of adherence to ART, or participate in psychosocial support programs, all of which are crucial factors in achieving viral load suppression (Martinez et al., 2014; Sherr et al., 2018). CALHIV infected through high-risk behaviors tend to show poorer adherence to

antiretroviral treatment and more irregular medical follow-up. Studies, particularly in the United States (MacDonell et al., 2013), suggest that vertically infected individuals generally have more experience with treatment, partly because they often have a parent living with HIV. This parental support, based on shared experience, can provide a more stable connection to HIV care services (Sherr et al., 2018). However, their prolonged exposure to treatment and healthcare services also presents challenges, such as adherence difficulties, the development of drug resistance, and extended exposure to stigma and other barriers (Lowenthal et al., 2014).

Vertically acquired infections generally receive earlier and more structured care compared to horizontally acquired infections (Sherr et al., 2018). CALHIV born to HIV-positive mothers typically benefit from early HIV detection during pregnancy and the immediate initiation of ART to prevent vertical transmission. Furthermore, they receive continuous monitoring throughout their development, facilitated by well-established maternal and child health programs. These programs provide regular follow-ups and medical consultations, including early HIV screening, prompt ART initiation, and ongoing psychosocial support, all of which enhance the likelihood of achieving viral load suppression from the early stages of infection (Nabukeera et al., 2021).

Conversely, CALHIV infected through horizontal transmission often lack access to such structured follow-up and early detection services. Due to their exclusion from maternal and child health programs, their diagnosis is frequently delayed until later in life, complicating their treatment and care. The lack of early interventions contributes to treatment failure and poor long-term HIV management, making achieving viral suppression more challenging (Ugwu & Eneh, 2014).

The association between horizontal HIV transmission and unsuppressed viral load among CALHIV reflects a complex interplay of factors, including diagnostic delays, social stigma, comorbidities, and the lack of structured follow-up. CALHIV infected through horizontal transmission face unique challenges that hinder their treatment adherence and increase the likelihood of failing to achieve viral suppression. Targeted strategies — such as improving access to early HIV testing, addressing stigma through education, and strengthening psychosocial support programs — are essential to reducing disparities between vertical and horizontal infections and improving health outcomes for CALHIV.

5.2.3. Advanced WHO clinical stages and their impact on viral suppression among children and adolescents living with HIV

The significant association between advanced WHO clinical stages and unsuppressed viral load (aOR = 4.8; 95 % CI: 2.1–10.8) observed in this study aligns with several previous studies conducted in East Africa (Abera et al., 2023; Fenta et al., 2021; Nabukeera et al., 2021; Osman et al., 2020; Quaker et al., 2024; Shumetie et al., 2021; Sibhat et al., 2020). Studies conducted in Ethiopia, Uganda, and Tanzania consistently demonstrated that patients at advanced WHO clinical stages had an increased risk of non-viral suppression under antiretroviral therapy. The study by Quaker et al. (2024), conducted on a large sample of 34,400 CALHIV in Tanzania, confirmed that CALHIV at advanced WHO stages had a significantly lower likelihood of achieving viral suppression, highlighting the scale of the issue nationally. Abera et al. (2023), in their study in Ethiopia with a sample of 492 patients, also highlighted this association, further reinforcing the conclusions on the impact of advanced WHO stages on viral suppression. Similarly, Nabukeera et al. (2021), in a series of 300 CALHIV in Uganda, emphasized the need for specific initiatives to strengthen treatment adherence among patients at WHO stage 4, in order to optimize viral

suppression. This relationship between advanced clinical stage and unsuppressed viral load illustrates the well-documented link between disease severity and treatment effectiveness in people living with HIV. Patients at advanced stages often have severely weakened immune systems, increased morbidity, and a higher risk of opportunistic infections, which impairs their ability to achieve optimal viral suppression.

The advanced WHO clinical stages (3 and 4) are significantly associated with compromised nutritional status, which not only impairs the response to antiretroviral therapy but also hinders viral load suppression. These stages are characterized by severe opportunistic infections, such as tuberculosis, severe bacterial infections (including Pneumocystis pneumonia, cryptococcal meningitis, etc.), and unexplained chronic diarrhea (Erjino et al., 2023; WHO, 2016). The chronic inflammation and increased energy requirements induced by these opportunistic infections, coupled with reduced food intake due to appetite loss, gastrointestinal disorders, and metabolic alterations, result in severe malnutrition and cachexia (WHO, 2016).

This deterioration in nutritional status further weakens the immune system, accelerating disease progression and reducing the effectiveness of ART. Moreover, studies have shown that patients in advanced WHO stages (3 and 4) are less likely to achieve viral suppression compared to those in stages 1 and 2, due to the deterioration of their immune status, which fosters increased viral replication (Abera et al., 2023; Fenta et al., 2021; Nabukeera et al., 2021; Erjino et al., 2023; Desta et al., 2020). Additionally, the presence of opportunistic infections at the initiation of ART presents an additional barrier to viral suppression, as it indicates already compromised immunity, thus reducing the treatment's effectiveness (Ssemwanga et al., 2020; Steegen et al., 2017). As a result, patients at advanced WHO stages are at an increased risk of poor treatment adherence and inadequate virological

responses, undermining their ability to achieve sustained viral suppression (Erjino et al., 2023). These findings underscore the importance of early and appropriate nutritional management for HIV patients, particularly those showing signs of advanced clinical progression.

Another reason explaining the association between advanced WHO clinical stages and viral load non-suppression is the high medication burden and treatment fatigue (Claborn et al., 2015; Jong et al., 2010). An Ethiopian study conducted by Gebreyesus et al. (2020) reported a statistically significant association between advanced WHO clinical stages and treatment fatigue. PLHIV at advanced stages often require complex treatment regimens, including antiretroviral therapy, prophylaxis for opportunistic infections (e.g., cotrimoxazole, fluconazole, isoniazid), and medications to manage HIV-related complications such as anemia or neuropathy. This increased medication burden contributes to treatment fatigue and raises the risk of drug interactions, side effects, and adherence difficulties (Claborn et al., 2015), which negatively impact viral load suppression.

HIV infection at an advanced stage is often associated with increased systemic inflammation and metabolic complications, making patients more susceptible to antiretroviral treatment toxicities, such as hepatotoxicity, nephrotoxicity, and neuropathy (Margolis et al., 2014; Teshome & Agezew, 2023; Getaneh et al., 2023). Side effects like nausea, vomiting, diarrhea, and peripheral neuropathies can compromise treatment adherence, leading to interruptions and virological failures (WHO, 2021). Given that non-adherence is a major factor in viral load suppression failure, it is crucial to manage these side effects effectively through rigorous clinical follow-up, treatment adjustments, and personalized support for each patient (Foka & Mufhandu, 2023).

Patients with advanced WHO clinical stages are often diagnosed too late or experience delays in initiating ART (Eamsakulrat et al., 2022). This delay can be attributed to either late presentation at healthcare facilities or a lack of access or connection to care. Several studies have shown that delayed initiation of ART is associated with less effective immune reconstitution, increased mortality, and lower viral load suppression rates compared to earlier treatment initiation (Muscatello et al., 2020; Grinsztejn et al., 2014; Ssebunya et al., 2017; Eamsakulrat et al., 2022). When ART is eventually started, the patient's immune system may already be severely compromised, limiting its ability to respond effectively to treatment, even under optimal conditions (Muscatello et al., 2020).

To enhance viral suppression in patients at advanced stages, a comprehensive approach is crucial. Prioritizing early HIV screening and immediate initiation of ART aligns with WHO's "Treat All" policy, as outlined in their updated consolidated guidelines for HIV treatment and prevention (WHO, 2016; 2019). This policy aims to provide ART to all HIV-positive individuals upon diagnosis, irrespective of disease stage, supporting the WHO's 95-95-95 targets. Timely implementation of this strategy is vital for improving care retention and achieving sustained viral suppression, ultimately reducing HIV-related morbidity and mortality (WHO, 2019). Increasing testing access, especially for high-risk groups, and integrating treatment initiation programs at diagnosis have demonstrated positive outcomes in terms of care retention and viral load suppression (Gwadz et al., 2015; Zanoni et al., 2017).

At the same time, comprehensive management of opportunistic infections, with improved access to rapid diagnostic tests and prophylactic treatments, is critical. This helps prevent ART interruptions due to these infections and enhances patient adherence (Fonsah et al., 2017). Integrating mental health services (Strasser & Gibbons, 2014; Smith Fawzi et al.,

2016; Nguyen et al., 2023; Haas et al., 2023) and peer support groups into HIV care (Okonji et al., 2020b; Chime et al., 2018; Mavhu et al., 2020) can also play a key role in improving adherence, particularly in the face of treatment fatigue and psychological distress often observed in advanced-stage patients (Claborn et al., 2015; Jong et al., 2010). Targeted adherence counseling, mobile interventions, and community-based ART distribution models are promising approaches to support care retention and improve viral load suppression rates (Foka & Mufhandu, 2023). Furthermore, for those experiencing severe side effects, it is important to offer more tolerable ART regimens, such as those based on dolutegravir, to enhance adherence and treatment effectiveness (Belfrage et al., 2023; Foka & Mufhandu, 2023; Ezenwosu et al., 2023; Hurbans & Naidoo, 2024; Wagner et al., 2024). Lastly, differentiated care models, such as intensified clinical follow-up, community ART refill programs, and decentralized care, can help overcome barriers to adherence, especially for patients with complex needs (Kwarisiima et al., 2017; Maskew et al., 2022; Bwire et al., 2023; Mavhu et al., 2020). Solutions like home ART delivery and teleconsultation can also provide additional support to patients facing mobility challenges or frequent hospitalizations (Iliyasu et al., 2025; Mdege & Chindove, 2014; Jo et al., 2021).

The present study highlights that advanced stages of HIV are strongly associated with unsuppressed viral load, emphasizing the need for targeted strategies to improve health outcomes. An approach combining early screening, management of opportunistic infections, psychosocial support, and optimization of therapeutic regimens can enhance viral suppression and reduce HIV-related morbidity and mortality. Furthermore, it is essential to continue research to explore new strategies, particularly in resource-limited settings where late diagnosis remains a major challenge (WHO, 2021). However, the impact of recent funding cuts to PEPFAR by the U.S. government could significantly hinder progress in addressing these challenges. Reduced funding may limit access to

critical HIV services, including early diagnosis, treatment, and comprehensive care, thereby exacerbating the burden of unsuppressed viral load and increasing HIV-related morbidity and mortality, particularly in low-resource settings. Continued investment in global HIV programs is essential to sustain progress in the fight against the epidemic.

5.2.4. Impact of antiretroviral therapy-related side effects on viral load suppression among children and adolescents living with HIV

Over the past decades, significant progress has been made with the introduction and widespread adoption of ART, which has transformed HIV from a once-fatal disease into a manageable chronic condition. This advancement has saved millions of lives, improved the quality of life of people living with HIV, and significantly reduced complications associated with the infection (Kumah et al., 2023). One of the primary goals of ART is to achieve and maintain viral suppression, meaning an undetectable viral load. Beyond improving individual patient health, viral load suppression plays a crucial role in preventing the transmission of the virus. Studies have shown that people living with HIV who maintain an undetectable viral load do not transmit the virus to their sexual partners (Rodger et al., 2019), a concept widely promoted under the slogan "Undetectable = Untransmittable" (Grace et al., 2022; Eisinger et al., 2019; Gashema et al., 2025; Huong et al., 2025). Therefore, viral suppression is a key indicator of treatment success, as it not only prevents long-term complications associated with HIV but also limits the transmission of the virus within communities (Rodger et al., 2019).

Despite these significant advances, adherence to ART remains a central challenge, especially among children and adolescents living with HIV. Multiple studies have emphasized that suboptimal adherence is frequently linked to ART-related side effects, which are a key predictive factor of non-adherence (Chesney, 2000). These side effects,

which include gastrointestinal disturbances, neurological symptoms, and chronic fatigue, can greatly impact patients' quality of life, causing them to interrupt treatment or inconsistently adhere to it (Fonsah et al., 2017).

In the present study conducted among children and adolescents living with HIV in Lubumbashi, we observed a significant association between ART-related side effects and unsuppressed viral load. These findings align with a growing body of research examining the link between treatment side effects and viral non-suppression. For instance, a recent study in Uganda by Brown et al. (2024) found that adolescents and young adults on ART who experienced side effects had a significantly lower likelihood of achieving viral suppression (OR = 0.46; 95 % CI: 0.22 – 0.95). These results suggest that inadequate management of side effects can be a major barrier to treatment effectiveness.

Similarly, in a cross-sectional study conducted in Nairobi, Kenya, Gachoka and Njoroge (2024) identified ART-related side effects as a significant factor contributing to viral non-suppression among children and young adolescents living with HIV. Among the 252 CALHIV under 15 years old, those who experienced treatment-related side effects had an increased risk of viral non-suppression (adjusted Prevalence Ratio = 3.01; 95 % CI: 1.37 – 6.62; p = 0.006). These findings highlight the critical role of side effects in viral non-suppression and underscore the importance of effectively managing treatment-related adverse effects, particularly in resource-limited settings.

Similarly, Nabukeera et al. (2021) conducted a study in Uganda on a cohort of children aged 0 to 14 years who were followed between January 2017 and March 2019 in Kampala. Their findings revealed a significant association between ART-related side effects and insufficient viral suppression. The researchers observed that children experiencing severe adverse effects were less likely to achieve an undetectable viral load, with an adjusted

incidence rate ratio of 1.77 (95 % CI: 1.06 – 2.97), indicating an increased risk of non-suppression. This study highlights the need for proactive management of side effects, including therapeutic adjustments and enhanced support for both children and their caregivers, to ensure continuous and effective treatment.

ART-induced side effects are prevalent and diverse, contingent on the specific medications prescribed, all contributing to a decline in patients' quality of life. Adverse effects like nausea, fatigue, gastrointestinal disruptions, skin rashes, and joint discomfort have the potential to hinder treatment adherence. Numerous patients, encompassing CALHIV, alter or halt their treatment regimen because of these manifestations, consequently jeopardizing therapy efficacy and impeding the achievement of VLS. Thus, it is imperative to effectively address these side effects to uphold adherence and enable patients to consistently adhere to their treatment plan.

The findings of these studies, conducted in various African settings (Nabukeera et al., 2021; Brown et al., 2024; Gachoka & Njoroge, 2024), reinforce the notion that side effects play a crucial role in viral non-suppression. This highlights the importance of addressing this concern in HIV treatment approaches, especially for vulnerable groups like CALHIV. Furthermore, these studies stress that managing side effects should extend beyond simple observation, encompassing customized interventions that empower patients to sustain their treatment regimen without sacrificing their quality of life.

Existing literature indicates that side effects are one of the main predictors of non-adherence to treatment (Zhang et al., 2016; Zhou et al., 2018). Patients, particularly those experiencing severe side effects, are more likely to miss medication doses or discontinue treatment entirely (Fonsah et al., 2017). This issue is particularly concerning for CALHIV, whose treatment regimens may be more complex due to necessary adjustments for growth

and development. If these side effects are not properly managed, they may hinder viral suppression and lead to treatment failure, increasing the risk of HIV-related morbidity and mortality.

The study by Zhou et al. (2018) found that the relationship between ART side effects and treatment adherence varied based on patients' level of knowledge about ART. Specifically, a negative association between side effects and adherence was observed among individuals with low to moderate knowledge of antiretroviral therapy. In contrast, this relationship was not significant in those with high ART knowledge, suggesting that a better understanding of treatment could mitigate the negative impact of side effects on adherence (Zhou et al., 2018). These findings highlight the importance of implementing targeted educational interventions focused on delivering practical information to improve adherence among people living with HIV (Zhou et al., 2018).

To address this issue, HIV treatment programs must adopt systematic strategies for managing ART-related side effects. Healthcare providers should be trained to proactively recognize and manage these side effects, including regular monitoring and treatment adjustments based on patients' specific needs. Additionally, using alternative treatment regimens with better tolerance profiles could help reduce side effects and improve adherence. For example, the introduction of new antiretrovirals, such as integrase inhibitors (e.g., dolutegravir), which have a more favorable side effect profile, may enhance adherence and maintain optimal viral suppression (Bruzzese et al., 2018; Townsend et al., 2022; Ezenwosu et al., 2023; Frange et al., 2019; Belfrage et al., 2023; White et al., 2025).

In addition to therapeutic adjustments, providing adequate psychosocial support and targeted counseling for CALHIV and their caregivers is essential to improve treatment adherence. Parents and guardians play a critical role in administering treatment to

CALHIV, and it is crucial that they are supported and informed to better understand the importance of regular medication adherence (Zhou et al., 2018). Follow-up interviews, where caregivers can ask questions and share concerns, not only help manage side effects but also strengthen patients' engagement in their treatment journey. Furthermore, it is essential for caregivers to have a good understanding of potential side effects and know how to respond to concerning symptoms.

Effective management of ART-related side effects in adolescents living with HIV also depends on open communication among healthcare providers, patients, and their families, which can enhance adherence and treatment effectiveness (Ahmed et al., 2023; Ammon et al., 2018; Audi et al., 2021; Strother et al., 2022). Caregiver support is crucial in assisting adolescents in handling side effects and adhering to their treatment (Ammon et al., 2018). Additionally, peer support interventions like peer support groups have demonstrated effectiveness in enhancing treatment adherence and retention in care in sub-Saharan Africa (Ahmed et al., 2023; Ammon et al., 2018). A comprehensive approach involving transparent communication, family support, and peer-based interventions is therefore vital for improving treatment outcomes in ALHIV.

Although ART has revolutionized HIV management, side effects remain a major challenge, particularly for CALHIV. Proactive management of these side effects, the adoption of better-tolerated treatment regimens, psychosocial support, and open communication between healthcare providers and patients are essential to improving treatment adherence and ensuring sustained viral suppression. Ultimately, a systematic, patient-centered approach will improve health outcomes for CALHIV, prevent HIV transmission, and reduce the morbidity and mortality burden associated with HIV. These

strategies are crucial for achieving global HIV goals while improving patients' quality of life and reducing virus transmission.

5.2.5. Poor adherence to antiretroviral therapy: A determinant of unsuppressed viral load among children and adolescents living with HIV

Adherence to ART is a fundamental pillar in HIV management, as it directly affects the effectiveness of treatment and viral load suppression (UNAIDS, 2023). Strict adherence to antiretroviral therapy is essential for maintaining an undetectable viral load, preventing disease progression, and reducing viral transmission (Iacob et al., 2017; Sahay et al., 2011; Kim et al., 2014). Good adherence also helps limit the emergence of drug resistance, ensuring an optimal and lasting therapeutic response (Muri et al., 2017). In contrast, insufficient or irregular adherence compromises treatment effectiveness, leading to increased viral load and exposing patients to severe clinical complications (Pham et al., 2022). Additionally, poor adherence may result in treatment failure and the need for more expensive and less accessible treatment regimens, exacerbating healthcare inequalities (Ajose et al., 2012). Therefore, improving adherence to ART is crucial to ensuring treatment success and enhancing the individual and collective benefits in the fight against HIV (Ford et al., 2018).

In this study, poor or fair adherence to ART (aOR = 90.8; 95 % CI: 45.8 – 179.9) was identified as the primary predictive factor for viral load non-suppression in CALHIV. This finding aligns with several studies conducted in sub-Saharan Africa among CALHIV (Djiyou et al., 2023; Mageda et al., 2023; Sibhat et al., 2020; Abera et al., 2023; Muri et al., 2017; Bitwale et al., 2021; Khamadi et al., 2023; Ally et al., 2023; Mchomvu et al., 2022; Quaker et al., 2024; Tsikhutsu et al., 2022; Mwangi et al., 2021; Mabizela & van Wyk, 2022; Mugo et al., 2023; Yiltok et al., 2020; Tanoh-Aka et al., 2021; Mukumbuta et

al., 2024), all underscoring the crucial role of treatment adherence in achieving viral suppression. These studies highlight that CALHIV with suboptimal adherence face a significantly higher likelihood of experiencing viral load non-suppression, jeopardizing their well-being and escalating the risk of long-term complications. Maintaining strict adherence to ART remains essential for ensuring sustained viral suppression and enhancing the quality of life for CALHIV.

Suboptimal adherence to ART in CALHIV results from a complex combination of biological, psychosocial, and structural factors (Laurenzi et al., 2022). Among these, HIV-related stigma remains one of the most influential. In sub-Saharan Africa, where the burden of the epidemic is particularly heavy, CALHIV often face double discrimination: first due to their serological status and second because of their age and dependency on adults for their care (Abelman et al., 2020). This stigma can lead to a refusal to disclose their status, fear of rejection by peers or the community, and social isolation, making regular treatment adherence difficult (Madiba & Josiah, 2019; Mburu et al., 2014; Hogwood et al., 2013; Gilbert et al., 2010). Furthermore, forgetfulness of doses is a frequent cause of poor adherence, especially among CALHIV who begin managing their treatment alone without adequate supervision (Kawuma et al., 2014). This issue is often amplified by therapeutic fatigue (pill fatigue), where the daily and prolonged use of antiretrovirals becomes a psychological burden, leading to irregular dosing or even treatment interruptions (Claborn et al., 2015; Merzel et al., 2008).

Another critical factor is the absence of support from a caregiver involved in the therapeutic follow-up. Many HIV-orphaned children or those living in unstable families lack a dedicated guardian capable of overseeing their treatment. The lack of parental or familial

support is linked to poor ART adherence and increased vulnerability to treatment interruptions (Gichane et al., 2018; Kikuchi et al., 2012; Cluver et al., 2016).

The lack of social support is also a major barrier. A child or adolescent without a supportive environment—at home, at school, or within the community—is more likely to neglect their treatment (Kihulya et al., 2022; MacCarthy et al., 2018, Cluver et al., 2016). Fear of being perceived differently or experiencing discrimination at school sometimes leads young individuals to avoid taking their medication in front of peers, compromising adherence (Madiba & Josiah, 2019). Additionally, the specific challenges of childhood and adolescence further complicate adherence to antiretroviral treatment. Unlike adults, children and adolescents must navigate significant transitional periods, such as entering school, adolescence, and gaining independence. These transitions can be stressful and impact motivation to adhere to long-term treatment (MacCarthy et al., 2018; Djiyou et al., 2023; Badejo et al., 2018). For example, the lack of privacy at school and managing social interactions can disrupt adherence as these young patients often face stigma and a lack of confidentiality in their school environment (MacCarthy et al., 2018). Furthermore, limited access to age-appropriate care, including specific psychosocial support and pediatric ART formulations, remains a challenge in many resource-limited countries (Penazzato et al., 2019).

Adolescents, often in a transition towards independence, also face economic barriers, including the challenge of accessing adequate nutrition, which can hinder their ability to adhere to treatment regularly (MacCarthy et al., 2018). Moreover, the stability of family support is crucial but frequently precarious. Many young patients have lost their biological parents, and the frequent changes in their caregiving environment, stemming from shifts in guardians, can exacerbate their situation (MacCarthy et al., 2018). These disruptions

can result in “drug holidays”, where adolescents, overwhelmed by managing multiple medications or dealing with personal issues, discontinue their treatment, jeopardizing viral suppression and increasing the likelihood of complications. Nevertheless, peer support, especially among young individuals living with HIV, proves to be a valuable resource for enhancing adherence, offering a support system of encouragement and empathy (MacCarthy et al., 2018).

Optimal adherence to antiretroviral treatment is a key factor for viral suppression and the reduction of morbidity and mortality among children and adolescents living with HIV. Therefore, it is crucial to implement targeted and tailored interventions to improve therapeutic adherence and ensure better virological outcomes. Among the most effective strategies, peer support groups play a crucial role by providing adolescents with a safe space to share experiences, express concerns, and receive emotional support (Audi et al., 2021). This approach not only reduces social isolation and perceived stigma but also helps strengthen the motivation of young patients by providing resilience models. Several studies conducted in sub-Saharan Africa have demonstrated that these interventions increase adherence to ART and improve retention in care (Ahmed et al., 2023; Okonji et al., 2020; Ndhlovu et al., 2021; Barker et al., 2019; Kiiry et al., 2024; Mark et al., 2019; Rencken et al., 2021). By promoting regular treatment adherence and facilitating the management of side effects, support groups offer a valuable solution for adolescents facing challenges with treatment adherence.

The use of mobile health technologies (m-Health) represents another promising approach to improving therapeutic adherence, especially among young people who tend to forget their medication. SMS reminders and mobile applications offer discreet and consistent support to patients while enhancing their autonomy in managing their treatment (Bigna et

al., 2014; Goldstein et al., 2023; Bezabih et al., 2021; Pop-Eleches et al., 2011; Lester et al., 2010; Maduka & Obin-West, 2013; Shet et al., 2014). Studies have shown that these digital interventions significantly improve adherence to ART by reducing forgetfulness and facilitating the integration of treatment into patients' daily lives (Uzma et al., 2011; Rodriguez zt al., 2012 ; Swendeman et al., 2015 ; Orrell et al., 2015 ; Chung et al., 2011). Due to their accessibility and flexibility, these tools allow for reminders tailored to the individual needs of patients, thus increasing their effectiveness and acceptability (Bezabih et al., 2021).

Family and community support also play a crucial role in improving adherence to ART. Stigma remains a major barrier to therapeutic adherence, and a supportive family and social environment is essential to ensure regular treatment intake. Research has shown that children and adolescents who receive active support from an engaged caregiver exhibit better treatment adherence and a reduced risk of therapeutic failure (Eticha & Berhane, 2014; Martin et al., 2007). Furthermore, the involvement of community leaders and teachers in HIV awareness efforts helps reduce stigma and fosters a more inclusive and compassionate approach to the care of CALHIV (Kihulya et al., 2022).

Therapeutic education is another key lever for motivating patients to maintain adherence to treatment. A better understanding of how ART works and its benefits can encourage adolescents to persevere, even in the face of side effects or medication fatigue (Oryokot et al., 2024). It is essential to explain to patients the potential side effects and how to manage them, while emphasizing the benefits of viral suppression, which not only preserves their health but also reduces the risk of virus transmission. The use of interactive tools such as educational videos, comics, and mobile applications can make learning more engaging and tailored to the needs of young patients (Bezabih et al., 2023; Aladin et al., 2023).

Adherence to ART among children and adolescents living with HIV is a major issue for ensuring effective viral suppression and improving their quality of life. It is essential to combine multiple complementary strategies to overcome barriers to therapeutic adherence. Peer support, mobile technologies, involvement of families and communities, and tailored therapeutic education are all approaches that, when implemented together, can improve treatment adherence and optimize virological outcomes. By integrating these interventions into care programs, it is possible to reduce morbidity and mortality related to HIV and foster a healthier future for CALHIV (WHO, 2016).

In conclusion, enhancing adherence to antiretroviral treatment is vital for achieving viral suppression and long-term outcomes in children and adolescents with HIV. Poor adherence to treatment raises the likelihood of treatment failure and virus transmission. Evidence-based interventions like peer support, mobile reminders, and cognitive-behavioral therapy are crucial (WHO, 2016). Psychosocial and community support help reduce stigma and boost patient motivation. The utilization of mobile technologies and simplified treatment regimens enhances adherence. The integration of these strategies into care programs has the potential to enhance viral suppression rates. However, the recent cessation of funding for HIV programs supported by PEPFAR could undermine these efforts. The withdrawal of financial support risks limiting access to critical HIV services, including adherence support programs, mobile health interventions, and community-based initiatives, potentially jeopardizing progress made in viral suppression and care for children and adolescents with HIV. Continued investment is essential to sustain and expand these programs, particularly in resource-limited settings, to ensure ongoing improvements in treatment adherence and health outcomes.

5.2.6. Predicting unsuppressed viral load among children and adolescents living with HIV: Logistic model performance and implications

The logistic regression model used in this study provides an in-depth understanding of the determinants of USVL among children and adolescents living with HIV. By identifying key factors influencing viral suppression, this analysis offers valuable insights for clinicians and public health policymakers striving to optimize antiretroviral therapy outcomes. The most influential variables include caregiver marital status, mode of HIV transmission, WHO clinical stage, ART adherence, and ART-induced side effects. These findings highlight the complexity of pediatric HIV management, emphasizing the need for a holistic approach that considers the clinical, psychosocial, and structural dimensions of the disease.

The model's performance evaluation indicates strong predictive capability, supported by rigorous statistical validation and high classification accuracy. The Linktest, a diagnostic test for model specification, confirms that the logistic regression was correctly defined, with highly significant coefficients for predicted values ($p < 0.0001$) and non-significant coefficients for squared values ($p = 0.900$). The absence of specification errors reinforces the reliability of the estimated associations, ensuring that the identified relationships between independent variables and viral suppression are robust and not artifacts of model misspecification.

To enhance the stability and reliability of the estimated coefficients, I conducted a bootstrap procedure with 1,000 replications. This technique assesses sample variability and helps mitigate potential data anomalies (Chong & Choo, 2011; Beran, 2008; Hesterberg, 2011). The findings support the consistency of the model's estimates, indicating that the identified risk factors for USVL are likely applicable to comparable populations.

The model's goodness of fit was assessed using the Hosmer-Lemeshow test, which yielded a p-value of 0.6747. This result indicates a strong alignment between observed and expected values, with no signs of overfitting or poor generalizability. A good model fit is crucial in clinical epidemiology, as a model that overly conforms to a specific dataset may not be applicable to other contexts (Hosmer Jr et al., 2013; Lemeshow & Hosmer Jr, 1982; Archer et al., 2004).

In terms of classification performance, the model demonstrates excellent discriminative ability, with an overall correct classification rate of 92.1 %. Specifically, a sensitivity of 85.2 % indicates that the majority of CALHIV with unsuppressed viral load are accurately identified, allowing for targeted interventions to be implemented for those in need of intensified support. The high specificity of 94.4 % confirms that the model accurately classifies individuals with suppressed viral load, minimizing the risk of false positives. Such precision is critical for ensuring efficient resource allocation and avoiding unnecessary interventions for patients responding well to treatment. The positive predictive value of 83.2% indicates that when a patient is classified as having an unsuppressed viral load, this classification is correct in most cases. Similarly, the negative predictive value of 95.1% guarantees strong confidence in identifying individuals who have achieved viral suppression.

However, a false negative rate of 14.8% highlights that a subset of at-risk patients remains undetected by the model, potentially limiting the effectiveness of intervention strategies based on this approach. The presence of false negatives suggests that the model could be improved by incorporating additional variables, particularly psychosocial and behavioral factors influencing adherence to treatment. Elements such as stigma, caregiver burden, and

perceptions of ART side effects could enhance the model's ability to more precisely identify the most vulnerable children and adolescents at risk of treatment failure.

The receiver operating characteristic (ROC) curve analysis confirms the model's strong discriminative power, with an area under the curve of 0.9581. A value this close to 1 indicates that the model is highly effective at distinguishing between patients with and without viral suppression. This metric, combined with high classification accuracy and sensitivity, further validates the model's robustness for clinical and epidemiological applications. The R-squared coefficient ($R^2 = 0.6871$) reveals that 68.71 % of the variance in USVL is explained by the variables included in the model. While this proportion suggests that the model captures a substantial portion of the determinants of viral suppression, nearly one-third of the variance remains unexplained. This gap indicates that other factors, such as socioeconomic conditions, healthcare accessibility, and patient education strategies, likely play significant roles in treatment adherence and virological success (Mcinziba et al., 2023; Hlophe et al., 2023).

Poor adherence to ART is a critical issue for viral suppression in CALHIV. Several interconnected factors contribute to non-adherence, including the caregiver's marital status, the mode of HIV acquisition, the WHO clinical stages, and adverse side effects of ART. Married caregivers may face challenges such as interpersonal conflicts or limited resources, leading to poorer adherence. In contrast, unmarried caregivers with strong support systems might better ensure treatment adherence. CALHIV who acquire HIV through horizontal transmission may experience stigma and emotional distress, further hindering adherence. Additionally, CALHIV diagnosed at advanced WHO clinical stages may face severe complications, while side effects of ART, such as gastrointestinal issues or fatigue, can further discourage consistent treatment, making adherence even more difficult.

These interconnected factors—caregiver's marital status, HIV acquisition method, WHO clinical stage, and ART side effects—collectively exacerbate the challenge of ensuring optimal adherence to ART. As these variables often work synergistically, they emphasize the need for a holistic, patient-centered approach to HIV care, addressing both the medical and psychosocial barriers to adherence.

Given the complexity of these contributing factors, the findings of this study carry significant strategic implications for improving CALHIV care. The strong link between ART adherence and viral load suppression underscores the need to strengthen adherence support interventions. Key recommendations include implementing personalized counseling programs, utilizing reminder technologies such as SMS messages and mobile applications (WhatsApp), and developing peer-support networks to encourage treatment compliance. Furthermore, since the primary caregiver's role is a critical determinant of USVL, initiatives aimed at enhancing caregiver competence and psychological well-being could positively impact viral load suppression outcomes. Previous studies have shown that well-informed and well-supported caregivers are more effective in ensuring consistent medication adherence among children and adolescents on ART. Another crucial aspect involves managing ART side effects, which have been identified as a potential barrier to adherence. Healthcare professionals should be trained to anticipate and mitigate these adverse effects by adjusting treatment regimens when necessary and equipping patients with strategies to better tolerate side effects.

While this study provides significant contributions to understanding USVL determinants, future research is necessary to further explore these observations. Integrating data on healthcare access, community perceptions of HIV, and structural barriers to adherence could enrich future analyses. Additionally, qualitative studies investigating the lived

experiences of CALHIV and their caregivers could offer a more nuanced perspective on the daily challenges of ART adherence and achieving VLS.

Overall, this logistic regression model serves as a powerful analytical tool for identifying factors associated with unsuppressed viral load among CALHIV. Its strong predictive capability, statistical robustness, and high accuracy make it a valuable model for public health strategies aimed at optimizing pediatric HIV care. However, improving its sensitivity and incorporating additional contextual factors remain crucial areas for further refinement. This study underscores the critical role of adherence support, caregiver involvement, and early clinical intervention in maximizing ART outcomes and reducing the burden of HIV among children and adolescents.

5.3. Facilitators and barriers to viral load suppression among adolescents living with HIV

Achieving VLS among ALHIV is a significant public health challenge worldwide. While the context in Lubumbashi, DRC, reflects many of the issues faced in other settings, both in resource-limited and high-income countries, it highlights the universal factors impacting ART success among ALHIV. These challenges—such as poverty, stigma, lack of support, and issues related to medication adherence—are experienced by adolescents across the globe. Using the socioecological model, this study identified specific barriers and facilitators to achieving VLS in Lubumbashi, revealing that both success and failure are influenced by multiple factors operating at various levels, including individual, family/ interpersonal, health service, and community. These factors have been shown to either hinder or facilitate ART adherence and the achievement of VLS among ALHIV.

The higher proportion of adolescents aged 16-19 years (89.7%) compared to those aged 13-15 years (10.3%) in our study can be attributed to differences in availability during recruitment. Older adolescents are generally more independent and able to attend appointments on their own, whereas younger adolescents often rely heavily on their parents or caregivers to accompany them. This dependency may have limited the participation of younger adolescents, as their attendance was contingent on their caregivers' availability and willingness to bring them to the study. This recruitment dynamic likely contributed to the age distribution observed in the sample. Participants in our study identified ART side effects, stigma, forgetting medication, lack of food, busy schedules, feeling healthy, travel, non-disclosure of HIV status, broken families, and lack of ART support as barriers to achieving VLS. In contrast, they identified confidence in ART efficacy, understanding ART's importance, establishing a routine, using reminders, managing side effects, engaging in peer support, maintaining open relationships with healthcare staff, and being motivated for someone else's sake as strategies for overcoming these barriers. These findings align with those from other qualitative studies identifying barriers and facilitators to achieve VLS. For instance, in Ghana (Ankrah et al., 2016) and Sierra Leone (Lahai et al., 2022), healthcare staff support, parental involvement, disease knowledge, and the perception of positive outcomes were emphasized as motivators for PLHIV to achieve VLS. Izudi et al. (2024) in Uganda noted the importance of understanding ART adherence, mental health support, peer support, personal reminders, and effective management of ART side effects. Similarly, Curioso et al. (2010) in Peru highlighted the role of living for his/her loved ones, reminders from family, routine establishment, positive outcomes, and confidence in drug efficacy as essential facilitators of achieving VLS.

Forgetting medication, stigma, and financial barriers were key obstacles to ART adherence among PLHIV in Ghana and Ethiopia (Ankrah et al., 2016; Bezabhe et al., 2014). A Botswana study also highlighted ART side effects, lack of food, and financial constraints as barriers for ALHIV (Yang et al., 2018). These findings align with ours and other studies (Izudi et al., 2024; Galea et al., 2018). In Peru, stigma, dietary challenges, busy schedules, and a sense of good health were identified as barriers to ART adherence (Curioso et al., 2010). This present study found that some ALHIV faced transportation difficulties, while others forgot medication due to religious activities, reflecting similar findings in Ethiopia (Bezabhe et al., 2014). This Ethiopian study showed that forgetting medication leads to USVL (Bezabhe et al., 2014), a phenomenon also observed in our study, where ALHIV experienced interruptions in ART due to busy social lives and school commitments. These findings underscore the necessity for interventions that target both practical and psychological barriers to enhance ART adherence and to achieve VLS.

Stigma and discrimination emerged as significant barriers to achieving VLS among ALHIV in our study, aligning with other studies identifying stigma as a major deterrent to ART adherence and VLS achievement. For instance, perceived stigma related to disclosure was highlighted as a key barrier among ALHIV in Ghana (Ankrah et al., 2016). Interventions to reduce stigma and promote social inclusion are crucial for improving health outcomes in this population. Although community facilitators were not included in our study, prior research underscores their vital role in enhancing ART adherence. Community outreach programs have been shown to reduce stigma, provide support networks, and improve both adherence and the overall quality of life for ALHIV (Badejo et al., 2023; Oryokot et al., 2024). Most ALHIV in our study achieved VLS after receiving counseling and psychological support, particularly when encountering stigma. They also expressed gratitude for the positive relationships with healthcare staff. This underscores

the significance of trust and open communication with HCWs, fostering a supportive environment for addressing HIV-related stigma and depression. These results are consistent with other studies that underscore the importance of strong relationships with HCWs and support systems, such as family reminders for medication, in achieving VLS (Biadgilign et al., 2009; Ankrah et al., 2016).

In Lubumbashi, some ALHIV encountered difficulties in maintaining consistent ART intake due to medication side effects, such as gastrointestinal problems, headaches, and fatigue, which hindered ART adherence and VLS achievement. This aligns with prior studies linking concerns about side effects to suboptimal VLS outcomes, despite adherence counseling (Ndikabona et al., 2021). Particularly, gastrointestinal issues like nausea, loss of appetite, and diarrhea serve as major barriers to sustained treatment, affecting VLS (Izudi et al., 2024; Ndikabona et al., 2021).

The finding that a lack of food is a significant barrier to achieving VLS, especially for ALHIV who are orphans or from financially constrained households, highlights the importance of addressing basic nutritional needs as part of ART support. Consistent with previous research (Gordon et al., 2021; Chhim et al., 2018; Izudi et al., 2024), this underscores the necessity of ensuring adequate food intake to improve ART adherence and, by extension, support VLS. Interventions should consider providing nutritional support or financial assistance to enhance medication adherence and prevent complications due to skipped doses. Addressing food insecurity is thus a critical component of comprehensive HIV care for ALHIV, as it directly impacts treatment outcomes and overall health (Cluver et al., 2016).

This study identified a significant barrier to achieving VLS: the lack of parental supervision during ALHIV medication intake. Despite caregivers administering medication, many

became preoccupied with other tasks and did not verify whether the medication was taken. Some ALHIV, facing challenges with their treatment, may conceal non-adherence by pretending to take the medication, which compromises achieving VLS. Similar to findings from a Peruvian study (Curioso et al., 2020), our research also demonstrates that orphaned ALHIV or those from disrupted families encounter challenges that detrimentally impact ART adherence, thereby impeding VLS. The absence of parental support, coupled with emotional and financial instability, plays a role in non-adherence and suboptimal outcomes. Previous studies underscore the crucial importance of family in aiding long-term treatment adherence and offering essential psychosocial support to achieve VLS (Galea et al., 2018; Ankrah et al., 2016; Johnson-Peretz et al., 2022; Lukyamuzi et al., 2021). These findings collectively emphasize the vital role of family involvement and consistent supervision in ensuring ART adherence and achieving optimal outcomes for ALHIV.

The present study also revealed that many ALHIV were not adhering to ART correctly due to not being informed of their HIV-positive status. This lack of disclosure led to confusion, as some ALHIV thought they were managing a chronic cough rather than HIV. Disclosing HIV status, however, can improve the quality of life, social support, immune recovery, and ART adherence, while non-disclosure increases the risk of loss to follow-up and is a significant barrier to achieving VLS (Izudi et al., 2024; Buma et al., 2015; Bulali et al., 2018; Akilimali et al., 2017).

In addition, being away from home and having busy schedules were identified as significant barriers to achieve VLS, aligning with findings from other studies (Gordon et al., 2021; Curioso et al., 2010; Bezabhe et al., 2018) showing that long travel distances and associated costs often result in missed appointments and ART non-adherence. Social

support and participation in peer groups were identified as crucial facilitators of VLS, improving HIV knowledge and ART adherence through interpersonal interactions and peer support (Gordon et al., 2021; Curioso et al., 2010; Badejo et al., 2023; Izudi et al., 2024).

5.4. Strengths of the study

This study presents several noteworthy strengths that significantly enhance its contributions to understanding VLS among CALHIV, their caregivers, and HCW involved in ART adherence.

First and foremost, the study offers a comprehensive exploration of determinants, barriers, and facilitators to achieve VLS from multiple perspectives. By including the views of CALHIV, their caregivers, and HCWs, the research captures a holistic understanding of the intricate dynamics influencing ART adherence and VLS. This multi-faceted approach is crucial, as it acknowledges the complex interplay between individual, familial, and healthcare provider influences on health outcomes. The study incorporates both quantitative and qualitative data, enriching the analysis and providing a well-rounded perspective on the factors affecting VLS. The quantitative data offers measurable insights into the prevalence and correlation of various factors, while the qualitative data provides rich, descriptive narratives that highlight the lived experiences of participants. This combination allows for a deeper understanding of the social, psychological, and cultural contexts surrounding ART adherence.

The use of standardized questionnaires, uniformly applied across all 21 HIV care clinics included in the quantitative phase of the study, ensured consistency, accuracy, and comparability of responses across all participants, which significantly reinforced the reliability and internal validity of the results. These validated tools, specifically designed to capture key psychosocial and clinical factors, enabled the systematic collection of high-

quality data. This methodological rigor enhances the credibility of the study's findings and supports their reproducibility in future research.

A major strength of the study is its focus on a representative sample of CALHIV, a particularly vulnerable and under-researched group, especially in SSA. By concentrating on this population, the study provides valuable insights into the unique challenges and health needs of CALHIV, offering critical information that can inform targeted interventions and policies aimed at improving their health outcomes. The sample's representativeness across diverse socio-demographic and clinical characteristics further strengthens the external validity of the findings, allowing them to be generalized to similar populations in other regions.

Moreover, the application of multiple logistic regression analysis was instrumental in identifying the key determinants of VLS. This advanced statistical method allowed for the control of confounding variables, enabling the identification of independent factors associated with USVL. The use of this robust analytical technique provided more precise and interpretable results, offering a clearer understanding of the predictors of VLS. This added rigor enhances the study's contributions to the field, identifying actionable factors that can be targeted in future interventions to improve VLS among CALHIV.

Furthermore, the substantial sample size in the qualitative phase of the study strengthens the validity of the study's findings. By conducting interviews until thematic saturation was achieved, the research ensured a nuanced understanding of the diverse factors affecting VLS. This commitment to reaching saturation underscores the thoroughness of the data collection process, allowing for an in-depth exploration of participants' lived experiences.

Another significant strength of this study is the application of the socioecological model as a guiding framework for interview development, data analysis, and result presentation.

The integration of social constructionist theory into the study provides a deeper understanding of how socio-historical and cultural contexts shape individual and collective experiences with ART adherence. Rather than focusing solely on the intrapsychic processes of individuals, social constructionist theory shifts attention to the social interactions and environmental factors that influence behaviors, including stigma, family dynamics, and community attitudes toward HIV. By incorporating this theoretical lens, the research recognizes that health outcomes are not just determined by personal behaviors but are also shaped by broader societal and cultural constructs.

This model is instrumental in structuring the research to consider the multiple layers of influence on VLS, from individual behaviors to broader socio-economic factors. By employing the socioecological model (Galea et al., 2018; Izudi et al., 2024), the study was able to consider the multilayered influences on ART adherence and VLS, encompassing individual, interpersonal, family, healthcare, and community levels. This framework allowed for a more holistic understanding of the complexities surrounding ART adherence, recognizing that factors such as personal motivation, family support, healthcare access, and community stigma are deeply interconnected. The socioecological approach also facilitated a broader examination of the interaction between these levels, highlighting the dynamic interplay between personal, social, and structural influences on health outcomes. This comprehensive perspective adds to the robustness of the study, offering insights that are not only contextually grounded but also potentially generalizable across similar settings. By focusing on these diverse levels of influence, the study captures the broader socio-historical and cultural context in which HIV care takes place, ultimately providing a more complete picture of the barriers and facilitators to VLS. By employing such a robust theoretical framework, the study enhances its scientific rigor and increases the potential for replicability in future research.

The qualitative component of the study is particularly valuable in identifying nuanced social and cultural factors that influence adherence to ART and VLS. By capturing the perspectives of various stakeholders, the findings can inform HCW and policymakers about the specific challenges that need to be addressed to enhance ART adherence among this vulnerable population.

In summary, the strengths of this study, including its comprehensive approach, integration of quantitative and qualitative data, substantial sample size, rigorous methodological framework, and valuable qualitative insights, contribute significantly to the understanding of VLS among CALHIV. The findings offer critical insights that can guide future research and interventions aimed at improving health outcomes for CALHIV.

5.5. Study limitations

This study presents several important limitations that must be taken into account when interpreting the findings. One primary limitation is the cross-sectional design, which restricts the ability to establish causal relationships between the identified determinants and USVL. While the study identifies various factors associated with USVL, it does not definitively ascertain whether these factors directly cause USVL. Additionally, the cross-sectional nature limits the ability to fully disentangle the temporal sequence between potential confounders, mediators, and the outcome, which constrains the interpretation of our multivariable logistic regression model. A longitudinal study design, which would track participants over time, would facilitate a more robust analysis of cause-and-effect relationships, thereby enhancing the understanding of how different determinants influence ART adherence and VLS.

The geographic focus of the research also poses limitations to the generalizability of the findings. Conducted exclusively in urban Lubumbashi, the study's results may not be

applicable to rural settings where socio-economic conditions and access to healthcare services differ significantly. These disparities in healthcare infrastructure, cultural attitudes toward HIV, and the quality of care can lead to varying experiences and outcomes in other regions of the DRC or SSA. Thus, while the findings are valuable within the context of Lubumbashi, caution should be exercised when attempting to extrapolate them to broader populations.

Another important limitation is the use of self-reported data, which may introduce social desirability bias. Participants could have provided responses they felt were more socially acceptable, affecting the accuracy of the data. This bias may mask the true experiences and challenges faced by ALHIV and their caregivers, hindering a full understanding of the barriers to achieving VLS.

Furthermore, certain unmeasured confounding factors may significantly influence ART adherence and health outcomes but were not accounted for in this study. Variables such as mental health conditions, levels of psychosocial support, and the economic status of participants could play a crucial role in determining ART adherence and achieving VLS. Moreover, although the multivariable logistic regression model included a broad set of candidate predictors, its estimates may still be affected by residual confounding from variables not captured in the routinely collected dataset. While we acknowledge that multiple tailored models can be informative for disentangling the specific roles of confounders, mediators, and effect modifiers, such an approach was beyond the primary scope of this study, which sought to deliver a concise and coherent set of determinants for programmatic and policy decision-making. We therefore consider the unified model not only appropriate but optimal for the current research objectives. Nevertheless, this is noted as a methodological consideration for future, more exploratory analyses aimed at unpacking the complex interrelationships between predictors.

The quantitative study faced substantial attrition, with 462 children lost to follow-up and 82 deceased during the observation period. It is plausible that many of these children were no longer receiving ART and had a higher likelihood of USVL. Given that the number lost to follow-up represents more than half of the final analytic sample, and that some deceased children likely had USVL, the estimated prevalence of USVL in this study may be biased downwards. This attrition bias should be considered when interpreting prevalence estimates, as it could lead to an underestimation of the true burden of USVL among CALHIV in this setting.

Lastly, while this study incorporates both quantitative and qualitative data, further qualitative research is warranted to deepen the understanding of the social, psychological, and cultural factors influencing ART adherence. A qualitative approach would help to identify key challenges faced by CALHIV, including stigma, the complexity of treatment regimens, and barriers to accessing healthcare services. Exploring factors such as family support, communication between caregivers and adolescents, and effective healthcare strategies would provide critical insights for developing tailored interventions aimed at improving adherence and VLS.

Despite these limitations, this study contributes valuable evidence regarding the barriers to achieving VLS among CALHIV by incorporating both quantitative and qualitative data. This dual approach enriches the understanding of the complexities surrounding ART adherence and VLS, highlighting the need for targeted interventions that address the specific challenges faced by this vulnerable population. The findings emphasize the importance of developing tailored strategies to improve ART adherence and overall treatment outcomes, informed by a comprehensive analysis of the social, psychological, and cultural factors influencing this population.

CHAPTER SIX

CONCLUSION

6.1. Summary of key findings from the study

The aim of this study was to explore the prevalence, determinants, barriers and facilitators to VLS among CALHIV on ART in Lubumbashi, DRC. Results revealed a high prevalence of USVL, reaching 24.7% among the 847 participants in this study. This finding highlights the significant challenges faced in achieving the 95-95-95 HIV targets, both at the sub-regional level in SSA, where 26.1% was reported among 169,949 CALHIV, a result comparable to ours (X^2=0.85; p=0.3564), and at the local level in Lubumbashi. Indeed, the prevalence of USVL observed in this study is in line with the general trend in the region, where VLS remains a difficult objective to achieve, due in particular to various socio-economic and healthcare obstacles. Key determinants of USVL identified in this study included poor ART adherence (aOR = 90.8; 95% CI: 45.8 – 179.9), advanced clinical stages of HIV (aOR = 4.8; 95% CI: 2.1 – 10.8), horizontal HIV transmission (aOR = 2.3; 95% CI: 1.2 – 4.5), ART side effects (aOR = 2.4; 95% CI: 1.3 – 4.5), as well as the fact that married caregivers of CALHIV were more likely to observe USVL (aOR = 2.8; 95% CI: 1.5 – 5.2). These results support the hypothesis that factors related to caregiver adherence and support are determinants of VL management in CALHIV.

Among the main barriers to achieve VLS, social stigma associated with HIV, lack of psychosocial support, and limited access to healthcare are the most frequently reported. These interconnected barriers, such as lack of family support and perceived discrimination in healthcare settings, complicate ART adherence and effective HIV management. In

particular, stigma, at both community and institutional levels, remains a major challenge that negatively influences CALHIV's motivation towards ART adherence.

However, facilitators were also identified, such as strong social support, management of ART side-effects, and reminder tools. Moreover, positive relationships with caregivers and personalized follow-up played a central role in the success of VLS. These findings support the hypothesis that an integrated care environment, which incorporates psychosocial support strategies, is essential for ART effectiveness and achieving VLS.

This study contributes to a comprehensive understanding of the specific challenges encountered by CALHIV in resource-limited settings like Lubumbashi.

6.2. Theoretical contribution

This study was grounded in a pragmatist paradigm (Morgan, 2014), which recognizes that complex public health issues such as VLS among CALHIV require the integration of complementary quantitative and qualitative approaches. Within this paradigm, theoretical positioning was not limited to the qualitative strand; rather, the socioecological model and social constructionist theory provided a unifying conceptual lens for the entire study, guiding the formulation of research questions, the choice of a convergent mixed-methods design, and the interpretation of integrated findings.

The integration of theoretical frameworks in this study enabled a comprehensive exploration of the factors influencing the achievement of VLS among CALHIV in Lubumbashi. By employing a mixed-methods approach, this research makes a significant contribution to understanding sustained VLS in CALHIV. Specifically, the quantitative component utilized a multiple logistic regression model to identify key determinants, while the qualitative component employed the socioecological model, enriched by insights from

social constructionist theory, to explore contextual factors that may affect VLS outcomes. The decision to employ a convergent mixed-methods design (Creswell & Plano Clark, 2018) was theoretically driven. The socioecological model's multi-level perspective aligned with the quantitative component's ability to identify statistical associations across individual, familial, and structural factors, while the qualitative component deepened understanding of how these factors operate in lived contexts—an approach consistent with social constructionist principles. Integrating both strands allowed for meta-inferences that neither method alone could have generated.

This issue has been a major concern in the DRC, as highlighted in 2021 following a review of the national HIV/AIDS program. The review revealed that only 11% of children living with HIV on ART achieved viral load suppression (PNLS, 2021). In contrast, the present study found that 75.32% of the 847 participants achieved sustained VLS. While these results are significantly higher than the national figures, they still fall short of the UNAIDS 95% target.

This study explored the complex factors influencing VLS among CALHIV by identifying key determinants. The logistic regression model used in the study highlighted the independence of four individual factors related to the CALHIV (poor adherence to ART, advanced clinical stages of HIV, horizontal HIV transmission, and ART side effects) and one family-related factor (caregiver marital status). This underscores the complexity of ART adherence outcomes and VLS.

By examining how barriers and facilitators operate at various levels—individual, interpersonal, family, health service, and community—the study underscores the complex, multi-layered factors that influence ART adherence and VLS outcomes among CALHIV.

The socioecological model, positing that behavior is influenced by interactions across different social and environmental levels, provides a valuable framework for understanding the range of factors impacting VLS. This approach reveals how individual-level factors, such as ART side effects, forgetting to take medication, lack of food, being too busy, feeling healthy and not perceiving the necessity of ART, and being away from home, are intertwined with broader familial, healthcare-related, and community influences. Family support was identified as a key factor in promoting ART adherence and achieving VLS, while lack of family involvement and fear of stigmatization were significant obstacles. In terms of health services, positive interactions and psychosocial follow-up were seen to encourage VLS. Overall, stigma and economic constraints were barriers to adherence, but social support networks were identified as facilitators for treatment uptake. These findings extend previous applications of the socioecological model in HIV research (Wanjala et al., 2024; Zuma et al., 2022) by focusing specifically on young people in a SSA context.

In addition, this study is informed by social constructionist theory, which emphasizes that knowledge and meanings are created through social interactions (Segre, 2016). Social constructionism highlights how stigma surrounding HIV, as well as norms around family structures and caregiving, shape CALHIV' experiences and understanding of their condition. For instance, the study found that CALHIV from broken families or who are double orphans faced unique challenges in achieving VLS. This suggests that the social construction of family roles and support systems can significantly affect health outcomes. The social constructionist lens also sheds light on the role of peer support clubs, psychosocial follow-up, and positive relationships with HCWs as facilitators of VLS. These support systems can help reconstruct the CALHIV' self-concepts and perceptions of living with HIV, enabling them to build positive identities around their health status. This aligns with prior research on the influence of social support on health behaviors (Okonji et al.,

2020; Strother et al., 2022), suggesting that peer interactions and positive healthcare relationships play a critical role in shaping CALHIV' adherence to ART and their ability to achieve VLS.

The integration of these datasets followed best practices in mixed-methods research, using joint displays and side-by-side comparisons (Guetterman et al., 2015) to ensure that the theoretical frameworks shaped both the identification of determinants and the interpretation of contextual nuances. This process made explicit the theoretical coherence between methods and findings, enhancing the explanatory power of the study.

Moreover, the application of the socioecological model in conjunction with social constructionist theory in this study underscores the importance of addressing stigma at multiple levels. Stigma persists as a major barrier to VLS, impacting not only the individual's adherence to ART but also influencing familial and community responses. Addressing these barriers requires interventions that challenge socially constructed stigma and promote understanding and acceptance of HIV within broader social contexts (Parker & Aggleton, 2007). This study advances theoretical discussions on ART adherence and VLS among CALHIV by revealing the intertwined socioecological and social constructionist dimensions of their experiences. It provides a basis for further research on how social and cultural constructions influence health behaviors, particularly in relation to chronic illness management within vulnerable populations.

By making the theoretical frameworks explicit across both methodological strands, this study advances the application of socioecological and social constructionist perspectives within a pragmatist mixed-methods paradigm. This integration not only strengthens the

theoretical contribution but also demonstrates the value of theory-informed methodological pluralism in addressing multifactorial public health challenges.

6.3. Linking quantitative and qualitative approaches

The integration of quantitative and qualitative approaches in this study enriches the theoretical framework of mixed methods research, providing a comprehensive view of the factors influencing adherence to ART and VLS among CALHIV in Lubumbashi. Using the socioecological model, the study offers an in-depth understanding of the dynamics influencing not only ART adherence but also VLS, a crucial objective for HIV management. The quantitative approach provides data on general trends in adherence, while the qualitative approach explores participants' perceptions, emphasing the importance of contextual and social factors in the success of ART. The study reveals that VLS is strongly influenced by individual factors (such as mode of acquisition, WHO clinical stages, and side effects), familial factors (including parental support and family structures), health-related factors (such as positive interactions), and community factors (including stigma and socioeconomic support). The socioecological model enables a more targeted approach to addressing obstacles to VLS and proposing more effective interventions. This study lays the groundwork for future research on adapting healthcare policies to consider the social, behavioral, and systemic factors that influence achieving VLS.

6.4. Understanding barriers and facilitators

Studies on adherence to ART and VLS among PLHIV indicate that adherence is influenced by various factors at the individual, interpersonal, community, and healthcare levels (Curioso et al., 2010; Galea et al., 2018; Izudi et al., 2024). Common barriers to adherence include ART side effects, stigma, limited social support, financial constraints,

and context-specific challenges in Lubumbashi, DRC. CALHIV, often reliant on caregivers for treatment, encounter issues related to a lack of disease awareness and insufficient or ineffective counseling. Moreover, adolescence brings about biological, psychological, and social changes that may impede CALHIV's adherence motivation.

Among the facilitators, family and peer support, as well as the use of electronic reminders, are crucial to improving adherence. Peer support groups reinforce commitment and provide a space for sharing experiences. Better communication between caregivers and CALHIV also optimizes adherence.

The analysis is grounded in the socioecological model, which delineates four levels of influence. Individually, the perception of the disease and medication management are pivotal. Interpersonally, support from caregivers and peers is crucial for adherence. Adherence at the community level is affected by stigma and cultural beliefs, whereas access to healthcare facilities and psychological support are fundamental at the healthcare level. As a result, VLS hinges on the intricate interplay of these factors, necessitating comprehensive, multidimensional interventions to enhance adherence and achieve VLS.

6.5. Development of a conceptual model

Based on the results of this study conducted on determinants, barriers, and facilitators to adherence to ART and VLS among CALHIV in Lubumbashi, we propose a conceptual model that illustrates the relationships between the key determinants of VLS. This model illustrates the dynamic interplay between individual, family, healthcare-related, and community factors (Figure 6.1).

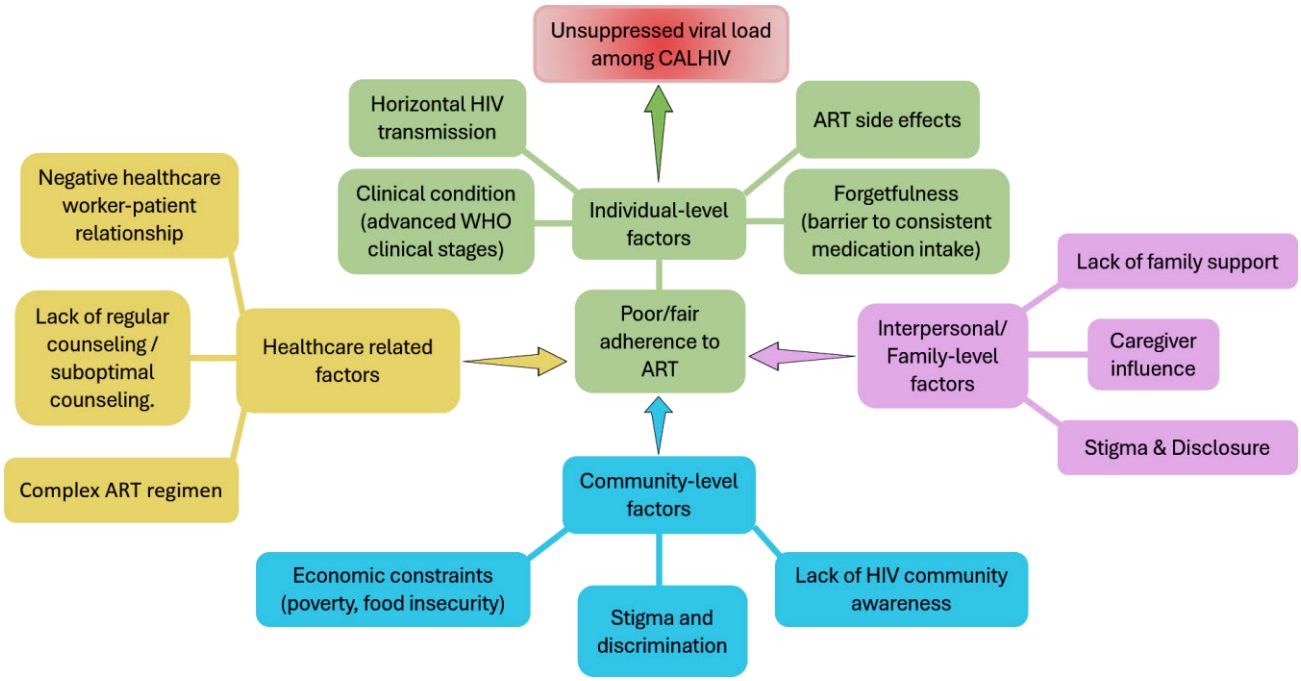

Figure 6.1 Conceptual model of determinants of unsuppressed viral load among CALHIV in Lubumbashi

This conceptual model offers a structured approach to developing tailored interventions for CALHIV, considering individual, family, community, and healthcare-related factors. Individual interventions may involve utilizing mobile ART reminder applications and providing personalized support through customized counseling sessions. Family-focused interventions could include training caregivers in HIV management, supporting the disclosure of HIV status, and enhancing family networks. Within healthcare services, it is essential to enhance the capabilities of caregivers, incorporate mental health services, and expand the availability of ART. Community and political initiatives, such as educational campaigns and subsidies for healthcare access, are vital in reducing stigma and enhancing ART adherence. Consequently, this model presents a practical and comprehensive strategy for understanding and addressing the determinants of VLS among CALHIV, particularly in the DRC, with potential applicability to similar settings.

6.6. Contribution to policy and practice

The results and theoretical perspectives from this study offer valuable insights for health policies striving to achieve the UNAIDS 95-95-95 targets, particularly in resource-limited settings like Lubumbashi. Integrating psychosocial and contextual dimensions into care programs for CALHIV is crucial to improve ART adherence and VLS.

6.6.1. Application to health policies to achieve UNAIDS 95-95-95 targets

UNAIDS aims for 95% of PLHIV to know their status, 95% of those diagnosed to be on ART, and 95% of those treated to achieve VLS (UNAIDS, 2014). In resource-constrained settings, various factors impact the attainment of these targets.

Early detection is crucial to improve the management of CALHIV. Implementing focused strategies in schools and communities could aid in the prompt detection of cases and access to essential care. It is vital to carry out awareness campaigns specifically designed for young people to reduce stigma and promote acceptance of their HIV status.

ART adherence depends on simplifying protocols, particularly by utilizing single-dose regimens and long-acting drugs. Integrated psychosocial support is crucial: training caregivers in psychological support, establishing peer support groups, and utilizing mobile reminders to enhance compliance.

Integrating HIV care into health systems is crucial. Decentralization of services, nutritional support, and ongoing training for caregivers encourage adherence by CALHIV. A comprehensive approach, combining medical and psychosocial interventions, is essential to achieve VLS.

6.6.2. Integrating psychosocial and contextual factors into the design of health programmes

This study demonstrates that the barriers to ART adherence encompass not just medical aspects but also psychological, social, and structural factors. The adherence to ART and the well-being of CALHIV are intricately linked to psychosocial considerations. Addressing stigma is paramount, necessitating awareness campaigns and caregiver training to mitigate discrimination within healthcare settings. Tailored psychological support and the incorporation of mental health services are equally imperative.

Family and educational support play a crucial role: training tutors and teachers helps create an environment conducive to ART adherence. Community programmes involving religious and community leaders promote social acceptance and reduce stigma.

While the free provision of ART and VL tests is essential, access to care remains challenging for some youth living in remote areas due to transportation difficulties to healthcare facilities. Deploying mobile clinics could help overcome these barriers and improve care. A comprehensive strategy that integrates medical treatment, psychosocial assistance, and community engagement is crucial for meeting the 95-95-95 targets and enhancing the well-being of CALHIV.

6.7. Impact of the suspension of PEPFAR funding on HIV care for children and adolescents in the Democratic Republic of the Congo: Challenges and urgent solutions

Since its launch in 2007 in the DRC, PEPFAR assistance has enabled over 5 million Congolese individuals to access HIV testing services and supported more than 200,000 PLHIV in initiating antiretroviral therapy (PEPFAR, 2022; U.S. Embassy in the DRC, 2025). These initiatives have led to a significant reduction in HIV-related mortality and

have contributed to progress toward achieving the UNAIDS 95-95-95 target by 2030. In July 2024, the DRC was recognized as one of the African countries closest to achieving these targets for the adult population (Gahongariye, 2024). However, additional efforts are needed to ensure that these advances also benefit CALHIV.

The announcement of the freeze on U.S. foreign aid on January 20, 2025, including the suspension of PEPFAR funding for 90 days (White House, 2025), poses a major threat to the care of CALHIV in the DRC. This interruption of funds could have dramatic consequences for an already vulnerable population. As of January 24, 2025, this suspension led to the immediate cessation of services, affecting both ongoing programs and new activities (Igoe M., 2025). In this context, PEPFAR faces organizational and operational challenges. In the DRC, as in other PEPFAR beneficiary countries, non-governmental organizations and HIV care clinics were ordered to cease activities, and many of them are now in a "closeout" phase, halting their service provision to PLHIV due to uncertainty about the future of the program (Doctors Without Borders, 2025; Nolen, 2025).

This funding suspension particularly affects the Free Distribution Points and Peer Support (PODIs) in Kinshasa, which are essential for the care of PLHIV in a context of stigma and poverty. The closure of these PEPFAR-supported care points leaves thousands without support, increasing the risk of advanced HIV. Moreover, Doctors Without Borders teams may be unable to meet the growing demand if the disruptions persist (Doctors Without Borders, 2025). On February 1, 2025, the U.S. government granted a limited waiver allowing the resumption of some essential services, primarily antiretroviral therapy and prevention of mother-to-child HIV transmission, but excluding other crucial activities

(Saldinger, 2025; Kates, 2025). HIV prevention programs targeting key populations, as well as those supporting orphans and vulnerable children, remain suspended (Kates, 2025).

The suspension of funding exposes CALHIV to an increased risk of treatment interruption, particularly due to shortages of pediatric antiretroviral drugs. This situation could lead to the development of drug resistance, further complicating their care and raising future treatment costs. Additionally, the shortage of pediatric ART formulations in the DRC could exacerbate this crisis, forcing some children to use inappropriate doses or share their medications with adults.

The discontinuation of funding could also result in heightened morbidity and mortality among CALHIV. Without consistent ART, these children and adolescents are vulnerable to rapid disease advancement, increasing the likelihood of severe complications like tuberculosis, malnutrition, and opportunistic infections (Doctors Without Borders, 2025). Additionally, the pause in mother-to-child transmission prevention programs would hinder the progress in decreasing new pediatric infections, putting at risk children born to HIV-positive mothers who would no longer receive the required prophylaxis.

Services for monitoring and supporting CALHIV would also face significant disruptions. These individuals necessitate psychosocial support to enhance treatment adherence and prevent psychological distress, including depression and anxiety. The discontinuation of support groups and counseling services would heighten the chances of treatment abandonment and HIV transmission.

In the long term, this funding suspension could hinder the progress made in addressing pediatric and adolescent HIV in the DRC. Treatment interruptions and reductions in testing services could decrease the viral suppression rate, thus promoting the spread of the

virus. Moreover, access inequalities may widen, particularly for the most impoverished families who cannot afford treatment, thereby exacerbating the stigma faced by CALHIV within their communities and schools. The cessation of funding would also affect prevention efforts among adolescents, who often face psychosocial challenges that reduce their motivation to adhere to treatment, increasing the risk of transmission to sexual partners.

In summary, the suspension of PEPFAR funding could reverse the progress made and jeopardize efforts to control the HIV epidemic in the country. Studies conducted in other African contexts highlight the potential consequences of such a reduction in funding. For example, a modeling study conducted in South Africa showed that a complete cessation of PEPFAR funding could result in 570,000 new infections and 600,000 additional HIV-related deaths by 2034 (Arvieux, 2025). Although these figures pertain to South Africa, they clearly illustrate the risks associated with reduced financial support in the fight against HIV.

In the face of this impending crisis, it is crucial to explore alternative funding sources to ensure the continuity of programs (Ratevosian et al., 2025). Sole reliance on PEPFAR exposes the DRC to fluctuations in foreign political decisions. Therefore, it is essential to mobilize national resources and explore other partnerships with local NGOs and the private sector. In the meantime, the national HIV response program and the Ministry of Health must implement a strategic plan to ensure the sustainability of care for PLHIV. To date, PLHIV continue to receive free care in HIV clinics through existing ARV stocks, and contracts with service providers remain in effect until the end of February 2025. However, as of March 2025, the management of these services will be fully assumed by the Congolese government, which will need to ensure the continuity of care. The interruption of U.S.

funding represents a major threat to the health of children and adolescents living with HIV in the DRC. It is urgent for the Congolese government and its partners to strengthen national funding, diversify support sources, and maintain essential services to prevent an irreversible deterioration of the country's epidemiological situation.

6.8. Implications for future research

The findings of this study contribute to filling knowledge gaps on ART adherence and VLS among CALHIV in the DRC. However, several aspects require further investigation. Various studies have explored the impact of psychosocial and contextual factors, such as stigma and family support, on ART adherence. For instance, a study conducted in Liberia revealed that high levels of stigma and inadequate informational support significantly increased ART nonadherence among PLHIV (Strother et al., 2022). The researchers recommended focusing on reducing stigma and enhancing continuous information from healthcare providers and families (Strother et al., 2022). Additionally, a systematic review underscored the significance of family-centered services in improving ART adherence and retention (Okonji et al., 2020). This review identified four critical treatment modalities: individual counseling, support groups, family-centered services, and treatment supporters, emphasizing the protective role of family in ART adherence (Okonji et al., 2020). Furthermore, the involvement of guardians and the challenges related to the transition from childhood to adolescence are frequently overlooked. Addressing these gaps is essential for developing comprehensive and effective interventions that promote ART adherence, achieve VLS, and improve long-term health outcomes for CALHIV.

Longitudinal studies are necessary to monitor changes in ART adherence and achieving VLS over the long term, assess the effectiveness of targeted interventions (support groups, electronic reminders), and analyze the impact of life transitions (schooling, transition to

adulthood, change of caregivers). Qualitative research should delve deeper into the cultural perceptions and challenges faced by caregivers, so that training and support for CALHIV can be better adapted. Finally, exploring structural and political factors, such as access to care and integrated care models, will help optimize support strategies and improve ART adherence for CALHIV in the DRC and elsewhere.

6.9. Interdisciplinary approaches

Improving ART adherence and achieving VLS among CALHIV necessitates an interdisciplinary approach that amalgamates insights from psychology, sociology, public health, and epidemiology. Through the integration of these diverse disciplines, they can enhance comprehension of the myriad factors influencing ART adherence and VLS, facilitating the formulation of more efficacious, context-specific intervention strategies for CALHIV.

6.9.1. Contribution of different disciplines to understanding viral load suppression

In psychology, VLS in CALHIV is highly dependent on ART adherence, which is influenced by cognitive and emotional factors. Perception of HIV, personal motivation, and acceptance of the diagnosis are essential for maintaining optimal compliance. Stigma and discrimination compromise adherence, making it crucial to develop behavioral interventions, such as cognitive-behavioral therapies, to overcome these barriers and improve VLS.

From a sociological point of view, family and community dynamics play a decisive role in ART adherence and, consequently, in VLS. Perceptions of HIV, shaped by cultural norms and social beliefs, influence continuity of care. Social inequalities, particularly in terms of gender and socioeconomic status, limit access to ART, thereby compromising VLS.

In public health, appropriate community strategies are essential to achieve VLS. Involving community leaders, providing psychosocial support, and integrating mental health and nutritional services can all contribute to enhancing ART adherence. Enhanced monitoring systems and targeted interventions have the potential to optimize VLS rates and decrease HIV transmission.

In epidemiology, longitudinal studies tracking CALHIV on ART provide valuable insights into the determinants of VLS. By identifying predictive factors of virological failure and evaluating the impact of public health policies over time, such studies will inform the development of more targeted intervention strategies. Long-term follow-up studies are essential to better understand the dynamics of ART adherence, identify early indicators of treatment failure, and refine public health approaches to ensure more effective and sustainable ART outcomes for CALHIV.

6.9.2. Importance of collaboration between key players

The integration of an interdisciplinary approach is essential to improve the management of CALHIV and promote VLS.

- *Greater coordination between care providers*

Joint training for doctors, psychologists, and social workers would provide holistic care for CALHIV, promoting VLS. The development of integrated clinics combining medical care, psychosocial support, and family accompaniment would ensure consistent follow-up and better control of VL, while reinforcing ART adherence.

- *Role of community organizations*

Community and religious leaders play a crucial role in reducing stigma, a major obstacle to VLS. Through the strengthening of support groups and the enhancement of access to

HIV services in rural areas, community interventions ensure better care, support ART adherence, and contribute to achieving VLS.

- *Commitment from political decision-makers*

The development of health policies guaranteeing equitable access to ART and resources to strengthen staff training and infrastructure is essential to achieve VLS. Public-private partnerships can ensure the continued availability of ART, facilitating access to care and contributing to VLS.

An interdisciplinary approach that integrates medical care, psychosocial support, and community interventions is essential for achieving the UNAIDS 95-95-95 targets and enhancing VLS among CALHIV.

6.10. Future studies

Building on the findings of our study on the factors influencing VLS in CALHIV, the following areas of future research are recommended:

1° *HIV-related mental health and cognitive function:* A study to assess the mental health and cognitive impacts of HIV and ART on CALHIV. This research would explore how psychological well-being correlates with ART adherence and VLS, addressing the psychological barriers that may hinder ART success.

2° *Longitudinal studies on ART long-term outcomes:* A longitudinal study to track the long-term health outcomes of CALHIV who experience delayed VLS. This research would focus on the development of HIV drug resistance, the occurrence of opportunistic infections, and overall survival rates, providing insight into the prolonged impacts of delayed VLS.

3° *Cost-effectiveness of intervention programmes:* A cost-effectiveness analysis to evaluate the economic viability of different intervention strategies aimed at improving VLS in CALHIV. This includes assessing the cost-effectiveness of psychosocial support, improved ART regimens, and community-based adherence support interventions.

4° *HIV resistance mechanisms:* A study to explore the role of HIV drug resistance in the inability to achieve VLS in CALHIV. This study would investigate mechanisms of resistance, with a particular focus on developing strategies for early detection and management to prevent ART failure.

These future studies are crucial for deepening our understanding of the complex factors influencing VLS in CALHIV. The results of these studies will help inform more effective interventions, improve ART outcomes, and guide public health strategies aimed at reducing HIV-related morbidity and mortality in this vulnerable population.

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APPENDIX A

INFORMED CONSENT FORM (English version)

Title of study: Unsuppressed viral load among Human Immunodeficiency Virus-positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators.

Principal investigator: Olivier K. Mukuku
Supervisor: Professor Kaymarlin Govender

Ethical Clearance Protocol Number: [N° HSSREC/00006817/2024]

Medical Ethics Committee of the University of Lubumbashi: [N° UNILU/CEM/036/2023]

Dear parent/guardian,

Good morning/afternoon. My name is Olivier Mukuku, and I am a student at the University of KwaZulu-Natal. As part of my studies, I am conducting research on HIV Viral Load Suppression. I would be grateful if you would consider participating in this study. Before you decide, you will be given detailed information about the study, have the opportunity to ask any questions, and receive a copy of this information sheet for your records.

We are inviting you to take part in a qualitative study into the experiences of adolescents living with HIV. The aim of this study is to gather valuable information about the challenges, needs and resources of adolescents living with HIV, in order to improve the support services available to them.

Before you decide to take part in this study, we ask you to read the information below carefully. Do not hesitate to ask questions if you need further clarification. Your participation is voluntary and you have the right to refuse or withdraw your consent at any time, without any negative consequences for you or your child.

The main aim of this study is to understand the experience of HIV-positive adolescents of adherence to antiretroviral treatment and viral load suppression. The information gathered will be used to improve support services and better meet the needs of adolescents living with HIV.

If you agree to take part, you will be invited to take part in a focus group with other parents/guardians of HIV-positive adolescents. Discussions will take place in a confidential and respectful environment. The focus group sessions will be recorded for later analysis, but the information gathered will be treated anonymously and confidentially. The interview will take approximately 45 to 60 minutes. We will make every effort to ensure that the interview is conducted at a time and place that is convenient and comfortable for you.

Your anonymity and the confidentiality of your answers will be strictly respected. The data collected will be used solely for research purposes and will not be disclosed to any unauthorized third party. Audio recordings will be stored securely and only members of the research team will have access to them.

Your participation in this study will contribute to a better understanding of the needs of HIV-positive adolescents and to improving the services available to them. There are no major risks associated with your participation, but you may feel emotionally affected by sharing your experience.

Your participation in this study is voluntary. You have the right to refuse to participate or to withdraw your consent at any time, without any negative consequences for you or your child. Your decision to participate or not will have no impact on the healthcare services you or your child receive.

By signing this form, you confirm that you have read and understood the information provided above. You consent to your participation in the study and to the use of the information collected for research purposes.

Name of parent/guardian: _____

Signature of parent/guardian: _____

Date : _____

Signature of researcher: _____

Date : _____

Please keep a copy of this form for your personal records.

Thank you very much for your participation and your valuable contribution to this study.

If you have any further questions or would like more information, please contact:

Dr Olivier Mukuku

Telephone: [redacted]

Email: [redacted]

Institut Supérieur des Techniques Médicales de Lubumbashi, Democratic Republic of the Congo

FORMULAIRE DE CONSENTEMENT ÉCLAIRÉ (French version)

Titre de l'étude : Suppression de la charge virale chez les enfants et adolescents séropositifs au VIH sous thérapie antirétrovirale à Lubumbashi, République démocratique du Congo : ampleur, déterminants, obstacles et facilitateurs.
Chercheur principal : Olivier K. Mukuku
Superviseur : Professeur Kaymarlin Govender

Ethical Clearance Protocol Number: [N° HSSREC/00006817/2024]

Medical Ethics Committee of the University of Lubumbashi: [N° UNILU/CEM/036/2023]

Chers parents/tuteurs,

Bonjour. Je m'appelle Olivier Mukuku et je suis étudiant à l'université de KwaZulu-Natal. Dans le cadre de mes études, je mène des recherches sur la suppression de la charge virale du VIH. Je vous serais reconnaissant de bien vouloir participer à cette étude. Avant de prendre votre décision, vous recevrez des informations détaillées sur l'étude, vous aurez la possibilité de poser des questions et vous recevrez une copie de cette fiche d'information pour vos dossiers.

Nous vous invitons à participer à une étude qualitative portant sur l'expérience des enfants infectés par le VIH. L'objectif de cette étude est de recueillir des informations précieuses sur les défis, les besoins et les ressources des enfants vivant avec le VIH, afin d'améliorer les services de soutien qui leur sont offerts.

Avant de prendre votre décision de participer à cette étude, nous vous demandons de lire attentivement les informations ci-dessous. N'hésitez pas à poser des questions si vous avez besoin de clarifications supplémentaires. Votre participation est volontaire et vous avez le droit de refuser ou de retirer votre consentement à tout moment, sans aucune conséquence négative pour vous ou votre enfant.

L'objectif principal de cette étude est de comprendre l'expérience des enfants infectés par le VIH sur l'adhérence au traitement antirétroviral et la suppression de la charge virale. Les informations recueillies seront utilisées dans le but d'améliorer les services de soutien et de mieux répondre aux besoins des enfants vivant avec le VIH.

Si vous acceptez de participer, vous serez invité(e) à prendre part à un focus groupe composé d'autres parents/tuteurs d'enfants infectés par le VIH. Les discussions se dérouleront dans un environnement confidentiel et respectueux. Les sessions de focus groupes seront enregistrées pour une analyse ultérieure, mais les informations recueillies seront traitées de manière anonyme et confidentielle. L'entretien durera environ 30 à 45 minutes. Nous ferons tout notre possible pour

que l'entretien se déroule à un moment et dans un lieu qui vous conviennent et vous mettent à l'aise.

Votre anonymat et la confidentialité de vos réponses seront strictement respectés. Les données recueillies seront utilisées uniquement à des fins de recherche et ne seront divulguées à aucun tiers non autorisé. Les enregistrements audios seront conservés de manière sécurisée et seuls les membres de l'équipe de recherche y auront accès.

Votre participation à cette étude contribuera à une meilleure compréhension des besoins des enfants infectés par le VIH et à l'amélioration des services qui leur sont offerts. Il n'y a pas de risques majeurs associés à votre participation, mais il est possible que vous vous sentiez émotionnellement affecté(e) en partageant votre expérience.

Votre participation à cette étude est volontaire. Vous avez le droit de refuser de participer ou de retirer votre consentement à tout moment, sans aucune conséquence négative pour vous ou votre enfant. Votre décision de participer ou de ne pas participer n'aura aucun impact sur les services de soins de santé que vous ou votre enfant recevez.

En signant ce formulaire, vous confirmez avoir lu et compris les informations fournies ci-dessus. Vous consentez à participer à l'étude et à ce que les informations recueillies soient utilisées à des fins de recherche.

Nom du parent/tuteur : _____
Signature du parent/tuteur : _____
Date : _____
Signature du chercheur : _____
Date : _____
Veuillez conserver une copie de ce formulaire pour vos dossiers personnels.

Merci beaucoup pour votre participation et votre contribution précieuse à cette étude.

Si vous avez des questions supplémentaires ou si vous souhaitez obtenir plus d'informations, veuillez contacter :

Dr Olivier Mukuku

Telephone: [redacted]

Email: [redacted]***r***

Institut Supérieur des Techniques Médicales de Lubumbashi, Democratic Republic of the Congo

APPENDIX B

CHILD ASSENT FORM

Title of study: Unsuppressed viral load among Human Immunodeficiency Virus - positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators.
Principal investigator: Olivier K. Mukuku
Supervisor: Professor Kaymarlin Govender

Ethical Clearance Protocol Number: [N° HSSREC/00006817/2024]

Medical Ethics Committee of the University of Lubumbashi: [N° UNILU/CEM/036/2023]

Dear [Child's Name],

Good morning/afternoon. My name is Olivier Mukuku, and I am a student at the University of KwaZulu-Natal. As part of my studies, I am conducting research on HIV Viral Load Suppression. I would be grateful if you would consider participating in this study. Before you decide, you will be given detailed information about the study, have the opportunity to ask any questions, and receive a copy of this information sheet for your records.

We would like to invite you to participate in our research study, which aims to understand the challenges and factors that affect HIV viral load suppression among adolescents in the Congo. We believe that your insights and experiences are crucial to helping us improve the well-being of HIV-positive adolescents.

Purpose of the study: The purpose of this study is to explore the barriers and facilitators that Congolese HIV-positive adolescents face in achieving viral load suppression. Your participation will help us gather important information to improve support and healthcare services for adolescents living with HIV.

Your role: If you agree to participate, you will be asked to share your thoughts and experiences in a confidential and supportive interview setting. We will respect your privacy and ensure that your identity remains confidential throughout the study.

Voluntary participation: Your participation in this study is entirely voluntary. You have the right to refuse to participate or withdraw from the study at any time without facing any negative consequences. Your decision will not affect the care or services you receive.

Confidentiality: Your personal information will be kept confidential. Any information shared during the study will be anonymized, and only the research team will have access to it. We will not use your name or any identifying information in our reports.

Duration of the interview: The interview will take approximately 30 to 45 minutes. We will make every effort to ensure that the interview is conducted at a time and place that is convenient and comfortable for you.

Benefits: While there may not be direct benefits to you, your participation will contribute valuable insights to the improvement of healthcare services for adolescents living with HIV. Your contribution may help enhance the support available to others facing similar challenges.

Risks: The study involves discussing personal experiences related to HIV. This may be emotionally sensitive. We will have a qualified and experienced counselor available for support during and after the interview.

Additional consent for future research

In addition to your participation in this study, we would like to ask your permission to use the data collected from you for future research projects. These projects will be related to the current study but may explore different aspects of HIV care and support for adolescents. Your data will remain confidential, and your identity will not be disclosed in any future research.

Please indicate if you agree to allow your data to be used for future research:

- Yes, I agree to the use of my data for future research: _____ (Initials)
- No, I do not agree to the use of my data for future research: _____ (Initials)

Contact Information: If you have any questions or concerns about the study, please feel free to contact Dr Olivier Mukuku (Tel: +[redacted]).

Permission: Before you decide whether or not to participate, we encourage you to discuss this study with your parent/guardian. We will also seek their permission for your involvement. Your parent/guardian may be present during the consent process.

I, the undersigned, have read and understood the information provided in this Child Assent Form. I agree to participate voluntarily in the study.

Child's Name (Print):_____

Child's Signature:_____

Date:_____

Parent/Guardian Consent: I, the undersigned, am the parent/guardian of the child named above. I have read and understood the information provided in this Child Assent Form. I give permission for my child to participate in the study.

Parent/Guardian Name (Print):_____

Parent/Guardian Signature:_____

Date:_____

Dr Olivier Mukuku

Telephone: [redacted]

Email: [redacted]

Institut Supérieur des Techniques Médicales de Lubumbashi, Democratic Republic of the Congo

FORMULAIRE D'ASSENTIMENT DE L'ENFANT (French version)

Chercheur principal : Olivier K. Mukuku
Superviseur : Professeur Kaymarlin Govender

Ethical Clearance Protocol Number: [N° HSSREC/00006817/2024]

N° approval of the Medical Ethics Committee of the University of Lubumbashi: UNILU/CEM/036/2023

Titre de l'étude : Suppression de la charge virale chez les enfants et adolescents séropositifs au VIH sous thérapie antirétrovirale à Lubumbashi, République démocratique du Congo : ampleur, déterminants, obstacles et facilitateurs.

Cher [Nom de l'enfant],

Bonjour. Je m'appelle Olivier Mukuku et je suis étudiant à l'Université de KwaZulu-Natal. Dans le cadre de mes études, je mène des recherches sur la suppression de la charge virale du VIH. Je vous serais reconnaissant de bien vouloir participer à cette étude. Avant de prendre votre décision, vous recevrez des informations détaillées sur l'étude, vous aurez la possibilité de poser des questions et vous recevrez une copie de cette fiche d'information pour vos dossiers.

Nous aimerions vous inviter à participer à notre étude de recherche, qui vise à comprendre les défis et les facteurs qui affectent la suppression de la charge virale du VIH chez les adolescents au Congo. Nous pensons que vos idées et vos expériences sont cruciales pour nous aider à améliorer le bien-être des adolescents séropositifs.

Objectif de l'étude : L'objectif de cette étude est d'explorer les obstacles et les facteurs facilitant la suppression de la charge virale chez les adolescents congolais séropositifs. Votre participation nous aidera à recueillir des informations importantes pour améliorer les services de soutien et de soins de santé destinés aux adolescents vivant avec le VIH.

Votre rôle : Si vous acceptez de participer, nous vous demanderons de partager vos réflexions et vos expériences dans le cadre d'un entretien confidentiel et positif. Nous respecterons votre vie privée et veillerons à ce que votre identité reste confidentielle tout au long de l'étude.

Participation volontaire : Votre participation à cette étude est entièrement volontaire. Vous avez le droit de refuser de participer ou de vous retirer de l'étude à tout moment sans subir de conséquences négatives. Votre décision n'affectera pas les soins ou les services que vous recevrez.

Confidentialité : Vos informations personnelles resteront confidentielles. Toute information partagée au cours de l'étude sera anonymisée et seule l'équipe de

recherche y aura accès. Nous n'utiliserons pas votre nom ni aucune information permettant de vous identifier dans nos rapports.

Durée de l'entretien

L'entretien durera environ 30 à 45 minutes. Nous ferons tout notre possible pour que l'entretien se déroule à un moment et dans un lieu qui vous conviennent et vous mettent à l'aise.

Avantages : Bien qu'il n'y ait pas d'avantages directs pour vous, votre participation apportera des informations précieuses pour l'amélioration des services de santé destinés aux adolescents vivant avec le VIH. Votre contribution peut aider à renforcer le soutien disponible pour d'autres personnes confrontées à des défis similaires.

Risques : L'étude implique de discuter d'expériences personnelles liées au VIH. Il peut s'agir d'un sujet émotionnellement sensible. Un conseiller qualifié et expérimenté sera à votre disposition pour vous soutenir pendant et après l'entretien.

Consentement supplémentaire pour de futures recherches :

En plus de votre participation à cette étude, nous aimerions vous demander la permission d'utiliser les données recueillies auprès de vous pour de futurs projets de recherche. Ces projets seront liés à l'étude actuelle mais pourront explorer différents aspects des soins et du soutien aux adolescents atteints du VIH. Vos données resteront confidentielles et votre identité ne sera pas divulguée dans le cadre d'une recherche future. Veuillez indiquer si vous acceptez que vos données soient utilisées pour des recherches futures :

- Oui, j'accepte que mes données soient utilisées pour des recherches futures : _____ (Initiales)
- Non, je n'accepte pas que mes données soient utilisées pour des recherches futures : _____ (Initiales)

Informations de contact : Si vous avez des questions ou des inquiétudes concernant l'étude, n'hésitez pas à contacter le Dr Olivier Mukuku (tél. : +2[redacted]).

Autorisation : Avant de décider de participer ou non à l'étude, nous vous encourageons à en discuter avec vos parents ou votre tuteur. Nous leur demanderons également leur autorisation pour votre participation. Votre parent/tuteur peut être présent lors de la procédure de consentement.

Je soussigné(e) ai lu et compris les informations fournies dans ce formulaire de consentement de l'enfant. J'accepte de participer volontairement à l'étude.

Nom de l'enfant (en lettres moulées) : _____

Signature de l'enfant:_____

Date:_____

Consentement du parent/tuteur : Je soussigné(e) suis le parent/tuteur de l'enfant nommé ci-dessus. J'ai lu et compris les informations fournies dans le présent formulaire d'assentiment de l'enfant. J'autorise mon enfant à participer à l'étude.

Nom du parent/tuteur (en lettres moulées) : _____

Parent/Gardien Signature:_____

Date:_____

Dr Olivier Mukuku

Téléphone : + +[redacted]

Courriel : [redacted]

Institut Supérieur des Techniques Médicales de Lubumbashi, République Démocratique du Congo

APPENDIX C

DATA COLLECTION FORM (for quantitative study)

Title of study: Unsuppressed viral load among Human Immunodeficiency Virus - positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators.

I. Section A: Child/adolescent's socio-demographic information and HIV status

1.1. Child age: ……. years (Date of Birth: …. /…../……)
1.2. Sex:
- Male O
- Female O

1.3. Educational level:
- Never been to school O
- Primary: Completed O Not completed O
- Secondary/High school: Completed O Not completed O

1.4. Currently living with/in
- At least one biological parent O
- A non-parent family member O
- Adoptive parents O
- Group housing O
- A non-family member O

1.5. Death of at least one parent from HIV/AIDS
- Yes O
- No O

1.6. Lifetime history of residence in group home for children with HIV/AIDS
- Yes O
- No O

1.7. Main occupation: ……
1.8. Orphan status
- Non-orphan O
- Only father died O
- Only mother died O
- Double orphan O

1.9. HIV status disclosure to child
- Yes O
- No O

1.10. Age of total disclosure
- <12 years O
- ≥12 years O

1.11. HIV status disclosure to others
- Yes O (if yes, to whom? ……..)
- No O

II. Section B: Caregiver's information

2.1. Caregiver relationship
- Parent O (if yes, which relationship? …….)
- Non-parent O

2.2. Caregiver marital status
- Single O
- Married O

2.3. Age of caregiver: ……. years

2.4. Caregiver HIV status
- Positive O
- Negative O
- Unknown O

2.5. Caregiver alcohol use
- Yes O
- No O

III. Child/adolescent's clinical information

3.1. Any other chronic disease
- Yes O
- No O

3.2. History of opportunistic disease since the HIV positivity
- Yes O
- No O

3.3. Tuberculosis status
- Positive O
- Negative O

3.4. Nutritional status
- Normal O
- Mild-moderate malnutrition O
- Severe malnutrition O

3.5. WHO HIV clinical stage
- I O
- II O
- III O
- IV O

3.6. HIV infection route
- Perinatal O
- Transfusion O
- Sexual contact O
- Unknown O

IV. Treatment information

4.1. History of treatment interruption since ARV initiation
- Yes O
- No O

4.2. ART adherence:
- Good (>95%) O
- Fair (85-95%) O
- Poor (<85%) O

4.3. Number of daily pills: ……

4.4. Adverse/side effects
- Yes O
- No O

4.5. ART changes

- Yes O
- No O

4.6. Cotrimoxazole prophylaxis

- Yes O
- No O

4.7. Isoniazid prophylaxis

- Yes O
- No O

4.8. ART duration: ……months (date of ART starting: …../……/…..)

4.9. Current ART regimen

- Efavirenz-based O
- Nevirapine-based O
- Protease inhibitor-based O
- Others: ……

V. Viral load: ……copies/ml

O <1000 copies/mL O ≥1,000 copies/mL

APPENDIX D

QUESTIONNAIRE STUDY (for qualitative study)

Title of study: Unsuppressed viral load among Human Immunodeficiency Virus-positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators.

I. Section A: Healthcare workers' focus group discussion

1.1. Healthcare workers' characteristics

- Age
- Sex
- Function in the HIV clinic care

1.2. Healthcare workers' questions

- How would you describe your experience working with adolescents with HIV?
- What are some of the health problems or opportunistic infections with which adolescents most often present?
- How often do adverse reactions to ARV occur?
- Do some of the adolescents with HIV you know have problems with adherence? What types of problems and why?
- When are the adolescents hospitalized?
- Have you experienced a time when two or more adolescents with HIV help each other?

II. Section B: Parents/Caregivers (guardians)' focus group discussion

2.1. Parents/Caregivers (guardians)' characteristics

- Relationship to adolescents
- Age
- Sex
- Status HIV
- Occupation
- Marital status
- Educational level

2.2. Parents/caregivers questions

- Has your adolescent learned to care for him/herself by, for example, taking his/her pills on time and eating well?
- What difficulties have you perceived that your son/daughter/charge has in managing his/her illness?
- Do you think that your son/daughter/charge knows to ask for help when s/he needs it?
- Would s/he be able to manage his/her own treatment?
- How do you help him/her take his/her ARV?

o

III. Section C: Adolescents' in-depth interview guide

3.1. Characteristics of adolescents that participated in the psychosocial support groups

- Sex
- Age
- HIV transmission route : perinatal, transfusion, sexual, unknown
- Currently living with/in: At least one biological parent, A non-parent family member, Adoptive parents, Group housing, A non-family member.
- Death of at least one parent from HIV/AIDS
- Lifetime history of residence in group home for children with HIV/AIDS
- Main occupation
- Orphan status: non-orphan, single orphan, double orphan
- WHO HIV clinical stage
- Adherence status: adherent, non-adherent

3.2. Adolescent questions

Knowledge of HIV

Q1. Can you explain what you know about HIV/AIDS?
Q2. Could you share how you contracted the infection?

General medication use

Q3. How many antiretroviral treatments (ART) are you currently on?
Q4. What are the names of the medications you're taking?
Q5. Can you tell me about when you first began taking these medications?
Q6. Are you taking any additional medications? How do you feel about the total number of medications you're on?
Q7. How did you feel during the first two weeks after starting your treatment?
Q8. Have you ever had your medication changed? If so, what was the reason for the change?
Q9. What do you think about your medication? Do you believe it's necessary?

Viral load suppression and Adherence

Q10. Are you familiar with what viral load is and how it affects your health?
Q11. In your opinion, what factors influence the suppression of your viral load?
Q12. What challenges do you face in taking your medication regularly and keeping your viral load suppressed?
Q13. On which day(s) of the week do you most often miss taking your medication?
Q14. Why do you think that happens?
Q15. Can you describe your experience at home when it comes to taking your medication?
Q16. How do you manage taking your medication while at school?
Q17. What has been the most difficult experience you've had with your medication?

Influence of others

Q18. How do you get along with the health workers at the clinic?
Q19. How is your relationship with the people who provide your medication?
Q20. How has this affected your attitude toward your medication?
Q21. How do you think living with or without your parents has influenced your ART management?
Q22. Do you talk about your HIV status with your friends or peers?
Q23. If not, what are the reasons behind that?
Q24. If yes, how has sharing your status impacted your commitment to taking your ARTs?

Alcohol/drug use

Q25. Do you drink alcohol, smoke, or use drugs like crack or cocaine?
Q26. If so, have you experienced hangovers or other effects? How does this impact your regular ART intake?

Conclusion

Q27. Is there anything else you'd like to share about your medications that we haven't covered today?

I have been asking you so many questions, is there anything you would like to ask me?

Thank you very much for your time.

Dr Olivier Mukuku

Telephone: **+**[redacted]

Email:[redacted]

Institut Supérieur des Techniques Médicales de Lubumbashi, Democratic Republic of the Congo

APPENDIX E

AGREEMENTS FOR ONSITE SUPPORT

Principal investigator: Olivier K. Mukuku
Supervisor: Professor Kaymarlin Govender

Ethical Clearance Protocol Number: [N° HSSREC/00006817/2024]

N° approval of the Medical Ethics Committee of the University of Lubumbashi: UNILU/CEM/036/2023

Letter of Support

[Date]

[Name of HIV Care Clinic] [Address] [City, Country]

Dear [Clinic Name],

Subject: Agreement for Onsite Support for Research Study Participants

I am writing to formalize an agreement between **Olivier Mukuku** conducting research for "**Unsuppressed viral load among Human Immunodeficiency Virus-positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators."** and [Name of HIV Care Clinic] for the provision of onsite support to research study participants.

Olivier Mukuku is currently conducting a research study titled "**Unsuppressed viral load among Human Immunodeficiency Virus-positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators."**, aiming to explore the barriers and facilitators to achieving viral suppression among HIV-positive adolescents in Lubumbashi. The study involves qualitative interviews with HIV-positive adolescents receiving antiretroviral therapy (ART) at your facility.

To ensure the well-being of research participants, it is essential to provide onsite support in the form of psychosocial assistance and further management. Therefore, we kindly request your cooperation in facilitating access to clinical psychologists and social workers for study participants who may require additional support during or after their participation in the research study.

By agreeing to this letter, [Name of HIV Care Clinic] commits to:

1. Providing access to clinical psychologists and social workers to offer psychosocial support to research study participants as needed.

2. Ensuring that appropriate measures are in place to address any adverse events that may arise during the study.
3. Collaborating closely with Olivier Mukuku and the research team to coordinate the provision of onsite support and ensure the well-being of participants.

This agreement will remain in effect for the duration of the research study, unless otherwise terminated by mutual agreement.

We appreciate your commitment to supporting this research endeavor and ensuring the ethical conduct of the study. If you have any questions or require further information, please do not hesitate to contact me.

Thank you for your cooperation.

Sincerely,

Dr Olivier Mukuku

Telephone: +[redacted]

Email: [redacted]

Institut Supérieur des Techniques Médicales de Lubumbashi, Democratic Republic of the Congo

APPENDIX F

SYSTEMATIC REVIEW REGISTRATION

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

The magnitude of viral load non-suppression and determinants in children and adolescents on antiretroviral therapy in Sub-Saharan Africa: a systematic review

From	To	Date	Subject
CRD-REGISTER	"[redacted]"	Wed, 2 Aug 2023 23:47:14 +0100	PROSPERO acknowledgement of receipt [451212]

NIHR | National Institute for Health and Care Research

PROSPERO
International prospective register of systematic reviews

Home | About PROSPERO | How to register | Service information Search | My PROSPERO | Logout: **Olivier Mukuku**

Register your review now | Edit your details

You have 1 records

My other records

These are records that have either been published or rejected and are not currently being worked on.

ID	Title	Status	Last edited
CRD42023451212	The magnitude of viral load non-suppression and determinants in children and adolescents on antiretroviral therapy in Sub-Saharan Africa: a systematic review	Registered	14/08/2023

t

APPENDIX G

APPROVAL LETTER FROM THE HUMANITIES & SOCIAL SCIENCES RESEARCH ETHICS COMMITTEE OF THE UNIVERSITY OF KWAZULU-NATAL

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

09 June 2024

Dr Olivier Mukuku (223152330)
School of Applied Human Sc
Howard College Campus

Dear Dr Mukuku,

Protocol reference number: HSSREC/00006817/2024
Project title: Unsuppressed viral load among human immunodeficiency virus-positive children and adolescents on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: magnitude, determinants, barriers, and facilitators.
Degree: PhD

Approval Notification – Full Committee Reviewed Protocol

This letter serves to notify you that your response received on 06 June 2024 to our letter of 15 May 2024 in connection with the above, was reviewed by the Humanities and Social Sciences Research Ethics Committee (HSSREC) and the protocol has been granted **FULL APPROVAL**

Any alteration/s to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach and Methods must be reviewed and approved through the amendment/modification prior to its implementation. In case you have further queries, please quote the above reference number.

PLEASE NOTE: Research data should be securely stored in the discipline/department for a period of 5 years.

Incidents of adverse events and serious adverse events (AEs and SAEs) should be reported in writing to HSSREC, the study sponsors, and any regulatory authority (where appropriate), within 7 working days of the occurrence for local sites and 14 days for all other South African sites.

This approval is valid for one year until 09 June 2025
To ensure uninterrupted approval of this study beyond the approval expiry date, a progress report must be submitted to the Research Office on the appropriate form 2 - 3 months before the expiry date. A close-out report to be submitted when study is finished.

HSSREC is registered with the South African National Health Research Ethics Council (REC-040414-040).

Yours faithfully

[redacted]

.....
Professor Dipane Hlalele (Chair)
/dd

Humanities & Social Sciences Research Ethics Committee
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Tel: +27 31 260 8350 / 4557 / 3587
Website: http://research.ukzn.ac.za/Research-Ethics/

APPENDIX H

APPROVAL LETTER FROM THE HAUT-KATANGA PROVINCIAL MINISTRY OF PUBLIC HEALTH

REPUBLIQUE DEMOCRATIQUE DU CONGO
PROVINCE DU HAUT-KATANGA

MINISTERE DE LA SANTE
ET COORDINATION DES AGENCES
DES NATIONS UNIES
Le Ministre

Lubumbashi, le 12 4 JUIL 2023

N°10.8/ /CAB/MIN.PROV/SANTE&C.O.N.U/HKAT/2023
001257

Transmis copie pour information à :

- Madame l'Inspecteur Provincial de la Santé du Haut-Katanga ;
- Monsieur le Chef de Division Provinciale de la Santé du Haut-Katanga

à LUBUMBASHI

Concerne : **Recommandation de recherches doctorales**

A Monsieur MUKUKU KABIRIKO Olivier,
étudiant à l'Université de Kwazulu Natal,
Durban, en Afrique du Sud,
Numéro d'étudiant : 223152330
à LUBUMBASHI

Monsieur,

Nous accusons bonne réception de votre lettre du 10 juillet 2023, relative à la demande d'une autorisation de faire des recherches dans les formations sanitaires de la Ville de Lubumbashi en rapport avec votre travail de thèse dont le sujet est intitulé « Suppression de la charge virale chez les enfants et adolescents infectés par le VIH à Lubumbashi, RDC : Prévalence, déterminants, barrières et facilitateurs ».

Y faisant suite, **nous vous autorisons de mener vos recherches doctorales** pour une durée d'une année allant du 25 juillet 2023 au 25 juillet 2024.

Nous vous encourageons et vous souhaitons bonne chance car ces recherches seront bénéfiques dans la prise en charge médicale de la communauté de notre province.

Sentiments patriotiques

Pro [redacted]

Adresse : 543, Av. Likasi *Commune de Lubumbashi* *Haut Katanga RDC*
E-mail : [redacted] *Tel : (+*[redacted]

APPENDIX G translated into English

Forwarded a copy for information to:
The Provincial Health Inspector for Haut-Katanga;

The Head of the Provincial Health Division of Haut-Katanga,

In Lubumbashi.
Re: Authorisation for doctoral research
To: Mr MUKUKU KABIRIKO Olivier, student at the University of KwaZuluNatal, Durban, South Africa, Student number: 223152330, in Lubumbashi.
Dear Sir,
We acknowledge receipt of your letter of 10 July 2023, concerning your request for authorizationto carry out doctoral research in the health facilities of the city of Lubumbashi in connection with your thesis on the subject of "Suppression of viral load in HIV-positive children and adolescents in Lubumbashi, DRC: Magnitude, determinants, barriers and facilitators".
We hereby authorize you to carry out your doctoral research for a period of one year, from 25 July 2023 to 25 July 2024.
We encourage you and wish you good luck, as this research will be beneficial to the medical care of the community in our province.
With patriotic sentiments.
Prof Dr Joseph NSAMBI BULANDA

APPENDIX I

APPROVAL LETTER FROM THE MEDICAL ETHICS COMMITTEE OF THE UNIVERSITY OF LUBUMBASHI

REPUBLIQUE DEMOCRATIQUE DU CONGO
UNIVERSITE DE LUBUMBASHI
COMITE D'ETHIQUE MEDICALE
[redacted]

CEM-UNILU

N° Approbation : UNILU/CEM/036/2023

Lubumbashi, le 02/12/2023

Objet : Non suppression de la charge virale chez les enfants et adolescents infectés par le VIH sous thérapie antirétrovirale à Lubumbashi, république démocratique du Congo : ampleur, déterminants, obstacles et facilitateurs.

Cher Mukuku Kabiriko Ollvier ;

Après lecture et examen de votre protocole par le Comité d'Ethique Médicale de l'Université de Lubumbashi (RD Congo).

Ayant revu le protocole susmentionné selon les normes éthiques nationales sur les études impliquant les êtres humains, le Comité a donné son approbation, sur des recommandations suivantes :

1. Respectez les règles de l'éthique médicale notamment en ce qui concerne la confidentialité des résultats individuels des personnes soumis au protocole ;
2. Réservez au Comité d'Ethique Médicale de l'Université de Lubumbashi un exemplaire du travail publié pour l'évaluation du respect de la procédure décrite dans votre protocole.

La présente approbation est valable pour la période allant du 03 décembre 2023 au 02 décembre 2025.

Veuillez agréer, Monsieur, l'expression de ma considération distinguée.

COMITE D'ETHIQUE MEDICALE Administration UNIVERSITE DE LUBUMBASHI

Le Président du Comité d'Ethique Médicale

Prof Dr Luboya Nathan
Président
[redacted]

Comité d'Ethique Médicale

Président
Prof Dr Luboya N. Oscar

1er Vice-Président
Prof Mujinga K. Norbert

2ème Vice-Président
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CT. Dr Kantong W. Gray
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IT. Tshimanga T. Erick

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Prof Dr Wembonyama O
Prof Dr Malengu MPE
Prof Bushabu KP
Prof Ngoy Fiema B.B.
Prof Dr Assumani YNA
Prof Banza LC
Prof Kakudji YP
Prof Dr Mwamba TA
Prof Dr Mbuyi MS
Prof Dr Lutala KT
Prof Kahumba
Prof Kasamba IE

E-mail : comethiqueunilu@gmail.com – Comite.Ethique@unilu.ac.cd
Cliniques Universitaires de Lubumbashi, Pav.5 – Ch.54.

APPENDIX H translated into English

N° approval: UNILU/CEM/036/2023

Subject: Unsuppressed viral load in HIV-positive children and adolescents in Lubumbashi, DRC: Magnitude, determinants, barriers and facilitators".

Dear Mukuku Kabiriko Olivier,

After reading and examination of your protocol by the Medical Ethics Committee of the University of Lubumbashi (DRCongo).

Having reviewed the above-mentioned protocol according to national ethical standards on studies involving human beings, the Committee has given its approval on the following recommendations:

1. Respect the rules of medical ethics, in particular with regard to the confidentiality of the individual results of persons undergoing the protocol;
2. Provide the University of Lubumbashi's Medical Ethics Committee with a copy of your published work for evaluation of compliance with the procedure described in your protocol.

This approval is valid for the period from December3rd, 2023to December 2nd, 2025.

Yours sincerely,

The Chairman of the Medical Ethics Committee

Prof Dr Luboya Numbi Oscar

APPENDIX J

CERTICATES OF TRAINING IN RESEARCH ETHICS

CERTIFICATE OF PARTICIPATION

PRESENTED TO

Olivier Mukuku

for participation in the
Research Ethics in
Practice Workshop

28th to 30th March 2022

[redacted]

Professor Kaymarlin Govender
RESEARCH DIRECTOR

[redacted]

Professor Tim Quinlan
FACILITATOR

HEARD

HEALTH ECONOMICS AND HIV AND AIDS RESEARCH DIVISION

TRREE

Zertifikat
Certificat
Certificado
Certificate

Promouvoir les plus hauts standards éthiques dans la protection des participants à la recherche biomédicale
Promoting the highest ethical standards in the protection of biomedical research participants

Certificat de formation - Training Certificate

Ce document atteste que - this document certifies that

Clinical Trials Centre
The University of Hong Kong

Olivier Mukuku

a complété avec succès - has successfully completed

Module 1 (2023) - Introduction to Research Ethics

du programme de formation TRREE en évaluation éthique de la recherche
of the TRREE training programme in research ethics evaluation

[redacted]

Professeur Dominique Sprumont
Coordinateur TRREE Coordinator

Release Date: 2024/05/23

APPROVED BY SIWF FMH ISFM
Programmes de formation continue (2 crédits)
Continuing Education Programs (2 credits)

Foederatio Pharmaceutica Helvetiae
FPH
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APPENDIX K

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APPENDIX L

FULL SEARCH TERMS OF PAPERS IN PUBMED

("children"[MeSH] OR "infant"[MeSH] OR "adolescent"[MeSH] OR "child"[Title/Abstract] OR "infant"[Title/Abstract] OR "adolescent"[Title/Abstract])

AND

("HIV-positive"[Title/Abstract] OR "HIV"[MeSH] OR "HIV-positive"[Title/Abstract] OR "HIV infection"[Title/Abstract])

AND

("antiretroviral therapy"[MeSH] OR "antiretroviral therapy"[Title/Abstract] OR "ART"[Title/Abstract])

AND

("viral load"[Title/Abstract] OR "virological failure"[Title/Abstract] OR "unsuppressed"[Title/Abstract] OR "viral suppression"[Title/Abstract])

AND

("risk factors"[MeSH] OR "risk factors"[Title/Abstract] OR "determinants"[Title/Abstract] OR "predictors"[Title/Abstract])

AND

("Benin"[Title/Abstract] OR "Burkina Faso"[Title/Abstract] OR "
"Botswana"[Title/Abstract] OR "Burundi"[Title/Abstract] OR "Cameroon"[Title/Abstract] OR "Central African Republic"[Title/Abstract] OR "Chad"[Title/Abstract] OR "Comoros"[Title/Abstract] OR "Congo"[Title/Abstract] OR "Democratic Republic of the Congo"[Title/Abstract] OR "Djibouti"[Title/Abstract] OR "Equatorial Guinea"[Title/Abstract] OR "Eritrea"[Title/Abstract] OR "Eswatini"[Title/Abstract] OR "Ethiopia"[Title/Abstract] OR "Gabon"[Title/Abstract] OR "Gambia"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "Guinea"[Title/Abstract] OR "Guinea-Bissau"[Title/Abstract] OR "Ivory Coast"[Title/Abstract] OR "Kenya"[Title/Abstract] OR "Lesotho"[Title/Abstract] OR "Liberia"[Title/Abstract] OR "Madagascar"[Title/Abstract] OR "Malawi"[Title/Abstract] OR "Mali"[Title/Abstract] OR "Mauritania"[Title/Abstract] OR "Mauritius"[Title/Abstract] OR "Mozambique"[Title/Abstract] OR "Namibia"[Title/Abstract] OR "Niger"[Title/Abstract] OR "Nigeria"[Title/Abstract] OR "Rwanda"[Title/Abstract] OR "Sao Tome and Principe"[Title/Abstract] OR "Senegal"[Title/Abstract] OR "Seychelles"[Title/Abstract] OR "Sierra Leone"[Title/Abstract] OR "Somalia"[Title/Abstract] OR "South Africa"[Title/Abstract] OR "South Sudan"[Title/Abstract] OR "Sudan"[Title/Abstract] OR "Togo"[Title/Abstract] OR "Uganda"[Title/Abstract] OR "United Republic of Tanzania"[Title/Abstract] OR "Zambia"[Title/Abstract] OR "Zimbabwe"[Title/Abstract])

APPENDIX M

FULL SEARCH TERMS OF PAPERS IN WEB SCIENCE

TS=("children" OR "infant" OR "adolescent")

AND

TS=("HIV-positive" OR "HIV" OR "HIV infection")

AND

TS=("antiretroviral therapy" OR "ART")

AND

TS=("viral load" OR "virological failure" OR "unsuppressed" OR "viral suppression")

AND

TS=("risk factors" OR "determinants" OR "predictors")

AND

TS=("Benin" OR "Burkina Faso" OR "Botswana" OR "Burundi" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo" OR "Democratic Republic of the Congo" OR "Djibouti" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Ivory Coast" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Togo" OR "Uganda" OR "United Republic of Tanzania" OR "Zambia" OR "Zimbabwe")

dd

APPENDIX N

FULL SEARCH TERMS OF PAPERS IN SCOPUS

TITLE-ABS-KEY("children" OR "infant" OR "adolescent")

AND

TITLE-ABS-KEY("HIV-positive" OR "HIV" OR "HIV infection")

AND

TITLE-ABS-KEY("antiretroviral therapy" OR "ART")

AND

TITLE-ABS-KEY("viral load" OR "virological failure" OR "unsuppressed" OR "viral suppression")

AND

TITLE-ABS-KEY("risk factors" OR "determinants" OR "predictors")

AND

TITLE-ABS-KEY("Benin" OR "Burkina Faso" OR " Botswana" OR "Burundi" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo" OR "Democratic Republic of the Congo" OR "Djibouti" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Ivory Coast" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome and Principe" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sudan" OR "Togo" OR "Uganda" OR "United Republic of Tanzania" OR "Zambia" OR "Zimbabwe")

APPENDIX O

LIST OF STUDIES EXCLUDED AT FULL-TEXT SCREENING STAGE IN THE SYSTEMATIC REVIEW

N°	Study	Reason
1	Yihun, B. A., Kibret, G. D., & Leshargie, C. T. (2019). Incidence and predictors of treatment failure among children on first-line antiretroviral therapy in Amhara Region Referral Hospitals, northwest Ethiopia 2018: A retrospective study. PloS one, 14(5), e0215300.	Wrong outcomes (Treatment failure was defined as clinical, immunological and virological failure. Virological failure was not available for all patients.)
2	Biney, I. J. K., Kyei, K. A., Ganu, V. J., Kenu, E., Puplampu, P., Manortey, S., & Lartey, M. (2021). Antiretroviral therapy adherence and viral suppression among HIV-infected adolescents and young adults at a tertiary hospital in Ghana. African Journal of AIDS Research, 20(4), 270-276.	Wrong study outcomes (viral suppression was defined by <400 copies/ml)
3	Vaz, P., Augusto, O., Bila, D., Macassa, E., Vubil, A., Jani, I. V., et al. (2012). Surveillance of HIV drug resistance in children receiving antiretroviral therapy: a pilot study of the World Health Organization's generic protocol in Maputo, Mozambique. Clinical infectious diseases, 54(suppl_4), S369-S374.	Wrong design (only children who have HIV drug resistance mutations after 12 months of ART)
4	Ndongo, F. A., Tejiokem, M. C., Penda, C. I., Ndiang, S. T., Ndongo, J. A., Guemkam, G., et al. (2021). Long-term outcomes of early initiated antiretroviral therapy in sub-Saharan children: a Cameroonian cohort study (ANRS-12140 Pediacam study, 2008–2013, Cameroon). BMC pediatrics, 21, 1-11.	Wrong study outcomes (viral suppression was defined by <400 copies/ml)
5	Alibi, M., Mwapasa, V., & Ngwalangwa, F. (2023). Retrospective cohort study comparing antiretroviral treatment outcomes among adolescents in Teen Clubs and Standard Care Clinics: Blantyre, Malawi. Journal of the International Association of Providers of AIDS Care (JIAPAC), 22, 23259582231172340.	Wrong study outcomes (viral failure was defined by >200 copies/ml)
6	Fokam, J., Nangmo, A., Wandum, C., Takou, D., Santoro, M. M., Nlend, A. E. N., et al. (2020). Programme quality indicators of HIV drug resistance among adolescents in urban versus rural settings of the centre region of Cameroon. AIDS research and therapy, 17, 1-10.	Wrong design (only children who have HIV drug resistance)
7	Musoke, P., Szubert, A. J., Musiime, V., Nathoo, K., Nahirya-Ntege, P., Mutasa, K., & ARROW Trial Team. (2015). Single-dose nevirapine exposure does not affect response to antiretroviral therapy in HIV-infected African children aged below 3 years. AIDS, 29(13), 1623-1632.	Wrong study outcomes (viral suppression was defined by <80 copies/ml)
8	Lowenthal, E. D., Marukutira, T., Tshume, O., Chapman, J., Anabwani, G. M., & Gross, R. (2015). Prediction of HIV virologic failure among adolescents using the pediatric symptom checklist. AIDS and Behavior, 19, 2044-2048.	Wrong study outcomes (viral suppression was defined by <400 copies/ml)

9	Ndongo, F. A., Texier, G., Penda, C. I., Tejiokem, M. C., Ndiang, S. T., Ndongo, J. A., et al. (2018). Virologic response to early antiretroviral therapy in HIV-infected infants: evaluation after 2 years of treatment in the Pediacam study, Cameroon. The Pediatric infectious disease journal, 37(1), 78-84.	Wrong study outcomes (viral suppression was defined by <400 copies/ml)
10	Badejo, O., Noestlinger, C., Jolayemi, T., Adeola, J., Okonkwo, P., Van Belle, S., et al. (2020). Multilevel modelling and multiple group analysis of disparities in continuity of care and viral suppression among adolescents and youths living with HIV in Nigeria. BMJ global health, 5(11), e003269.	Wrong study population (aged 10-24 years)
11	Sebunya, R., Musiime, V., Kitaka, S. B., & Ndeezi, G. (2013). Incidence and risk factors for first line antiretroviral treatment failure among Ugandan children attending an urban HIV clinic. AIDS research and therapy, 10, 1-10.	Wrong study outcomes (viral suppression was defined by <2000 copies/ml)
12	Dires, Y. M., Manyazewal, T., & Charlotte, H. (2021). Virological Non-Suppression and Associated Factors Among Adolescents and Youth Living with HIV in Ethiopia: A Facility-Based Case-Control Study. https://doi.org/10.21203/rs.3.rs-1014693/v1	Wrong study population (aged 12-24 years)
13	Gill, M. M., Herrera, N., Guilaze, R., Mussa, A., Dengo, N., Nhangave, A., et al. (2023). Virologic outcomes and ARV switch profiles 2 years after national rollout of dolutegravir to children less than 15 years in southern Mozambique. The Pediatric Infectious Disease Journal, 42(10), 893-898.	Wrong study population (only children on DTG-based regimen)
14	Sisay, M. M., Ayele, T. A., Gelaw, Y. A., Tsegaye, A. T., Gelaye, K. A., & Melak, M. F. (2018). Incidence and risk factors of first-line antiretroviral treatment failure among human immunodeficiency virus-infected children in Amhara regional state, Ethiopia: a retrospective follow-up study. BMJ open, 8(4), e019181.	Wrong outcomes (Treatment failure was defined as clinical and immunological failure.)
15	Miti, S., Handema, R., Mulenga, L., Mwansa, J. K., Abrams, E., Frimpong, C., et al. (2020). Prevalence and characteristics of HIV drug resistance among antiretroviral treatment (ART) experienced adolescents and young adults living with HIV in Ndola, Zambia. PLoS One, 15(8), e0236156.	Wrong study population (aged 15-24 years)
16	Koske, V. C., Otieno, M. O., & Mambo, B. W. (2023). Treatment factors associated with viral suppression among adolescents on antiretroviral therapy in Kenya. World Journal of Advanced Research and Reviews, 2023, 18(03), 1296–1306.	Wrong outcomes (No definition of viral suppression)
17	van Wyk BE, Kriel E, Mukumbang FC. (2020). Two-year viral load suppression among adolescents receiving antiretroviral therapy in the Cape Metropole, South Africa, 2013 - 2015: A retrospective cohort analysis. S Afr Med J, 110(12):1213-1217.	Wrong outcomes (No definition of viral suppression)
18	Kibalama Ssemambo, P., Nalubega-Mboowa, M. G., Owora, A., Serunjogi, R., Kironde, S., Nakabuye, S., et al. (2021). Virologic response of treatment experienced HIV-infected Ugandan children and adolescents on	Wrong study outcomes (viral suppression was defined by <400 copies/ml)

	NNRTI based first-line regimen, previously monitored without viral load. BMC pediatrics, 21, 1-11.	
19	Nasuuna, E., Kigozi, J., Babirye, L., Muganzi, A., Sewankambo, N. K., & Nakanjako, D. (2018). Low HIV viral suppression rates following the intensive adherence counseling (IAC) program for children and adolescents with viral failure in public health facilities in Uganda. BMC public health, 18, 1-9.	Wrong study population (only children and adolescents with viral failure)
20	Devendra, A., Kohler, M., Letsika, M., Khooa, H., Motaboli, L., Lerotholi, M., et al. (2022). HIV viral suppression in children and adolescents two years after transition to dolutegravir: a multicentre cohort study. AIDS, 10-1097.	Wrong outcomes (definition of the outcome: viraemia greater than 50 copies/ml)
21	Chanie ES, Feleke DG, Emiru TD, et al. Viral load undetectable state and predictors among children and adolescents living with HIV in South Gondar, Ethiopia, 2023: an 8-year retrospective cohort study. BMJ Open 2024;14:e083206. doi:10.1136/ bmjopen-2023-083206	Wrong outcomes (definition of the outcome: viraemia greater than 50 copies/ml)
22	Kekitiinwa A, Szubert AJ, Spyer M, Katuramu R, Musiime V, Mhute T, Bakeera-Kitaka S, Senfuma O, Walker AS, Gibb DM; ARROW Trial Team. Virologic Response to First-line Efavirenz- or Nevirapine-based Antiretroviral Therapy in HIV-infected African Children. Pediatr Infect Dis J. 2017 Jun;36(6):588-594. doi: 10.1097/INF.0000000000001505. PMID: 28505015; PMCID: PMC5533213.	Wrong outcomes (definition of the outcome: viraemia greater than 80 copies/ml and 400 copies/ml)
23	Casalini, C., Bateganya, M., Akolo, C., Sanwo, O., Idemudia, A., Nwaokoro, P., ... & Pandey, S. R. (2023). Increasing multimonth dispensing of antiretrovirals and assessing the effect on viral load suppression among children and adolescents receiving HIV services in Nigeria. Plos one, 18(6), e0286303.	Wrong study outcomes (Multimonth dispensing coverage and optimized regimen coverage)
24	Osayi, E. O., Ajayi, O., Onyeji, J., Isichei, M., Sagay, A. S., & Anderson, A. (2024). The prevalence of internalized stigma and its association with HIV viral suppression among fully disclosed adolescents and young adults living with HIV (AYLHIV) receiving HIV care in an HIV clinic in Plateau State, Nigeria. Plos one, 19(5), e0303360.	Wrong study population (aged 10-26 years)
25	Wilson, K., Onyango, A., Mugo, C., Guthrie, B., Slyker, J., Richardson, B., ... & Kohler, P. (2022). Kenyan HIV clinics with youth-friendly services and trained providers have a higher prevalence of viral suppression among adolescents and young adults: results from an observational study. Journal of the Association of Nurses in AIDS Care, 33(1), 45-53.	Wrong study population (aged 10-24 years)
26	Rugemalila, J., Kunambi, P. P., Amour, M., Sambu, V., Kisonjela, F., Rugarabamu, A., ... & Aboud, S. (2024). Trends and correlates in HIV viral load monitoring and viral suppression among adolescents and young adults in Dar es Salaam, Tanzania. Tropical Medicine & International Health, 29(9), 792-800.	Wrong study population (aged 10-24 years)
27	Kangethe, J., Nduati, P., & Mutai, K. (2020). Virological suppression among HIV infected adolescents and youths	Wrong study population (aged 10-24 years)

	receiving ART in the National Teaching and Referral Hospital in Kenya. Clin J HIV AIDS, 4(1), 38-43.	
28	Dow, D. E., & Bartlett, J. A. (2014). Dolutegravir, the second-generation of integrase strand transfer inhibitors (INSTIs) for the treatment of HIV. Infectious diseases and therapy, 3, 83-102.	Wrong outcomes (definition of the outcome: viraemia greater than 400 copies/ml)
29	Nlend, A. E. N., Motaze, A. N., Ndiang, S. T., & Fokam, J. (2017). Predictors of virologic failure on first-line antiretroviral therapy among children in a referral pediatric center in Cameroon. The Pediatric Infectious Disease Journal, 36(11), 1067-1072.	Wrong outcomes (definition of the outcome: viraemia greater than 5,000 copies/ml)
30	Van Dijk, J. H., Sutcliffe, C. G., Munsanje, B., Sinywimaanzi, P., Hamangaba, F., Thuma, P. E., & Moss, W. J. (2011). HIV-infected children in rural Zambia achieve good immunologic and virologic outcomes two years after initiating antiretroviral therapy. PloS one, 6(4), e19006.	Wrong outcomes (definition of the outcome: viraemia greater than 400 copies/ml)
31	Amani-Bosse C, Dahourou DL, Malateste K, Amorissani-Folquet M, Coulibaly M, Dattez S, Emieme A, Barry M, Rouzioux C, N'gbeche S, Yonaba C, Timité-Konan M, Mea V, Ouédraogo S, Blanche S, Meda N, Seguin-Devaux C, Leroy V. Virological response and resistances over 12 months among HIV-infected children less than two years receiving first-line lopinavir/ritonavir-based antiretroviral therapy in Cote d'Ivoire and Burkina Faso: the MONOD ANRS 12206 cohort. J Int AIDS Soc. 2017 Apr 25;20(1):21362.	Wrong outcomes (definition of the outcome: viraemia greater than 500 copies/ml)
32	Njuguna, I., Neary, J., Mburu, C., Black, D., Beima-Sofie, K., Wagner, A. D., ... & John-Stewart, G. (2020). Clinic-level and individual-level factors that influence HIV viral suppression in adolescents and young adults: a national survey in Kenya. Aids, 34(7), 1065-1074.	Wrong study population (aged 10-24 years)
33	Umar, E., Levy, J. A., Bailey, R. C., Donenberg, G., Hershow, R. C., & Mackesy-Amiti, M. E. (2019). Virological non-suppression and its correlates among adolescents and young people living with HIV in Southern Malawi. AIDS and Behavior, 23, 513-522.	Wrong study population (aged 13-24 years)
34	Nsanzimana, S., Rwibasira, G. N., Malamba, S. S., Musengimana, G., Kayirangwa, E., Jonnalagadda, S., ... & Justman, J. E. (2022). HIV incidence and prevalence among adults aged 15-64 years in Rwanda: Results from the Rwanda Population-based HIV Impact Assessment (RPHIA) and District-level Modeling, 2019. International Journal of Infectious Diseases, 116, 245-254.	Wrong outcomes (definition of the outcome: viraemia greater than 400 copies/ml)
35	Puga, D., Cerutti, B., Molisana, C., Bader, J., Faturiyele, O., Ringera, I., ... & Labhardt, N. D. (2016). Still far from 90-90-90: virologic outcomes of children on antiretroviral therapy in nurse-led clinics in Rural Lesotho. The Pediatric infectious disease journal, 35(1), 78-80.	Wrong outcomes (definition of the outcome: viraemia greater than 80 copies/ml)

SAMPLE SIZE CALCULATION BASED ON DETERMINANTS OF UNSUPPRESSED VIRAL LOAD

To calculate the required sample size for the second objective—identifying determinants of unsuppressed viral load (USVL)—we relied on proportions derived from previous studies that reported significant associations with adherence (Abera et al., 2023), ART side effects (Gachoka et al., 2025), and WHO clinical stage (Sibhat et al., 2020). The calculations were performed using **Stata 16**, applying the following syntax:

power twoproportions p1, test(chi2) effect(oratio) oratio(2)

The Fleiss formula for two independent proportions was applied using the following assumptions:

- Confidence level: 95%
- Power: 80%
- Ratio of unexposed to exposed: 1
- Two-sided test

The following determinants were used to estimate the minimum sample size:

Table S1. Sample size calculation for second objective based on selected determinants of USVL

Determinant	Exposure Category	Reference study	*p1* (n/N in unexposed group)	OR assumed	Estimated *p2*	Power	Alpha	Total Sample Size
Adherence	Poor adherence	Abera et al. (2023)	9.4% (40/425)	2.0	17.2%	80%	5%	596
ART side effects	Reported side effects	Gachoka et al. (2025)	9.6% (22/230)	2.0	17.5%	80%	5%	586
WHO clinical stage	Advanced stage (III & IV)	Sibhat et al. (2020)	17.9% (66/369)	2.0	30.4%	80%	5%	368

p1 corresponds to the proportion of unsuppressed viral load in the unexposed group, while *p2* is derived based on the assumed odds ratio of 2.

These calculations support the adequacy of our final sample size (n = 847), which far exceeds the minimum required for robust multivariable modeling.

References

Abera NM, Alemu TG, Agegnehu CD. Incidence and predictors of virological failure among HIV infected children and adolescents on first-line antiretroviral therapy in East Shewa hospitals, Oromia Region, Ethiopia: A retrospective follow up study. *PLoS One*. 2023;18(11):e0289095. https://doi.org/10.1371/journal.pone.0289095

Gachoka LN, Njoroge A. Viral load monitoring practices and correlates of viral non-suppression among children and young adolescents living with HIV in Kiambu County, Kenya. *SAGE Open Pediatr*. 2025;12:30502225251311664.

Sibhat M, Kassa M, Gebrehiwot H. Incidence and predictors of treatment failure among children receiving first-line antiretroviral treatment in general hospitals of two zones, Tigray, Ethiopia, 2019. *Pediatr Health Med Ther*. 2020;11:85–94.

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LOGISTIC REGRESSION MODEL PERFORMANCE FOR VIRAL LOAD SUPPRESSION

Table S2. Classification Table

	Unsuppressed viral load (D ≠ 0)	Suppressed viral load (D = 0)	**Total**
Predicted Positive (+)	180	28	208
Predicted Negative (–)	29	610	639
Total	209	638	847

Table S3. Diagnostic performance metrics of the model

Metric	**Value**
Sensitivity (Pr(+D))	86.12%
Specificity (Pr(–~D))	95.61%
Positive Predictive Value (Pr(D+))	86.54%
Negative Predictive Value (Pr(~D–))	95.46%
False Positive Rate (Pr(+~D))	4.39%
False Negative Rate (Pr(–D))	13.88%
False Positive Rate for Classified Positive (Pr(~D+))	13.46%
False Negative Rate for Classified Negative (Pr(D–))	4.54%
Correctly Classified	93.27%

1° Model overview

- Number of observations: 847
- Area under the ROC curve (AUC): 0.9699
- Pseudo R^2: 0.6745
- Log likelihood: –154.055
- Likelihood ratio Chi^2 (2 df): 638.39
- p-value: < 0.0001

2° Hosmer-Lemeshow goodness-of-fit test

- Number of groups: 10
- Chi^2 (df = 8): 3.01
- p-value: 0.9340

Interpretation: The high p-value indicates a good fit; there is no significant difference between observed and predicted probabilities.

3° Link test for model specification

Table S4. Linktest results for model specification

Predictor	Coefficient	Std. Error	z	p-value	95% CI
_hat	0.970	0.074	13.14	<0.001	[0.825, 1.114]
_hatsq	–0.024	0.028	–0.86	0.391	[–0.079, 0.031]
_cons	0.114	0.206	0.55	0.581	[–0.290, 0.518]

Interpretation: The significant _hat and non-significant _hatsq indicate no model specification error.

4° Sensitivity/Specificity curve and ROC curve

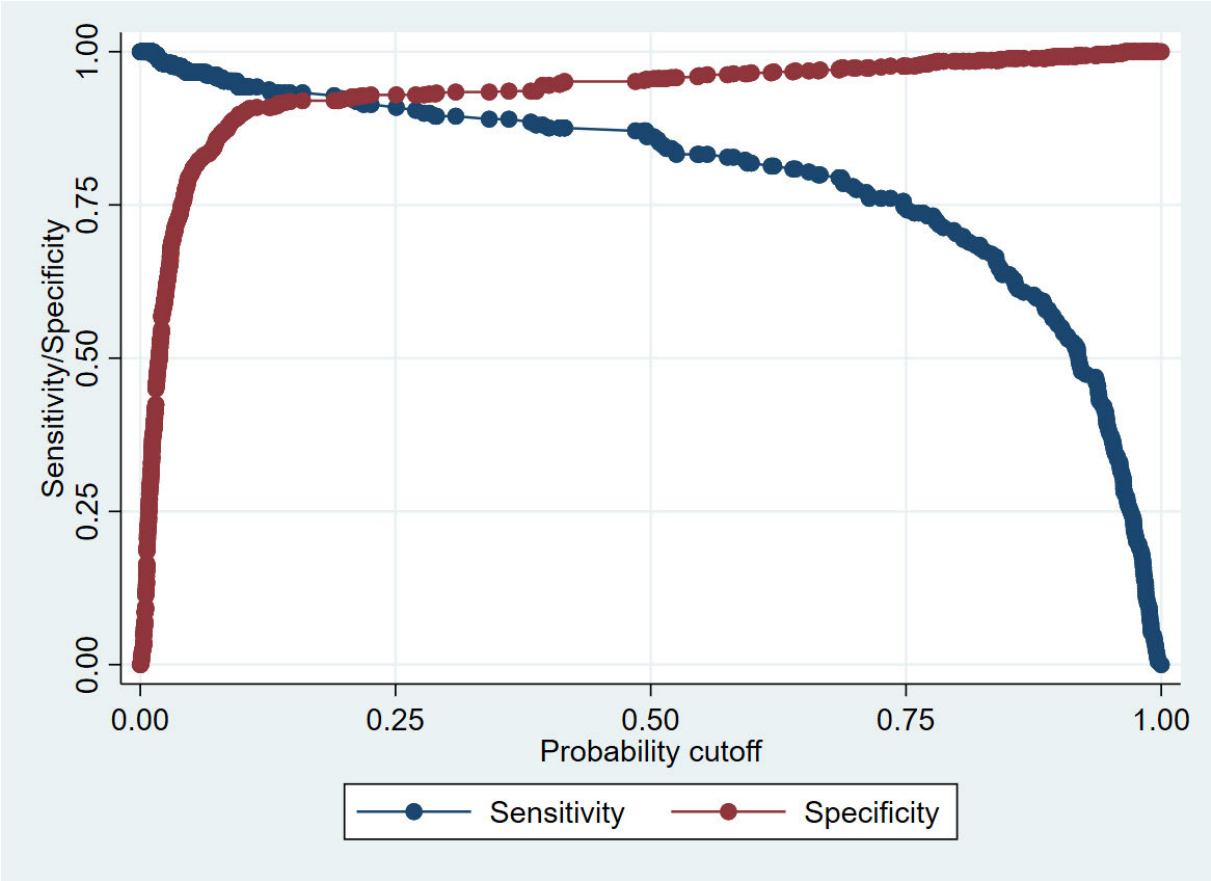

Figure S1. Model performance metrics for distinguishing children and adolescents living with HIV with suppressed and unsuppressed viral load

nn

The ROC curve showing the model's discrimination ability (AUC = 0.9699) has been included below:

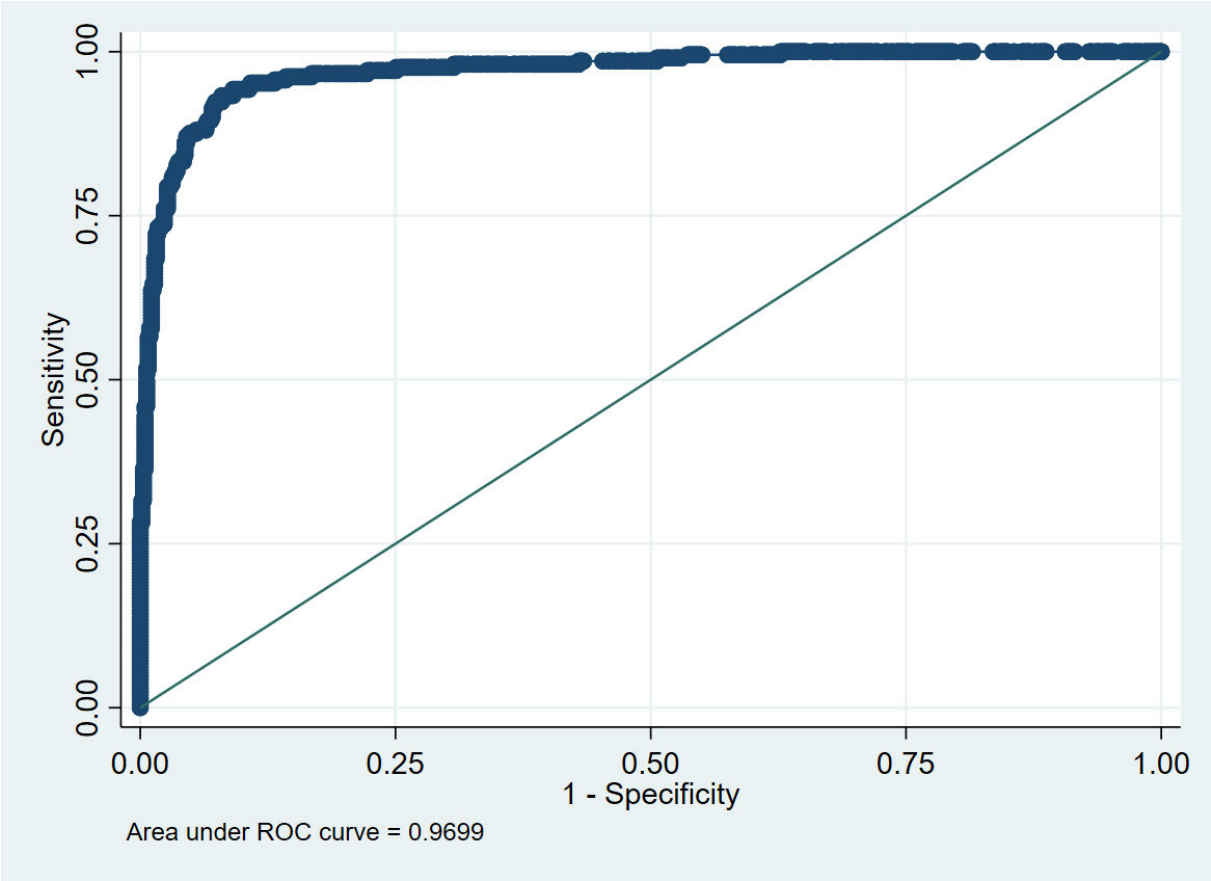

Figure S2: ROC curve for logistic model predicting unsuppressed viral load

Table S5. Variance Inflation Factor (VIF) for independent variables

Variable	Category	VIF	1/VIF
CALHIV's age	5-9 years	6.15	0.1627
	10-14 years	7.36	0.1359
	15-19 years	10.37	0.0965
CALHIV's educational level	Primary	4.88	0.2048
	Secondary	5.87	0.1705
	Higher/University	2.25	0.4444
Currently living with/in	A non-parent family member	2.10	0.4752
	Adoptive parents	2.14	0.4674
	Group housing	1.35	0.7428
Orphan status	At least one biological parent died	1.46	0.6848
	Double orphan	2.87	0.3485
Caregiver's age	≥40 years	1.74	0.5737
Caregiver's sex	Male	1.29	0.7741
Caregiver's HIV status	Negative	2.09	0.4787
	Unknown	1.96	0.5104
Caregiver's marital status	Married	1.22	0.8184
HIV infection route	Horizontal	1.53	0.6550
HIV status disclosure to CALHIV	Yes	2.23	0.4492
HIV status disclosure to others	No	1.17	0.8567
WHO clinical stage	3-4	3.63	0.2752
Nutritional status	Moderate/ Severe malnutrition	1.63	0.6122
History of TB in the last 6 months	Yes	3.62	0.2764
Isoniazid prophylaxis	No	1.42	0.7066
ART adherence	Poor/Fair	2.08	0.4809
History of ART interruption since ART initiation	Yes	1.32	0.7578
ART-induced side effects	Yes	1.76	0.5680
ART duration	6-24 months	1.41	0.7079
	25-48 months	1.20	0.8338
Current ART regimen	Nevirapine based regimen	1.34	0.7475
	Efavirenz based regimen	1.40	0.7128
Mean		**2.69**	

Multicollinearity diagnostics showed no concerning levels of collinearity among the independent variables, with a mean Variance Inflation Factor (VIF) of 2.69—well below the commonly accepted threshold of 10.

Magnitude and characteristics of unsuppressed HIV viral load in children and adolescents on antiretroviral therapy in sub-Saharan Africa: a systematic review and meta-analysis

Olivier Mukuku, Kaymarlin Govender, Stanislas Okitotsho Wembonyama, Yannick Nkiambi Kiakuvue

Summary

Background HIV/AIDS remains a major health issue in sub-Saharan Africa, especially among children and adolescents, with a substantial proportion of people with HIV having unsuppressed viral loads despite the availability of antiretroviral therapy (ART), complicating efforts to manage and control the epidemic. We aimed to estimate the prevalence of unsuppressed viral load and identify the factors contributing to this issue among children and adolescents living with HIV on ART in sub-Saharan Africa.

Methods In this systematic review and meta-analysis, we assessed data from Web of Science, Google Scholar, Scopus, PsycINFO, Embase, PubMed (MEDLINE), EBSCOhost Research Databases, and Wiley Online Library, as well as grey literature searches. We included studies published between Jan 1, 2010, and Nov 30, 2024 that focused on children and adolescents (aged <20 years) on ART in sub-Saharan Africa and reported on factors related to viral load suppression, defined by a viral load of less than 1000 copies per mL. Eligible studies included observational and interventional designs. Data appraisal and extraction were conducted by two independent reviewers from the author group, with summary data extracted from published reports. The primary outcome assessed was the prevalence of unsuppressed viral loads, with meta-analysis performed using STATA software to calculate prevalence and associated factors. The study is registered with PROSPERO (CRD42023451212).

Findings From an initial 13 121 identified articles, 52 studies involving 169 949 children and adolescents on ART met the inclusion criteria. Prevalence of unsuppressed viral load among children and adolescents in sub-Saharan Africa was 26·47% (95% CI 23·06–29·87); specifically, 26·01% (20·51–31·52) for studies in children (<15 years), 24·76% (17·36–32·16) for studies in adolescents (10–19 years), and 28·52% (23·33–33·72) for studies in a combined group of children and adolescents. Factors associated with unsuppressed viral load included younger age (<5 years), male sex, rural residence, orphan status, attendance at a level 1 or 2 health-care facility, HIV status not disclosed, poor ART adherence, advanced WHO clinical stage of HIV, low CD4 cell counts, history of opportunistic infections, nevirapine-based treatment regimen, drug substitution history, and not receiving co-trimoxazole prophylaxis. This meta-analysis showed a significant heterogeneity across the included studies, as evidenced by I^2=99·66% and p<0·0001.

Interpretation Unsuppressed viral load among children and adolescents is a key concern in sub-Saharan Africa, and is influenced by sociodemographic, clinical, immunological, and treatment-related factors. Addressing these issues through targeted interventions and improved ART adherence strategies is crucial for better health outcomes.

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Introduction

The scourge of HIV/AIDS has been one of the most daunting health challenges of the past few decades.[1] Antiretroviral therapy (ART) has transformed HIV from a fatal disease into a manageable condition, improving survival and quality of life for millions of people.[2] However, the fight continues, especially in sub-Saharan Africa, which bears two-thirds of the global HIV burden, underscoring the need for effective ART management.[3]

In 2023, 1·4 million (95% CI 1·1–1·7 million) of the 39·9 million people living with HIV globally were children younger than 15 years old.[3] Sub-Saharan Africa accounted for approximately 66% of all HIV cases and 86% of children younger than 15 years living with HIV worldwide.[3] Around 590 000 (430 000–920 000) children aged 0–14 years living with HIV did not have access to ART in 2023.[3] ART coverage among adolescents and adults aged 15 years and older was 77% (95% CI 62–90), but only 57% (41–75) among children younger than 15 years, with even lower viral load suppression rates: 48% (39–60) for children compared with 73% (66–81) for adolescents and adults. The persistent gaps in early diagnosis and access to effective treatment led to approximately 76 000 (53 000–110 000) child deaths in 2023, with 73% of these occurring in children younger than 10 years. Despite representing just 3% of people

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Prevalence and determinants of unsuppressed HIV viral loads among children and adolescents living with HIV on antiretroviral therapy in Lubumbashi, Democratic Republic of the Congo: a retrospective cross-sectional study

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ABSTRACT

Background Despite global improvements in antiretroviral therapy (ART) access for children and adolescents living with HIV (CALHIV), a significant proportion continue to experience unsuppressed viral load (USVL). Limited studies focus on the factors contributing to USVL among CALHIV in the Democratic Republic of the Congo (DRC), especially in the context of evolving treatment landscapes. Understanding these determinants is crucial for enhancing ART outcomes.

Objective This study aimed to determine the prevalence of USVL and identify factors associated with USVL among CALHIV receiving ART in Lubumbashi, DRC.

Design A multicentre retrospective cross-sectional study was conducted. Data were gathered using an observational checklist based on assessing patient file data and entered into Microsoft Excel. Analysis was performed using STATA V.16. Variables with a p value of 0.20 from the bivariable analysis were included in a multivariable logistic regression model, and significant variables ($p<0.05$) were retained in the final model.

Setting and participants The study was conducted at 21 HIV care clinics in Lubumbashi from June to September 2024. It included 847 CALHIV aged 0–19 years who had been on ART for at least 6 months and had at least one available VL result.

Primary outcome measure The rate of USVL among CALHIV, defined as achieving a VL below 1000 copies/mL, in those who had been on ART for at least 6 months.

Results The prevalence of USVL among CALHIV was 24.68% (209/847; 95% CI: 21.89% to 27.69%). Multivariable logistic regression analysis revealed that CALHIV with married caregivers were more likely to have USVL (adjsuted OR, aOR=2.4; 95% CI: 1.2 to 5.0). Other factors associated with USVL included horizontal HIV transmission (aOR=2.3; 95% CI: 1.0 to 5.2), advanced WHO clinical stages (aOR=3.5; 95% CI: 1.0 to 13.7), poor/fair ART adherence (aOR=107.8; 95% CI: 50.3 to 231.1) and ART-induced side effects (aOR=3.8; 95% CI: 1.9 to 7.9).

Conclusions The high rate of USVL among CALHIV in Lubumbashi highlights the need to strengthen ART adherence support, manage treatment side effects and improve early diagnosis and follow-up, particularly for those infected through horizontal transmission or presenting with advanced clinical stages. Special attention should also be given to caregiver-related factors, including marital status, which may influence treatment outcomes.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Use of standardised questionnaires: The use of a validated questionnaire ensured the consistency and comparability of responses, reinforcing the reliability of the results obtained.

⇒ Representative children and adolescents living with HIV (CALHIV) sample: The study focuses on a vulnerable group, CALHIV, providing valuable information on a subgroup often under-represented in research, particularly in sub-Saharan Africa.

⇒ Cross-sectional design limitation: The study uses a cross-sectional design, which limits the ability to establish causality between the identified determinants and the outcome, unsuppressed viral loads.

⇒ Geographical limitation: The study's focus on Lubumbashi restricts the generalisability of the findings. Differences in healthcare systems, socioeconomic factors and cultural contexts across other regions of the Democratic Republic of the Congo or sub-Saharan Africa may yield different results.

⇒ Lack of qualitative exploration: The study did not account for factors like mental health, psychosocial support or economic status, nor did it include a qualitative component to explore social, psychological and cultural barriers such as stigma and healthcare access, which could have impacted antiretroviral therapy adherence and viral load suppression.

PLOS ONE

RESEARCH ARTICLE

Barriers and facilitators to HIV viral load suppression among adolescents living with HIV in Lubumbashi, Democratic Republic of the Congo: A qualitative study

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Abstract

Background

Antiretroviral therapy (ART) has been pivotal in improving the lives of adolescents living with HIV (ALHIV) globally. However, achieving and maintaining viral load suppression (VLS) among ALHIV remains a significant challenge, with difficulties reported in various settings, including places like Lubumbashi, in the Democratic Republic of the Congo. Despite the availability of ART, several barriers to optimal ART adherence and achieving VLS persist among this population. This qualitative study aimed to explore the factors influencing ART adherence and achieving VLS among ALHIV in Lubumbashi.

Methods

In-depth interviews were conducted with 39 ALHIV (22 female, 17 male) receiving ART and 14 caregivers (9 female, 5 male) participating in their treatment. ALHIV were purposively selected based on criteria including being HIV-positive, on ART, informed of their HIV status, and aged 13-19 years. Caregivers were purposively sampled based on their involvement in the treatment and care of the ALHIV. Focus group discussions were held with 16 healthcare workers (HCWs) (10 female, 6 male), including doctors, nurses, and pharmacists, who had at least one year of experience caring for ALHIV in the selected clinics. The sessions were audio-recorded, transcribed, and analyzed using a thematic approach to identify recurring themes and patterns. Data analysis was guided by the socioecological model, examining factors at the individual, interpersonal, health service-related, and community levels. NVivo 14 software was used for data management and analysis.

Results

The key barriers to achieving VLS identified included economic challenges, stigma and discrimination, forgetfulness, and a lack of family support. Factors such as strong social