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MSc in Epidemiology & Biostatistics

PROJECT REPORT

Determinants of Virologic Failure and Prevalence of Resistance Mutations among Human Immunodeficiency Virus (HIV) - Infected Children and Adolescents Aged 18 Months to 18 Years on Antiretroviral Therapy at Livingstone Teaching Hospital, Zambia

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Date of Submission: 20/01/2026

Acceptance

ACCEPTANCE CERTIFICATE

This dissertation, entitled "Determinants of virologic failure and prevalence of resistance mutations among Human Immunodeficiency Virus (HIV) - infected children and adolescents aged 18 months to 18 years on antiretroviral therapy at Livingstone Teaching Hospital," was prepared and submitted by Jones Mwewa in partial fulfillment of the requirements for the Master's degree in Epidemiology & Biostatistics, and is hereby accepted.

Supervisor's name: Dr Steward Mudenda

Signature: 

Date: 19th January 2026

Declaration

I, Jones Mwewa, declare that this dissertation is my own original work and that it has not been submitted to any other institution for the award of a degree or qualification. All sources of information used have been duly acknowledged.

Signature: 

Date: 19th January 2026

Dedication

This dissertation is dedicated to my family for their constant encouragement, patience, and support throughout my academic journey. I also dedicate this work to all children and adolescents living with HIV, whose experiences continue to inspire efforts toward improving HIV care and treatment outcomes.

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I would like to express my sincere gratitude to my supervisor, Dr. Steward Mudenda, for the guidance, support, and feedback provided throughout the development of this dissertation. I am grateful to the School of Postgraduate Studies, University of Lusaka, for providing the academic environment that made this study possible.

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Definition of Key Terms

Adherence: is the extent to which a patient/client acts in accordance with the prescribed interval and dose of a dosing regimen (Specialist Pharmacy Service, 2023).

Antiretroviral therapy: is an HIV treatment that uses a combination of two or more antiviral drugs to achieve viral load suppression (Cleveland Clinic, 2023).

Cumulative incidence: a proportion that estimates the risk of individuals who will experience an event or develop a disease during a specified period (VEDANTU, n.d.).

Disease determinants: a group of variables, such as specific disease agents and environmental factors, that directly or indirectly influence the frequency or distribution of a disease (Australian Institute of Health and Welfare, 2024)

Drug resistance refers to a state in which cancer cells or microorganisms, such as bacteria or viruses, fail to respond to a drug that is typically effective in killing or weakening them (EBSCO Information Services, Inc. | www.ebsco.com, 2023).

Infection: the invasion and growth of microorganisms in the body (Felman, 2020).

Mutation: is an alteration in the genetic material (genome) of cells of a living organism or virus that is more or less permanent and can be transmitted to the cell or virus's descendants (Gilchrist, 2019).

Prevalence: this is the number of affected persons present in the population at a specific time divided by the number of persons in the population at that time (www.sciencedirect.com, n.d.).

Viral load: is the amount of Human Immunodeficiency Virus in the blood of a host (MedlinePlus, 2022).

Abbreviations

- Antiretroviral therapy - (ART)
- Children and adolescents living with HIV (CALHIV)
- Differentiated Service Delivery (DSD)
- Dolutegravir (DTG)
- Enhanced Adherence Counseling - (EAC)
- Highly Active Antiretroviral Therapy - (HAART)
- Health Belief Model - (HBM)
- Health Research Authority - (NHRA)
- High Efficacy of Dolutegravir - (INSTIs)
- Human Immunodeficiency Virus - (HIV)
- Integrase Strand Transfer Inhibitor – (INSTI)
- Livingstone Teaching Hospital - (LTH)
- Non-Nucleoside Reverse Transcriptase Inhibitor – (NNRTI)
- Nucleoside Reverse Transcriptase Inhibitor – (NRTI)
- Protease Inhibitor – (PI)
- Social Ecological Model - (SEM)
- Tenofovir - (TDF)
- Virologic Failure - (VF)

Abstract

Virologic failure is a major challenge in the management of Human Immunodeficiency Virus (HIV) among children and adolescents on antiretroviral therapy (ART). This study aimed to identify the prevalence of virologic failure, identify its determinants, and describe the pattern of HIV drug resistance mutations among HIV-infected children and adolescents aged 18 months to 18 years receiving ART at Livingstone Teaching Hospital.

A facility-based cross-sectional study was conducted among 418 children and adolescents living with HIV. Virologic failure was defined as a viral load of ≥1,000 copies/mL. Data on socio-demographic, socio-economic, and clinical characteristics were collected from medical records and patient interviews. Logistic regression analysis was used to identify factors associated with virologic failure. Genotypic resistance testing was performed among participants with virologic failure to assess resistance mutations.

The prevalence of virologic failure was 19.14%. Poor adherence to ART was the strongest predictor of virologic failure, with affected participants having significantly higher odds of failure. Adolescents were more likely to experience virologic failure compared to younger children. Low caregiver income and food insecurity were also independently associated with virologic failure. Drug resistance analysis showed no major NRTI resistance mutations, while NNRTI resistance mutations were common, particularly the K103N mutation. Resistance to integrase strand transfer inhibitors was rare.

In conclusion, virologic failure among children and adolescents at Livingstone Teaching Hospital was mainly driven by poor adherence and socio-economic vulnerability rather than widespread drug resistance. Strengthening adherence support, implementing adolescent-friendly HIV services, and integrating socio-economic and nutritional support into HIV care are critical to improving treatment outcomes in this population.

CHAPTER ONE – Introduction

1.1 Background

The introduction of antiretroviral therapy (ART) fundamentally changed the trajectory of the Human Immunodeficiency Virus (HIV) infection, allowing children living with the virus to survive into adolescence and adulthood (Mutanga et al., 2019). Antiretroviral therapy (ART) aimed to suppress viral replication, restore immune function, and prevent morbidity and mortality (WHO, 2021). Among Antiretroviral therapy (ART) outcomes, virologic suppression is the cornerstone, as failure to achieve or sustain suppression leads to immunological decline, opportunistic infections, and the emergence of drug-resistant virus strains (UNAIDS, 2022).

Globally, children and adolescents remained disproportionately affected by gaps in Human Immunodeficiency Virus (HIV) treatment outcomes. By 2021, an estimated 1.7 million children aged 0–14 years were living with the Virus, with 160,000 new infections and 98,000 deaths in this age group (UNICEF, 2021). In sub-Saharan Africa, which bears over 80% of the global burden of pediatric Human Immunodeficiency Virus (HIV) virologic failure among children and adolescents was widespread, ranging between 20% and 35% in several studies (Bernheimer et al., 2015).

In Zambia, despite making substantial progress in combating Human Immunodeficiency Virus (HIV), Children and adolescents continued to lag behind adults, with earlier estimates suggesting that only about 53% of Human Immunodeficiency Virus (HIV) infected children achieved viral suppression (Cai et al., 2023). Adolescents in particular faced elevated risks of non-adherence, disengagement from care, and treatment failure compared to younger children and adults (Mutanga et al., 2019). To address these disparities, Zambia introduced Dolutegravir (DTG)-based regimens into pediatric and adolescent treatment guidelines in 2020. Dolutegravir (DTG) is a potent integrase inhibitor with a high barrier to resistance, a favorable side-effect profile, and once-daily dosing, making it suitable for adolescents who struggle with adherence (Turkova et al., 2021).

Livingstone Teaching Hospital (LTH) – Centre of Excellence is a referral hub for Southern Province, serving both urban and rural populations. The hospital provides specialized pediatric and adolescent Human Immunodeficiency Virus (HIV) services, with programmatic support from national and international partners. Despite its advanced infrastructure, several barriers compromised outcomes for children and adolescents, such as socio-economic hardship,

Geographic barriers, Cultural beliefs and stigma and adolescent-specific challenges including peer pressure and mental health issues. (Zambia MoH, 2020). Even with the DTG rollout, pediatric HIV treatment outcomes remained under pressure. Evidence suggested that multiple interlinked determinants, ranging from socio-economic and cultural barriers to clinical and ART-related issues, contributed to virologic failure and resistance mutations among children. Therefore, despite infrastructure and expertise, challenges such as poverty, food insecurity, transportation barriers, traditional medicine practices, faith healing, and stigma affect adherence and contribute to virologic failure (Moomba & Van Wyk, 2019). These contextual issues underscore the importance of evaluating treatment outcomes during the DTG era (2021–2024). Understanding determinants of virologic failure and the prevalence of resistance mutations in children during the DTG era is critical to strengthening pediatric HIV treatment outcomes in this high-burden setting. Studying these determinants within the context of Livingstone Teaching Hospital during the DTG era (2021–2024) is critical to improving pediatric outcomes and sustaining Zambia's progress toward epidemic control. Therefore, this study investigated the determinants of virologic failure and prevalence of resistance mutations among Human Immunodeficiency Virus (HIV)-infected children and adolescents aged 18 months to 18 years on antiretroviral therapy at Livingstone Teaching Hospital.

1.2 Statement of the Problem

Despite global and national progress in scaling up dolutegravir-based ART, virologic failure among children and adolescents remained a critical public health challenge. The consequences of failure are severe. While adult populations in Zambia have been relatively well-studied, there was a significant knowledge gap regarding the prevalence and determinants of virologic failure among children and adolescents, as well as the resistance mutations that arise under DTG-based regimens. Livingstone Teaching Hospital – Centre of Excellence serves as a referral hub for paediatric Human Immunodeficiency Virus care in Southern Province. However, no systematic study was done to determine the extent of virologic failure and the patterns of resistance mutations in children and adolescents during the DTG era (2021–2024). Without such evidence, health workers lacked the data required to tailor adherence interventions, pick effective regimens, and inform policy on paediatric HIV management.

This research, therefore, addressed a critical gap in knowledge by investigating the determinants of virologic failure and characterizing resistance mutations in this vulnerable group. Findings contributed to enhancing clinical management, programmatic planning, and national HIV control efforts in Zambia.

1.3 Justification of the Study

Despite significant advancement in the scale-up of antiretroviral therapy (ART), virologic failure among children and adolescents living with HIV was a major public health challenge, particularly in low and middle-income countries. Children and adolescents represented a unique population with distinct social, biological, and behavioral vulnerabilities that can negatively affect treatment outcomes. In Zambia, limited local evidence existed on the combined influence of socio-demographic, clinical, socio-economic, and behavioural factors on virologic failure among this age group.

Livingstone Teaching Hospital provides HIV care to a large paediatric and adolescent population. However, the routine programme data collected were often insufficient to verify why some patients fail to achieve viral suppression. In addition, there was little or no documentation on the prevalence and patterns of HIV drug resistance mutations among children and adolescents experiencing virologic failure in this setting. Without the information, clinicians and programme managers can face challenges in making timely and informed treatment decisions.

This study therefore provides local, evidence-based data on the determinants of virologic failure and the prevalence of resistance mutations among HIV-infected children and adolescents. The findings will inform targeted interventions to enhance adherence, guide clinical management, strengthen adolescent HIV services, and support policy formulation aimed at achieving sustained viral suppression and improved health outcomes in this vulnerable population.

1.4 Research Aim and Objectives

1.4.1 Research Aim

To investigate the determinants of virologic failure and prevalence of resistance mutations among Human Immunodeficiency Virus (HIV)-infected children and adolescents aged 18 months to 18 years on antiretroviral therapy at Livingstone Teaching Hospital – Centre of Excellence during the DTG era (2021–2024).

1.4.2 Specific objectives

I. To identify socio-economic determinants (e.g., caregiver income, food security, distance to clinic, caregiver/adolescent education level) associated with virologic failure among Human Immunodeficiency Virus (HIV)-infected children and adolescents at Livingstone Teaching Hospital.

II. To determine clinical and ART-related factors (e.g., antiretroviral therapy regimen type, adherence patterns, treatment duration, co-infections, history of antiretroviral therapy switch) associated with virologic failure in children and adolescents on DTG-based ART regimens.

III. To establish the prevalence and mutation profiles of Human Immunodeficiency Virus (HIV) drug resistance among children and adolescents with confirmed virologic failure at Livingstone Teaching Hospital.

IV. To compare virologic outcomes between children (18 months–14 years) and adolescents (15–18 years) to determine age-related differences in treatment failure and resistance patterns.

1.5 Research Questions

1. What is the prevalence of virologic failure among HIV-infected children and adolescents aged 18 months to 18 years receiving antiretroviral therapy at Livingstone Teaching Hospital?

2. What socio-demographic, socio-economic, and clinical factors are associated with virologic failure among children and adolescents on ART?

3. Is adherence to antiretroviral therapy associated with virologic failure among HIV-infected children and adolescents?

4. What is the prevalence and pattern of HIV drug resistance mutations among children and adolescents experiencing virologic failure at Livingstone Teaching Hospital?

1.6 Scope of the Study

This study was conducted at Livingstone Teaching Hospital in Southern Province, Zambia. It focuses on HIV-infected children and adolescents aged 18 months to 18 years who receive antiretroviral therapy at the facility. The study assesses socio-demographic, socio-economic, and clinical factors associated with virologic failure, as well as patterns of HIV drug resistance mutations among participants with unsuppressed viral load.

The study is limited to patients attending Livingstone Teaching Hospital and therefore did not fully represent children and adolescents receiving HIV care in other health facilities. The cross-sectional design also limits the ability to establish causal relationships. However, the findings provide important insight into treatment outcomes and challenges within the study setting and will be relevant for informing local HIV programme improvements.

CHAPTER TWO - Literature Review

2.1 Introduction

This chapter reviewed existing literature related to virologic failure and resistance mutations among children and adolescents living with Human Immunodeficiency Virus (HIV). The review is structured to align with the study objectives, covering global, regional, national, and local contexts. The literature highlights socio-economic, clinical, and antiretroviral therapy (ART)-related determinants of virologic failure; the prevalence and patterns of resistance mutations; and differences between children and adolescents.

2.2 Global Perspective

Globally, children and adolescents remained disproportionately affected by Human Immunodeficiency Virus (HIV). In 2021, an estimated 1.7 million children aged 0–14 years were living with Human Immunodeficiency Virus (HIV), while adolescents aged 15–18 years contributed substantially to AIDS-related deaths (UNAIDS, 2022; UNICEF, 2021). ART coverage among children lags behind adults; only 52% of children had access to ART compared to 76% of adults (WHO, 2021). Several studies reported virologic failure rates of 20–35% in adolescents across diverse settings (Bernheimer et al., 2015; Boerma et al., 2017). Factors contributing to this include poor adherence, treatment fatigue, psychosocial distress, transition challenges, and limited youth-friendly services (Nachega et al., 2016; Crowell et al., 2020). Drug resistance in children is a major threat: estimates suggested up to 50% of children experiencing failure harbor NNRTI resistance mutations (Clutter et al., 2016). Children and adolescents living with HIV represent a significant proportion of the HIV burden, particularly in sub-Saharan Africa. Despite expanded access to ART, viral suppression rates among this population remained lower compared to adults. Children and adolescents faced unique challenges related to growth, development, dependence on caregivers, and disclosure of HIV status, stigma, and long-term treatment fatigue.

2.3 Regional Perspective: Sub-Saharan Africa

In sub-Saharan Africa, poverty and food insecurity remained the primary drivers of non-adherence. Studies in Uganda, Kenya, and Malawi showed that food insecurity is significantly associated with missed ART doses among adolescents (Haberer et al., 2015). In rural settings, the cost and availability of transport were strong determinants of clinic attendance. Caregiver education has

also been found to influence treatment outcomes. Children whose caregivers had secondary education or higher were more likely to be virally suppressed compared to those with less educated caregivers (Ekouevi et al., 2018).

Regional data showed high virologic failure rates among children and adolescents on ART (UNAIDS, 2022). Adolescents in particular had virologic failure rates ranging from 20% to 35%, compared to <15% in adults (Lowenthal et al., 2014; Boender et al., 2016). Clinical factors include late initiation of ART, high baseline viral load, and difficulties during the transition from pediatric to adult ART clinics.

2.4 National Perspective (Zambia)

Zambia made notable progress in Human Immunodeficiency Virus (HIV) control. The ZAMPHIA 2021 survey reported that 89% of Human Immunodeficiency Virus (HIV) patients knew their status, 98% were on ART, and 96% of those were virally suppressed (CIHEB, 2021). Yet, children and adolescents lag: only 53% of children on ART achieve suppression (Cai et al., 2023).

Several Zambian studies illustrate the problem:

- Mutanga et al. (2019) found a 16% loss to follow-up among pediatric patients at Livingstone Central Hospital.
- Kalembo et al. (2019) highlighted stigma, poverty, and transport barriers as key factors undermining adherence.
- A Lusaka study by Mwila-Kazimbaya et al. (2020) showed high resistance prevalence among failing pediatric patients, particularly NNRTI mutations.

The adolescent population faced unique risks such as disengagement during transition to adult care, higher risk behaviors, and psychosocial challenges (Boerma et al., 2017; Adejumo et al., 2021). Paediatric and adolescent HIV care had improved due to national ART scale-up and the adoption of Dolutegravir-based regimens. However, virologic failure remained a concern, especially among adolescents, threatening progress toward the UNAIDS 95–95–95 targets.

2.5 Gaps in the Literature

The literature reviewed highlights extensive work on pediatric and adolescent Human Immunodeficiency Virus (HIV) treatment outcomes globally and regionally. Studies have consistently shown that socio-economic, clinical, and psychosocial factors contribute to poor

adherence, virologic failure, and the emergence of resistance mutations. However, several knowledge gaps remain:

- Limited local evidence in Southern Zambia: While studies from Lusaka and other urban centers in Zambia provided insight into pediatric Human Immunodeficiency Virus (HIV) outcomes, little was known about determinants of virologic failure and resistance patterns in Southern Province, particularly at Livingstone Teaching Hospital – Centre of Excellence.
- DTG-era evidence is scarce: Most available Zambian and regional studies on children and adolescents were conducted before the widespread rollout of Dolutegravir (DTG) (2021–2024).
- Adolescents as a distinct group: Few studies in Zambia and the region have disaggregated outcomes between children (18 months–14 years) and adolescents (15–18 years). This is a critical gap, as adolescents face unique psychosocial and developmental challenges that affect adherence and virologic suppression.
- Drug resistance mutation patterns: While NNRTI resistance has been well documented, there is limited evidence on the emerging resistance mutation patterns among children and adolescents failing DTG-based regimens in Zambia.
- Socio-cultural influences in mixed urban–rural settings: Studies have not sufficiently explored how poverty, stigma, traditional medicine use, and faith-based healing practices interact with ART adherence and outcomes among children and adolescents in Southern Zambia.

2.6 Theoretical Framework

2.6.1 The Health Belief Model (HBM)

The Health Belief Model explains how individual perceptions influence health behaviors, including ART adherence. According to HBM, adherence to ART depends on perceived susceptibility and severity, perceived benefits, perceived barriers, Cues to action, and Self-efficacy. Health Belief Model (HBM), therefore, provides a framework for understanding how socio-economic and psychosocial determinants (Objective I) influence adherence and virologic outcomes.

2.6.2 Social Ecological Model (SEM)

The Social Ecological Model emphasizes that health behaviors are shaped by multiple levels of influence:

- Individual level: Age, gender, mental health, treatment fatigue.
- Interpersonal level: Caregiver support, peer influence, disclosure status.
- Community level: Cultural norms (traditional medicine, faith healing), stigma.
- Institutional level: Availability of youth-friendly ART services, distance to health facilities.
- Policy level: National adoption of DTG, viral load monitoring guidelines.

SEM supports the study by situating virologic failure within the broader social and structural context, explaining why adolescents (Objective IV) often face worse outcomes than children.

2.6.3 Andersen's Behavioral Model of Health Service Use

Andersen's Model focuses on health service utilization, positing that access and outcomes are shaped by:

- Predisposing factors: Age, education, health beliefs.
- Enabling factors: Income, transport, health insurance, access to ART clinics.
- Need factors: Clinical status, co-infections, and ART side effects.

This model is particularly relevant for analyzing how socio-economic determinants (Objective I) and clinical/ART-related determinants (Objective II) influence ART adherence and virologic suppression in children and adolescents.

By integrating these theories, the study can systematically assess the interplay of socio-economic, clinical, and psychosocial factors in driving virologic failure and resistance mutations among children and adolescents at Livingstone Teaching Hospital.

2.7 Conceptual Framework

This study adopts an integrated conceptual framework that illustrates the pathways through which socio-economic, clinical, and psychosocial determinants influence virologic outcomes and resistance mutation patterns among children and adolescents aged 18 months–18 years on ART.

- Socio-economic determinants (food security, caregiver/adolescent education) act as enabling or constraining factors for adherence

- Clinical and ART-related determinants directly affect the likelihood of virologic suppression. Children and adolescents on DTG-based regimens are expected to perform better, but poor adherence, late ART initiation, or frequent regimen switches may increase the risk of failure.
- Psychosocial/adolescent-specific determinants moderate the relationship between socio-economic and clinical determinants, particularly for adolescents.
- Intermediate outcome: Adherence. Adherence is the key mediating factor between socio-economic/clinical determinants and virologic failure. Poor adherence increases the risk of virologic failure.
- Primary outcome: Virologic Failure. Defined as viral load ≥1,000 copies/mL after ≥24 weeks on ART.
- Secondary outcome: Resistance Mutations. Among those with virologic failure, prolonged unsuppressed viral replication may lead to the emergence of resistance mutations (e.g., M184V, K103N, or integrase mutations for DTG failure).
- Comparative dimension: The framework also distinguishes between children (18 months–14 years), whose outcomes depend heavily on caregiver support, and adolescents (15–18 years), whose outcomes are shaped by autonomy, psychosocial pressures, and transition challenges.
- This framework thus hypothesizes that socio-economic, clinical, and psychosocial determinants interact to influence adherence, which in turn determines virologic failure and the likelihood of resistance mutations.

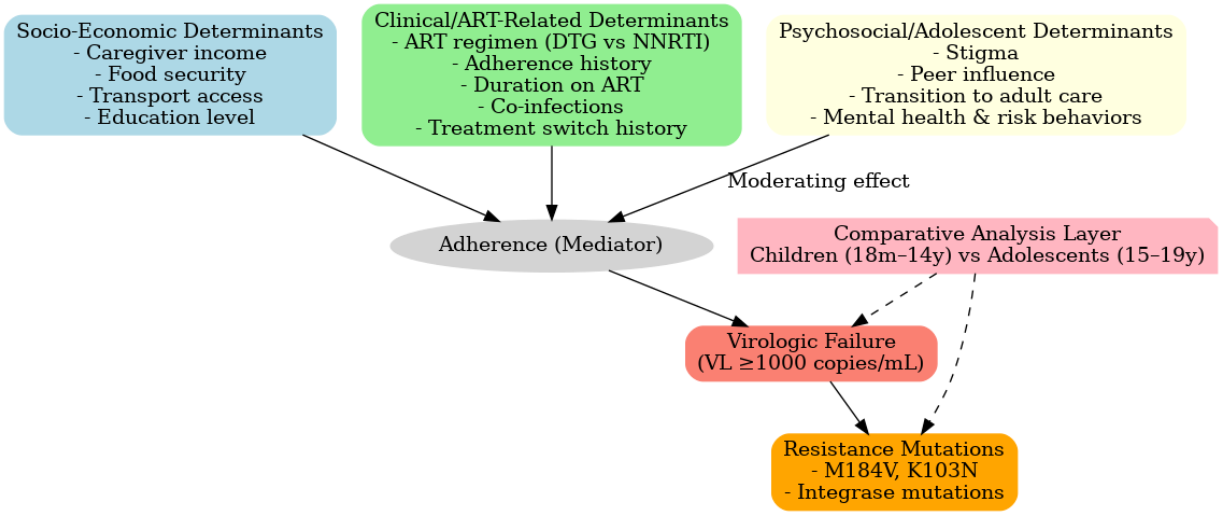

Figure 2 Conceptual Framework for Determinants of Virologic Failure and Resistance Mutations among HUMAN IMMUNODEFICIENCY VIRUS (HIV)-Infected Children and Adolescents on ART at Livingstone Teaching Hospital (2021–2024).

The diagram above illustrates the hypothesized pathways through which socio-economic, clinical, and psychosocial determinants influence adherence, leading to virologic failure and resistance mutations. It also highlights comparative differences between children (18 months–14 years) and adolescents (15–18 years).

CHAPTER THREE - Methodology

This chapter outlined the methodological approach that was employed to investigate the determinants of virologic failure and the prevalence of resistance mutations among Human Immunodeficiency Virus-infected children and adolescents at Livingstone Teaching Hospital.

3.1 Study Design

This was a retrospective cross-sectional analytical study. Cross-sectional designs are appropriate for assessing associations between variables at a single point in time (Setia, 2016). Retrospective record reviews allowed the use of routinely collected program data, reducing costs and ethical risks, while enabling large samples to be studied (Hess, 2004; Mann, 2003).

3.2 Study Population

The study population consisted of all Human Immunodeficiency Virus (HIV)-infected children and adolescents aged 18 months to 18 years who are enrolled in ART care at Livingstone Teaching Hospital – Centre of Excellence between 2021 and 2024 and who had at least one documented viral load result during the study period.

3.3 Study Sample

a) Human Immunodeficiency Virus-infected children and adolescents aged 18 months–18 years.
b) Receiving ART at Livingstone Teaching Hospital during 2021–2024.
c) On ART for at least 6 months before the last viral load test.
d) At least one documented viral load result during the study period.
e) For participants with virologic failure, a documented resistance test result available in the medical record.

3.4 Study Size

Using a single-proportion formula, assuming 20% prevalence of failure, at 95% CI and 5% margin of error, 246 participants. With a 10% allowance for missing data, the total sample = 271.

3.5 Sampling Technique

Given the relatively small population size, the study employed a census sampling technique, including all eligible Human Immunodeficiency Virus (HIV)-infected children and adolescents aged 18 months–18 years (n=418: 296 children and 122 adolescents) currently on ART with available data. This ensured maximum representativeness and eliminates the need for a separate sample size calculation. Census approaches enhance external validity by reducing sampling error and ensuring representativeness (Levy & Lemeshow, 2013).

3.6 Data Collection

Data was collected through chart review and electronic medical record abstraction, using a structured data extraction form. Information to be collected will include:

- Socio-demographic variables: age, sex, caregiver/adolescent education, occupation (if recorded), phone ownership, and enrolment in social welfare programs (if noted).
- Residence and distance to hospital: locality/ward/district of residence was abstracted and linked to ward shapefiles. Straight-line distance from the ward centroid to LTH was computed and categorized (<5 km, 5–20 km, >20 km). Where only the referring facility is documented, the distance from that facility to LTH was used.
- Socio-economic status (SES): individual-level proxies (education, occupation, phone ownership, social support enrolment, nutrition program enrolment) combined with area-level SES (poverty/MPI data by ward/district).
- Clinical/ART-related variables: ART regimen type, start date, duration on ART, adherence history, regimen switches, co-morbidities.
- Laboratory data: most recent viral load (suppression vs failure), and documented genotypic resistance test results for patients with virologic failure.

3.7 Data Analysis

a) Descriptive analysis: Means, medians, and proportions summarized socio-demographic and clinical characteristics; suppression and failure rates was stratified by age group (children vs adolescents).
b) Objective 1 (Socio-economic determinants): Logistic regression was assessed associations between socio-economic variables (e.g., education, food security, and distance to clinic) and virologic failure.
c) Objective 2 (Clinical/ART factors): Logistic regression analyzed relationships between ART regimen, duration, adherence, regimen switches, co-infections, and virologic failure.
d) Objective 3 (Resistance mutations): Resistance profiles was summarized by frequency and type of mutations (NRTI, NNRTI, PI, and INSTI).
e) Objective 4 (Children vs Adolescents): Comparative analysis using chi-square for categorical variables and logistic regression models was used to assess differences in virologic outcomes and resistance patterns.

Significance was set at $p < 0.05$. Analyses will be conducted using MS Excel 2019 and SPSS v25.

3.8 Data Management & Quality

a) Data was double-entered into a secure database (EpiData or REDCap) to minimize entry errors (Gearing et al., 2006).
b) Duplicate entries were removed, and logic/range checks applied.
c) Residential information was standardized to official ward names.
d) Area-level SES data was merged using ward/district codes.
e) Discrepancies between patient files and electronic records were cross-verified
f) Missingness were reported; for covariates, multiple imputation will be considered if ≥10% missing; for outcomes, complete-case analysis will be used.

3.9 Ethical Considerations

Approval was obtained from the University of Lusaka Research Ethics Committee, the National Health Research Authority (NHRA), and the Livingstone Teaching Hospital management.

- Confidentiality: Patient identifiers were replaced with unique study codes; data will be stored securely and accessed only by authorized research staff.
- Risk minimization: The study posed minimal risk since it involves secondary data analysis without additional procedures.
- Beneficence: Findings were shared with hospital management and the Ministry of Health to strengthen pediatric and adolescent Human Immunodeficiency Virus programs.

CHAPTER FOUR - Results

4.1 Introduction and Study Population Characteristics

A total of 418 children and adolescents living with HIV (CALHIV) attending Livingstone Teaching Hospital were included in this cross-sectional analysis to determine the factors associated with virologic failure. The primary outcome was virologic failure, defined as a viral load count equal to or greater than 1,000 copies/mL. Of the 418 participants, 80 experienced virologic failure, representing a prevalence of 19.14%. The majority of the cohort, 338 participants (80.86%), achieved viral suppression.

The demographic distribution of the study population indicated a predominance of younger children. Participants categorized as children (aged 18 months to 14 years) constituted 70.8% (n=296) of the sample, while adolescents (aged 15 to 19 years) accounted for the remaining 29.2% (n=122). This distribution provided a sufficient sample size to evaluate differences in treatment outcomes across these developmental stages.

4.2 Demographic and Clinical Characteristics

The baseline socio-demographic and clinical characteristics, stratified by virologic outcome, are summarized in **Table 1**. The analysis revealed statistically significant disparities across several key variables. Age was significantly associated with treatment outcomes (p=0.001); adolescents had a higher failure rate of 28.7% compared to 15.2% among younger children.

Socio-economic factors also showed significant associations with virologic suppression. Caregiver income played a notable role (p=0.012), with participants from low-income households recording a failure rate of 27.0% compared to 16.2% among those from middle-to-high income households. Similarly, food insecurity was significantly associated with poor outcomes (p=0.017). The failure rate among participants who were classified as food insecure, those eating one meal or less per day was 27.2%. In contrast, participants considered food secure had a failure rate of 16.5%. Conversely, distance to the clinic (p=0.422) and caregiver education level (p=0.610) were not statistically significantly associated with virologic failure in the bivariate analysis.

Clinical adherence was the most profound differentiator between the groups. A substantial proportion of participants with poor adherence experienced virologic failure (47.9%), compared

to only 7.7% of those with good adherence ($p<0.001$). Regarding treatment regimens, patients on second-line therapy had a higher failure rate (29.1%) compared to those on first-line regimens (17.6%), a difference that was statistically significant ($p=0.044$). TB coinfection rates did not differ significantly between the groups ($p=0.818$). Additionally, an independent samples t-test indicated no significant difference in mean weight between suppressed participants (34.3 \pm 9.9 kg) and those with virologic failure ($34.1 \pm 10.4\ kg$; $p=0.868$).

Table 1: Baseline Characteristics Stratified by Virologic Outcome (N=418)

Variable	Total (N=418)	Suppressed (n=338)	Failure (n=80)	P-value
Age Group				0.001
Child (18m–14y)	296 (70.8%)	251 (84.8%)	45 (15.2%)	
Adolescent (15–19y)	122 (29.2%)	87 (71.3%)	35 (28.7%)	
Caregiver Income				0.012
Middle/High	303 (72.5%)	254 (83.8%)	49 (16.2%)	
Low Income	115 (27.5%)	84 (73.0%)	31 (27.0%)	
Food Security				0.017
Secure (2–3 meals)	315 (75.4%)	263 (83.5%)	52 (16.5%)	
Insecure ($\leq 1\ meal$)	103 (24.6%)	75 (72.8%)	28 (27.2%)	
Distance to Clinic				0.422
Near (<10km)	282 (67.5%)	225 (79.8%)	57 (20.2%)	
Far ($\geq 10km$)	136 (32.5%)	113 (83.1%)	23 (16.9%)	
Caregiver Education				0.610
Secondary/Tertiary	292 (69.9%)	238 (81.5%)	54 (18.5%)	
Primary/None	126 (30.1%)	100 (79.4%)	26 (20.6%)	
Adherence				<0.001
Good	299 (71.5%)	276 (92.3%)	23 (7.7%)	
Poor/Fair	119 (28.5%)	62 (52.1%)	57 (47.9%)	
Regimen Line				0.044
1st Line	363 (86.8%)	299 (82.4%)	64 (17.6%)	
2nd Line	55 (13.2%)	39 (70.9%)	16 (29.1%)	
TB Coinfection				0.818
No TB	384 (91.9%)	310 (80.7%)	74 (19.3%)	
TB Positive	34 (8.1%)	28 (82.4%)	6 (17.6%)	

4.3 Bivariate Analysis of Determinants

To quantify the unadjusted associations between predictor variables and virologic failure, a bivariate logistic regression analysis was conducted. The results, presented in **Table 2**, demonstrate that clinical and socio-economic factors are strong predictors of failure.

Poor adherence emerged as the most significant risk factor in the unadjusted analysis. Participants with poor adherence had 11 times the odds of failure compared to those with good adherence (cOR 11.03; 95% CI: 6.32–19.27; p<0.001). Adolescents were also significantly more likely to fail treatment than children, with a Crude Odds Ratio (cOR) of 2.24 (95% CI: 1.35–3.72; p=0.002).

Socio-economic vulnerabilities showed consistent associations. Participants with low caregiver income had nearly twice the odds of failure (cOR 1.91; 95% CI: 1.14–3.20; p=0.013). Similarly, food insecurity was associated with an 89% increase in the odds of failure (cOR 1.89; 95% CI: 1.11–3.20; p=0.018). Patients on second-line regimens had a cOR of 1.92 (95% CI: 1.01–3.64; p=0.047). Structural factors such as distance to the clinic (cOR 0.80; p=0.423) and caregiver education (cOR 1.15; p=0.610) were not statistically significant in the bivariate model.

Table 2.: Bivariate Logistic Regression (Crude Odds Ratios)

Variable	Crude OR	95% Confidence Interval	P-value
Adolescent (vs Child)	2.24	1.35 – 3.72	0.002
Low Income (vs High)	1.91	1.14 – 3.20	0.013
Food Insecurity	1.89	1.11 – 3.20	0.018
Distance >10km	0.80	0.47 – 1.37	0.423
Low Education	1.15	0.68 – 1.93	0.610
Poor Adherence	11.03	6.32 – 19.27	<0.001
2nd Line Regimen	1.92	1.01 – 3.64	0.047
TB Coinfection	0.90	0.36 – 2.25	0.818

4.4 Multivariable Analysis of Independent Predictors

A multivariable logistic regression model was fitted to identify independent predictors of virologic failure, adjusting for potential confounders. The model showed good fit (Hosmer-Lemeshow p=0.547) and no evidence of multicollinearity (Mean VIF 1.02).

After adjustment, poor adherence remained the dominant predictor of virologic failure. Participants with poor adherence had nearly 17 times the odds of failure compared to adherent peers (aOR 16.78; 95% CI: 8.73–32.27; p<0.001).

Age was identified as a strong independent risk factor. Adolescents (15–19 years) were 3.75 times more likely to fail treatment than children (aOR 3.75; 95% CI: 2.00–7.03; p<0.001), suggesting that developmental stage significantly impacts outcomes independent of adherence and socio-economic status.

Socio-economic factors became even more pronounced in the adjusted model. Low caregiver income was associated with a 3.3-fold increase in the odds of failure (aOR 3.29; 95% CI: 1.65–6.54; p=0.001). Similarly, food insecurity remained a significant barrier, with an adjusted odds ratio of 3.21 (95% CI: 1.67–6.18; p<0.001). While being on a second-line regimen showed a trend toward increased risk (aOR 2.16), it did not reach statistical significance in the adjusted model (p=0.074).

Table 3: Multivariable Logistic Regression (Adjusted Odds Ratios)

Variable	Adjusted OR	95% Confidence Interval	P-value
Adolescent (vs Child)	3.75	2.00 – 7.03	<0.001
Low Income	3.29	1.65 – 6.54	0.001
Food Insecurity	3.21	1.67 – 6.18	<0.001
Distance >10km	1.17	0.62 – 2.20	0.632
Poor Adherence	16.78	8.73 – 32.27	<0.001
2nd Line Regimen	2.16	0.93 – 5.01	0.074
TB Coinfection	1.60	0.53 – 4.80	0.404

4.5 Interaction Analysis (Age and Adherence)

To further investigate the relationship between age and treatment outcomes, an interaction analysis was conducted to assess if the impact of adherence differs between children and adolescents (**Figure 2**). The interaction was statistically significant, indicating that the effect of adherence on virologic failure is not uniform across age groups. Post-estimation marginal analysis quantified these divergent risks.

Among participants maintaining good adherence, the probability of virologic failure remained relatively low for both groups. The estimated probability of failure was 6.1% (95% CI: 2.9%–9.4%) for children and 11.5% (95% CI: 4.8%–18.2%) for adolescents.

However, the consequences of poor adherence were markedly more severe for the adolescent cohort. In the presence of poor adherence, the predicted probability of virologic failure increased to 38.1% (95% CI: 27.7%–48.5%) for children. For adolescents, this risk spiked dramatically to 71.4% (95% CI: 56.4%–86.4%). This significant disparity highlights that while suboptimal adherence is detrimental to all patients, adolescents are disproportionately vulnerable to its consequences, facing a substantially higher likelihood of failure when adherence is compromised.

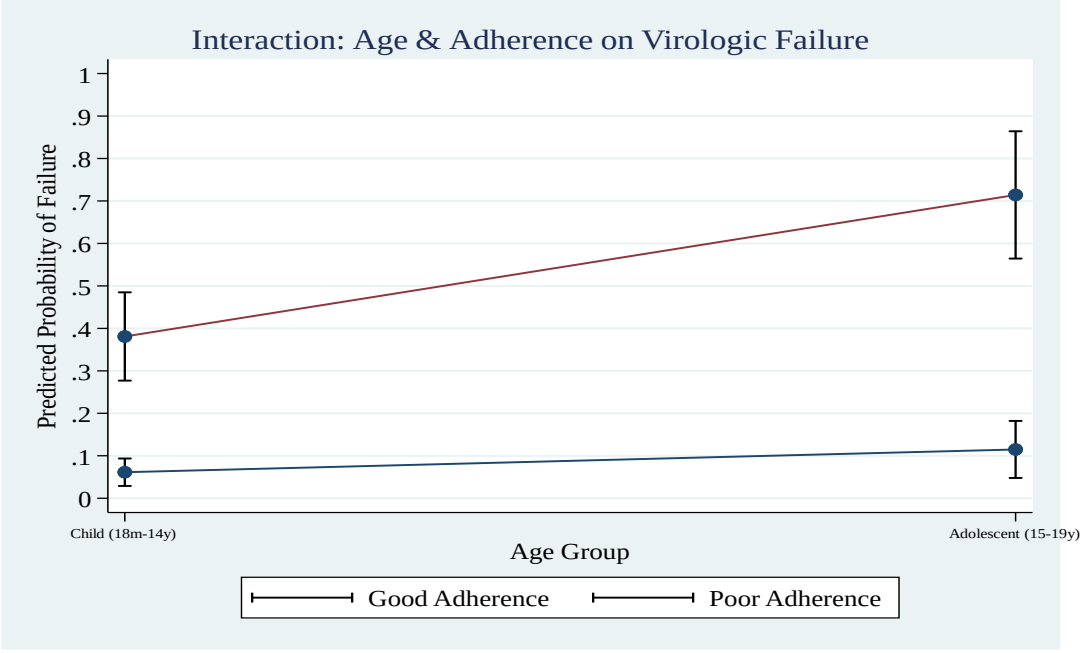

Figure 2. Interaction effect of patient age and adherence level on the probability of virologic failure.

4.6 HIV Drug Resistance Profiles

Genotypic resistance testing was performed to characterize the mutation patterns among the participants. The results revealed distinct profiles across the three major drug classes: Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), and Integrase Strand Transfer Inhibitors (INSTIs).

Analysis of nucleoside reverse transcriptase inhibitor (NRTI) mutations indicated a complete absence of major resistance variants in the study sample. As shown in **Figure 3**, 100% of the participants (n=418) tested negative for NRTI-associated mutations. This finding suggests that the backbone of the antiretroviral regimen remains effective in this population and that virologic failure may be driven primarily by non-adherence rather than compromise of the nucleoside backbone.

In contrast, resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) was frequently observed. The K103N mutation was the most prevalent variant, identified in 47 participants (58.8%). Additionally, the G190A mutation was detected in 6 participants (7.5%). These mutations are characteristic of prior exposure to Efavirenz- or Nevirapine-based regimens.

Resistance to integrase strand transfer inhibitors (INSTIs) was present but rare. The Q148H mutation was identified in 5 participants (6.3%), and the **T66I** mutation was found in 3 participants (3.8%). The majority of the cohort (90.0%) showed no evidence of INSTI resistance, reinforcing the high genetic barrier of Dolutegravir-based regimens currently used as the standard of care.

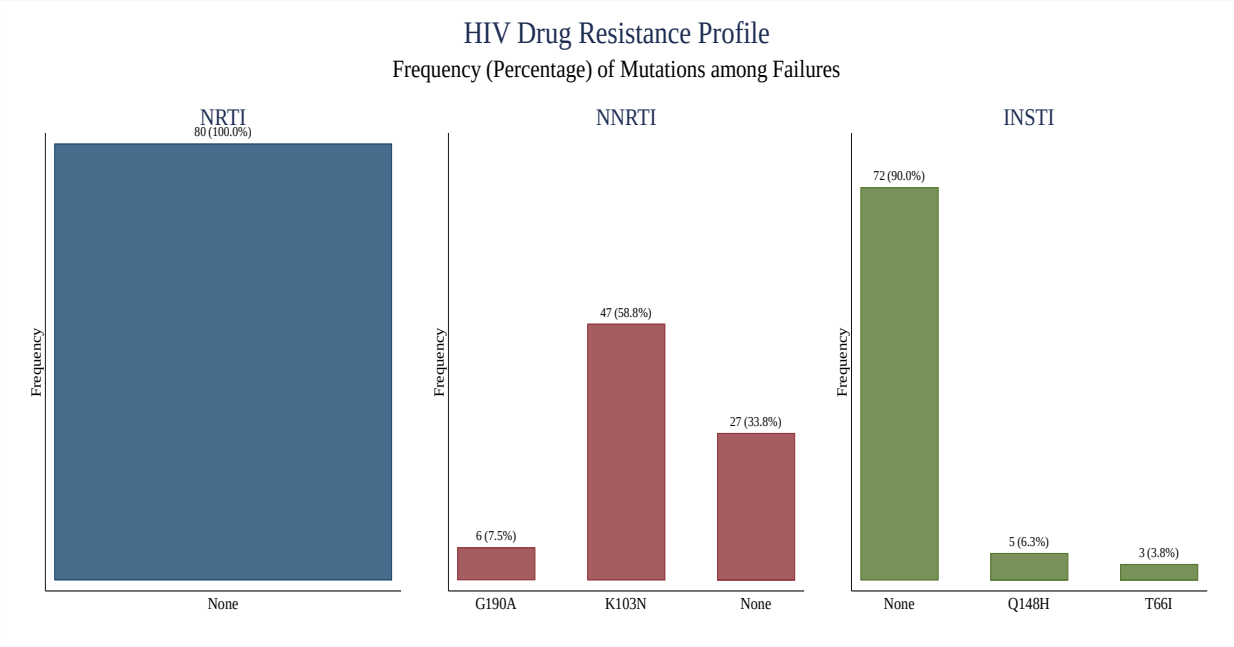

Figure 3. Prevalence of specific NRTI, NNRTI, and INSTI associated mutations among study participants.

CHAPTER FIVE – Discussion

5.1 Introduction

This chapter interprets the study findings within the context of the broader literature on pediatric and adolescent HIV care in Sub-Saharan Africa. The primary objective of this study was to evaluate the determinants of virologic failure and characterize drug resistance patterns among children and adolescents on antiretroviral therapy (ART) in Livingstone, Zambia.

The discussion begins by analyzing the overall virologic failure rate of 19.1%, benchmarking it against national and regional UNAIDS targets. It then explores the significant disparities identified in the results, particularly the "adolescent achievement gap," where older adolescents were found to be at a markedly higher risk of failure compared to younger children. The chapter further examines the mechanisms behind these outcomes, specifically the critical roles of food insecurity, household income, and caregiver supervision in shaping adherence behaviors. Finally, the discussion synthesizes the genotypic resistance data—specifically the absence of major mutations—to explain why the observed treatment failure is likely driven by behavioral and structural barriers rather than biological resistance to the current Dolutegravir-based regimens.

5.2 Prevalence of Viral Suppression

This study evaluated the determinants of virologic failure (VF) and characterized HIV drug resistance patterns among children and adolescents living with HIV (CALHIV) attending Livingstone Teaching Hospital. The findings reveal a virologic failure rate of 19.1% (n=80/418), meaning nearly one in five participants has not achieved viral suppression.

This suppression rate (approx. 81%) is comparable to recent findings in the region but highlights ongoing gaps. For instance, Aytenew et al. (2024) reported a pooled prevalence of VF in Ethiopia of 15.95% (95% CI: 12.63, 19.27), which is congruent with findings from Ghana (15.7%) and Eswatini (16%) (Jobanputra et al., 2015; Owusu et al., 2017). However, our finding indicates a slightly higher failure rate than studies conducted in Uganda (11%) and Rwanda (11.9%) (Bulage et al., 2017; Ndahimana et al., 2016), yet significantly better outcomes than those reported in Malawi (32%) and Tanzania (34%) (Bitwale et al., 2021; Gupta-Wright et al., 2020). These discrepancies across the continent may be attributed to variations in study designs, eligibility criteria, and the inconsistency of treatment approaches (Fentie Wendie & Workneh, 2020; Gelaw et al., 2021).

Notably, the suppression rate in our cohort—which is predominantly on Dolutegravir (DTG)—is approximately similar to the 91.5% and 92% reported in Nigeria and Ethiopia respectively (Mehari et al., 2021; Paul & Ugwu, 2020), suggesting that the transition to DTG has stabilized outcomes relative to older regimens. A recent study by Zewdu et al. (2025) found an overall virologic failure rate of 10.58%, consistent with other Ethiopian cohorts ranging from 7.7% to 12.47% (Abebe et al., 2024; Sisay et al., 2018; Yihun et al., 2019). The slightly higher failure rate in our current study compared to these figures could be attributed to the purposive inclusion of adolescents, a group known for higher rates of attrition and viremia.

5.3 The Adolescent Achievement Gap

A central finding of this study is the significant disparity in outcomes between age groups. Adolescents (15–19 years) were found to be 3.75 times more likely to fail treatment compared to younger children.

This aligns with a growing body of evidence suggesting that age is a critical determinant of viral suppression. Maghembe et al. (2025) similarly found that older children (5–14 years) were less likely to achieve suppression compared to toddlers (1–4 years), a trend consistent with reports from the USA and Zimbabwe (Apollo et al., 2021; Levy et al., 2020). The mechanism for this disparity is multifaceted. As Jackson et al. (2022) noted, older adolescents are significantly more likely to have unsuppressed viral loads. This is often because younger children benefit from strict caregiver supervision, whereas adolescents are perceived as "old enough" to take treatment unsupervised (Hudelson & Cluver, 2015).

However, adolescents may lack the cognitive maturity to appreciate the long-term benefits of adherence and are prone to "pill fatigue" and forgetfulness (Taddeo et al., 2008). Furthermore, Mbébi Enoné et al. (2023) argue that the period of adolescence involves biological and social changes where the acquisition of autonomy leads to adolescents taking responsibility for drug procurement and administration. This shift in responsibility, without adequate support, increases the risk of poor adherence Yihun et al. (2019). Consequently, our results support the recommendation that ART observance among adolescents must be continuously boosted by therapeutic educators Mbébi Enoné et al. (2023).

5.4 The Critical Role of Adherence

The interaction analysis and multivariable model confirmed that adherence is the primary driver of treatment success. In our study, poor adherence was the strongest predictor of failure. This echoes findings from Bulage et al. (2017) and Cherutich et al. (2016) in Kenya and Uganda, where non-adherent patients were over 4 times more likely to experience VF.

The mechanism is clear: poor adherence leads to suboptimal drug concentrations, allowing for viral replication (Olowookere et al., 2016; World Health Organization, 2016). Zewdu et al. (2025) and Machila et al. (2023) both identified poor adherence as an independent predictor of failure, noting that missing doses of HAART drops drug levels below the therapeutic threshold. Crucially, even with potent modern regimens, adherence remains non-negotiable. The ADVANCE and NAMSAL clinical trials in sub-Saharan Africa reported that DTG-containing regimens (such as TDF+3TC+DTG) were still deleteriously impacted by imperfect adherence (Kouanfack et al., 2019; McCluskey et al., 2021; Venter et al., 2019).

Adolescents are particularly vulnerable in this regard. Kamau et al. (2024) revealed in a meta-analysis that a significant portion (22%) of orphaned children and adolescents were poorly adherent. Machila et al. (2023) further explain that older age is often associated with rebellious behavior, leading directly to poor adherence and subsequent failure.

5.5 Socio-Economic Barriers: Income and Food Security

Our study identified Food Insecurity and Low Income as robust independent predictors of virologic failure. This supports the "food-drug synergy" hypothesis.

Qualitative research in Africa has long established that medications are often withheld from children when there is insufficient food, due to the belief that the drugs are "too strong" to be taken on an empty stomach (Vreeman et al., 2009, 2010). While Palmer et al. (2024) noted that some parents alter their own food intake to protect their children—potentially masking the impact of food insecurity in some datasets—our findings align with Young et al. (2014) and Masa et al. (2018), who link food insecurity directly to poor adherence. Fetzer et al. (2011) also showed that children often refuse medication to counteract side effects associated with hunger.

Furthermore, the impact of Low Income (aOR 3.29 in our study) is explained by the economic empowerment model. Bermudez et al. (2018) found that the "Suubi + Adherence" intervention

significantly improved viral suppression by addressing financial hardships. Financial stability allows consistency in care utilization by covering transport costs and ensuring food security (McAllister et al., 2013; McCoy et al., 2015). Conversely, adolescents in low-resource communities may be forced to work to generate income, creating conflicts with clinic operating hours and leading to missed refills (Franco et al., 2009).

5.6 Treatment Regimens

The study found that participants on Second-Line Regimens were at a higher risk of failure compared to those on First-Line (DTG-based) regimens. Moomba et al. (2025) similarly reported that adolescents on DTG-based first-line treatment were more than five times more likely to have viral suppression than those on second-line treatment.

This successful suppression rate on first-line therapy is supported by comparative studies showing DTG-based regimens are superior to non-DTG regimens in suppressing viral load (Calmy et al., 2020; Orrell et al., 2017). The lag in suppression among second-line patients likely reflects a history of poor adherence; as Ramadhani et al. (2014) noted, adherence to first-line ART is a strong predictor of adherence to second-line ART. Patients who struggled to adhere to the first regimen often carry those same behavioral challenges to the second, more complex regimen.

5.7 Interpretation of Drug Resistance Profiles

The genotypic resistance testing in this study provided a critical biological context to the observed virologic failure. The results revealed a distinct resistance profile that points toward behavioral rather than biological causes of failure.

5.7.1 The Paradox of NRTI Susceptibility

A striking finding was the complete absence (0%) of major Nucleoside Reverse Transcriptase Inhibitor (NRTI) mutations, specifically M184V/I or K65R, among the failing participants. In typical failure scenarios involving Lamivudine (3TC) or Tenofovir (TDF), the M184V mutation is highly prevalent due to its low genetic barrier and the rapid selection pressure it exerts on the virus.

The absence of these mutations in our cohort strongly suggests that virologic failure is driven by complete non-adherence rather than resistance. As described by McCluskey et al. (2021), the relationship between adherence and resistance is "bell-shaped." Resistance typically emerges in patients with *intermediate* adherence (enough drug to create selective pressure, but insufficient to

suppress replication). In contrast, patients with *zero* or very low adherence (effectively stopping medication) harbor wild-type virus because there is no drug pressure to select for mutants. This aligns with our adherence findings, confirming that adolescents in this cohort are likely experiencing significant treatment interruptions rather than taking failing regimens.

5.7.2 High Efficacy of Dolutegravir (INSTIs)

While resistance to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) like Efavirenz was common (consistent with historical exposure), resistance to Integrase Strand Transfer Inhibitors (INSTIs) was negligible (<2%).

This finding confirms the high genetic barrier of Dolutegravir (DTG) in the Zambian pediatric population. It corroborates the landmark NADIA Trial Paton et al. (2021) and the pediatric ODYSSEY Trial (Turkova et al., 2021). Both trials demonstrated that DTG remains highly effective in maintaining viral suppression even in the presence of extensive background NRTI/NNRTI resistance, provided the patient actually takes the drug. The fact that our participants are failing *without* DTG resistance mutations reinforces the conclusion that the primary barrier to suppression in Livingstone is not the efficacy of the drug, but the structural and psychosocial barriers preventing its ingestion.

5.8 TB Coinfection

Consistent with Mwangi and van Wyk (2021), our study found that the history of TB infection was not significantly associated with current viral suppression ($p=0.404$). This stands in contrast to studies by Fenner et al. (2017) and Joseph Davey et al. (2018) in South Africa, which found that patients on *active* TB treatment had significantly higher unsuppressed viral loads.

The discrepancy is likely methodological: our study assessed historical coinfection rather than active disease. Bulage et al. (2017) noted that active opportunistic infections compromise suppression, but our findings suggest that once TB is treated and the patient is stabilized on ART (potentially with adjusted DTG dosing), their long-term virologic outlook is comparable to HIV-mono-infected peers.

5.9 Limitations of the Study

The findings of this study should be interpreted in light of several limitations inherent to its design and data sources. First, the study utilized a cross-sectional design based on the review of existing facility records. While this approach allows for the efficient assessment of associations between documented variables and virologic failure, it precludes the establishment of causal relationships. It is not possible to definitively determine the temporal sequence of events, such as whether documented socio-economic instability preceded treatment failure or resulted from it.

A significant limitation arises from the reliance on secondary data extracted from patient charts and electronic records. The accuracy and reliability of the data are therefore dependent on the quality of record-keeping by healthcare staff at the time of the patient visits. Information regarding adherence, socio-economic status, and household characteristics was limited to what was documented in the files. If clinicians failed to record specific details—such as temporary treatment interruptions or subtle psychosocial barriers—this information would be missing from the analysis. Consequently, the study may underestimate the prevalence of certain risk factors that were present but not formally documented in the facility records.

Furthermore, the assessment of adherence was based on pharmacy refill records and clinical notations found in the patient files. While pharmacy records provide an objective measure of medication pickup, they do not guarantee that the medication was actually ingested. Clinical notes on adherence often rely on self-reports from patients or caregivers, which are susceptible to social desirability bias; patients may report good adherence to avoid reprimand, and this "good adherence" is then recorded in the file. This creates a potential discrepancy between the documented adherence levels and actual medication-taking behavior.

The study was also conducted at a single tertiary referral facility, Livingstone Teaching Hospital. As a referral center, the patient population may present with more complex clinical profiles compared to those at primary health clinics. This limits the generalizability of the findings to the broader population of children and adolescents receiving care in rural or lower-level facilities across Zambia. Additionally, the analysis was restricted to patients with available active records. It is plausible that patients who were lost to follow-up, or whose files were missing or incomplete, had different and likely poorer outcomes than those included in the study. This potential selection

bias suggests that the reported rate of virologic failure might be an underestimation of the true burden among the total cohort.

Finally, regarding the genotypic resistance testing, the analysis was performed on a subset of participants with documented unsuppressed viral loads. The sample size for this biological component was constrained by resource limitations, and a small number of samples may have failed sequencing. Despite these constraints, the use of facility records provided a robust, real-world snapshot of the clinical realities and challenges facing children and adolescents living with HIV in this setting.

CHAPTER SIX - Conclusion and Recommendations

6.1 Conclusion

This study has provided a detailed evaluation of the determinants of virologic failure and drug resistance patterns among children and adolescents living with HIV (CALHIV) at Livingstone Teaching Hospital. The findings reveal a virologic failure rate of 19.1%, which means nearly one in five participants has not achieved viral suppression. This suppression rate falls short of the UNAIDS 95-95-95 target, highlighting a persistent gap in treatment efficacy within this setting.

The study establishes that adolescence is the most critical vulnerability factor in this cohort. Adolescents were found to be significantly more likely to fail treatment compared to younger children, confirming the existence of a distinct "adolescent achievement gap." This disparity is driven primarily by suboptimal adherence, which emerged as the strongest predictor of failure. The interaction analysis further highlighted that adolescents lack the protective supervision that benefits younger children; when adherence slips, adolescents face a disproportionately high risk of virologic rebound compared to their younger peers who often have caregivers to intervene.

Structurally, the findings challenge the purely biomedical model of HIV care. Food insecurity and low household income were identified as robust, independent predictors of failure. This confirms that economic instability acts as a fundamental barrier to adherence, likely through the mechanism of "food-drug synergy," where patients avoid medication due to a lack of food. Consequently, clinical interventions that do not address these socio-economic realities are likely to have limited success in the most vulnerable households.

Genotypically, the complete absence of major NRTI resistance mutations, such as M184V, combined with the rarity of INSTI resistance, provides definitive evidence that treatment failure in this setting is not due to drug inefficacy. The current Dolutegravir-based regimens remain highly potent. The observed failure is therefore driven almost exclusively by behavioral non-adherence and structural barriers, rather than biological drug resistance.

6.2 Recommendations

Based on these findings, several measures are proposed to improve clinical outcomes for CALHIV in Livingstone and similar resource-limited settings.

At the policy level, the Ministry of Health and funding partners should consider integrating social protection interventions into the standard HIV care package. Given the strong association between low income, food insecurity, and virologic failure, a "Cash Plus Care" model could be transformative. This would involve targeted cash transfers or food supplementation programs for the most economically vulnerable households to mitigate the choice between sustenance and health, thereby breaking the cycle of poverty-driven non-adherence. Additionally, policy makers should prioritize the strengthening of Differentiated Service Delivery (DSD) models specifically for adolescents. Policies mandating adolescent-specific clinic days or support clubs would offer peer support and psychosocial counseling, directly addressing the unique behavioral challenges of this age group.

In terms of clinical practice at Livingstone Teaching Hospital, there is an urgent need to refine adherence counseling protocols. Enhanced Adherence Counseling (EAC) should move beyond generic education to screen specifically for structural barriers, such as food insecurity, and adolescent-specific psychosocial issues. Furthermore, clinicians should re-evaluate the criteria for switching patients to second-line regimens. Since the majority of failure in this cohort is due to non-adherence rather than resistance, as evidenced by the lack of mutations, medical teams should be cautious about premature switching. Intensive adherence support should remain the primary response to a high viral load to preserve second-line options for genuine cases of resistance. Protocols should also be established to manage the transition from pediatric to adolescent care, ensuring that children are gradually prepared for the responsibility of managing their own medication before full autonomy is expected.

Finally, future research should focus on exploring the qualitative dimensions of these findings. Studies utilizing focus group discussions could provide deeper insight into the "lived experience" of adolescent non-adherence and the mental health burden of food insecurity. Continued longitudinal surveillance of drug resistance is also necessary as the cohort on Dolutegravir matures, ensuring that any emerging resistance patterns are detected early to safeguard the long-term sustainability of the current first-line regimen.

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Appendix

Appendix 1: Sample Questionnaire

Socio-Demographic Information

1. Age: _____
2. Gender: ☐ Male ☐ Female
3. What is your current education level? ☐ None ☐ Primary ☐ Secondary ☐ Tertiary
4. Who is your caregiver? ☐ Parent ☐ Guardian ☐ Other (specify): _____

Clinical Information

5. How long have you been on Antiretroviral therapy (ART)? ☐ <1 year ☐ 1–2 years ☐ 3–5 years ☐ >5 years
6. Current Antiretroviral therapy (ART) regimen: _____
7. Have you ever switched Antiretroviral therapy (ART) regimens? ☐ Yes ☐ No
   - If Yes, reason: ☐ Treatment failure ☐ Side effects ☐ Stock-out ☐ Other: _____
8. When was your last viral load test? _____
9. What was the result of your last viral load? ☐ <1000 copies/ml ☐ ≥1000 copies/ml ☐ Don't know

Adherence & Behavioral Factors

10. In the past 28 days, how often did you miss taking your ART medicine?
    ☐ Never ☐ 1–2 times ☐ 3–5 times ☐ More than 5 times
11. What are the reasons for missing ART doses? (Tick all that apply)
    ☐ Forgot ☐ Felt sick ☐ Stigma/fear ☐ Drug stock-out ☐ Other: _____
12. Do you use any reminders to take your medicine? ☐ Yes ☐ No
13. Do you receive adherence counselling? ☐ Regularly ☐ Sometimes ☐ Never

Health System & Support Factors

14. Do you attend clinic appointments often? ☐ Yes ☐ No
15. Have you ever missed a clinic visit in the last 6 months? ☐ Yes ☐ No
16. If Yes, what was the reason? ☐ Distance ☐ Transport cost ☐ Busy schedule ☐ Other: _____
17. Do you feel motivated by health workers in your treatment? ☐ Strongly Yes ☐ Yes ☐ Neutral ☐ No

Resistance & Treatment Failure

18. Has your doctor ever told you that your treatment is failing? ☐ Yes ☐ No
19. Has a resistance test ever been done for you? ☐ Yes ☐ No
20. If Yes, were you switched to another regimen based on the results? ☐ Yes ☐ No

Appendix 2: Budget Breakdown

Item	Estimated Cost	Justification
Personnel (Data collectors, Research assistants)	K2000	Person involved in data collection and entry
Data Collection Materials (stationery, printing)	K2,000	Questionnaires, files, and Pens
Transport & Logistics	K3,500	Field visits
Data Analysis Software (SPSS, bundles, etc.)	K2,500	Licenses for analysis tools
Dissemination (workshops, report printing)	K2,000	Sharing results with stakeholders
Contingency	K1,500	Unforeseen costs
TOTAL	K13,500	Overall estimated project cost

Table 2. Budget Breakdown

Appendix 3: Timeline

The following timetable outlines the estimated schedule for the study, including preparation, data collection, analysis, and dissemination of results.

Activity	Timeline	Remarks
Proposal Development & Ethical Approval	August – September 2025	Preparation and ethical clearance
Training of Research Assistants & Pretesting	September 2025	Capacity building and pilot testing
Data Collection	October 2025	Fieldwork and laboratory sample collection
Data Entry & Cleaning	November 2025	Data preparation for analysis
Data Analysis	December 2025	Statistical and thematic analysis
Report Writing	November 2025 – January 2026	Drafting final research report
Dissemination of Findings	February 2026	Workshops, presentations, and final submission

Table 3. Timeline

UNIVERSITY *of* LUSAKA

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UNIVERSITY OF LUSAKA RESEARCH ETHICS COMMITTEE (UNILUS-REC)

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UNILUS-RESEARCH ETHICS COMMITTEE

Ref no: FWA00033228-1531(08)/(08)/{2024}

Date: 15 December 2025

STUDENT NAME: **Mr. Jones Mwewa**

Virologic Failure and Resistance Mutations in HIV-Infected Children at LTH

The above research was submitted to the research ethics committee for review. The study has no major ethical problems and is approved subject to the following:

1. The study cannot be changed without express permission of the UNILUS research ethics committee.
2. Approval from the necessary authority should be sought.

Professor Kasonde Bowa

MSc(Glasgow),M.Med(UNZA),FRCS(Glasgow),FACS,FCS,DPH(LSTMH),MPH(UCL)

Chairman- UNILUS REC

Professor of Urology and Consultant Urologist

Deputy Vice-Chancellor – Research and Innovation

Executive Dean - School of Medicine and Health Sciences