Pediatric Antiretroviral Treatment Uptake, Treatment Adherence, Regimen Switches, and Retention in Care in Namibia

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Pediatric Antiretroviral Treatment Uptake, Treatment Adherence, Regimen Switches, and Retention in Care in Namibia

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The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to assure the availability of quality pharmaceutical products and effective pharmaceutical services to achieve desired health outcomes. Toward this end, the SIAPS result areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms to improve access to medicines, and increasing quality pharmaceutical services.

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Key Words

ART, pediatric, lost to follow-up (LTFU), ART regimen, regimen switches, EDT, MoHSS, SIAPS, Namibia

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CONTENTS

List of Figures

List of Tables

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ACRONYMS AND ABBREVIATIONS

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
EDT	Electronic Dispensing Tool
HIV	human immunodeficiency virus
HMIS	Health Management Information System
LTFU	lost to follow-up
mEDT	Mobile Electronic Dispensing Tool
MoHSS	Ministry of Health and Social Services
MSH	Management Sciences for Health
PEPFAR	President's Emergency Fund for AIDS Relief
PII	personally identifiable information
PLHIV	people living with HIV
PMTCT	prevention of mother-to-child transmission (of HIV)
SIAPS	System for Improved Access to Pharmaceuticals and Services
SPS	Strengthening Pharmaceutical Systems
TB	tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNAM	University of Namibia
USAID	United States Agency for International Development
WHO	World Health Organization

DEFINITION OF TERMS

Active patient: A patient who has been registered and receives regular ART at a given public health facility and who has not missed his/her last appointment by 30 days or more

Lost to follow-up patient: A patient who has not attended the ART clinic or pharmacy at which they are registered for more than 90 days since the last scheduled appointment and whose whereabouts are unknown to the clinic staff

Outreach site: A public health facility, usually a health center or a clinic, to which health workers from the district hospital in the respective district travel once or twice a month to provide health services (usually ART) that are not usually available at that facility

Transferred out patient: A patient who is registered in the ART program at a facility and is later formally sent to another facility accompanied by a transfer letter signed by a medical officer or nurse at the original facility

Treatment supporter: A relative, friend, or acquaintance to a patient on ART who is supposed to assist the patient to improve adherence to ART, attendance at ART clinic appointments, as well as offer other support

Regimen switch: A change of a pediatric ART patient's regimen from the MoHSS-approved ART guidelines' recommended first line to second line antiretrovirals (ARVs)

The regimens are as documented in Namibia's ART guidelines of 2007, 2010, and 2014 (table 1).

Table 1: Recommended ART regimens for children in Namibia by year

Year	First line	Second line	Substitute
2007	D4T/3TC/NVP (stavudine/ lamivudine/nevirapine)	ABC + ddI + LPV/r (abacavir + didanosine + lopinavir/ritonavir)	
2010	• D4T/3TC as pediatric fixed-dose combination (FDC) plus LPV/r suspension • (D4T/3TC/NVP as pediatric FDCs) • AZT (zidovudine)/3TC/ NVP • TDF (tenofovir)/3TC/ NVP	• ABC + AZT + 3TC + LPV/r) • ABC + AZT + 3TC + [NVP or EFV (efavirenz)] • TDF + AZT + 3TC + [NVP or EFV]	
2014	• ABC/3TC/LPV/r • ABC/3TC/EFV • TDF/FTC (emtricitabine) (or 3TC)/EFV	• ABC + AZT + 3TC + LPV/r • ABC + AZT + 3TC + EFV • TDF + AZT + 3TC + LPV/r • TDF + AZT + 3TC + EFV	• AZT for ABC • NVP for EFV

EXECUTIVE SUMMARY

Background

Namibia has a decentralized public health system with 14 administrative regions. It is challenged by a dual burden of HIV and AIDS and tuberculosis (TB). AIDS is among the top 10 causes of death in Namibia, and antenatal HIV prevalence was 16.9% in 2014. ART has been available in the private sector in Namibia since 1997. The national ART programme was launched in June 2003 with funding from the President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund. In March 2015, an estimated 240,000 Namibians were living with HIV; over 136,000 patients were receiving ART in the public sector, 8% percent (10,578) of whom were pediatric patients. All children and adolescents under 15 years are eligible for ART in Namibia. Dispensing of ARVs in the public sector is captured through the Electronic Dispensing Tool (EDT), which is available in 51 main ART sites. EDT mobile is now available in approximately 20 primary health care facilities.

Methodology

A programmatic and policy-relevant longitudinal analysis of routinely collected pediatric data (<1 year, 1–4 years, 5–9 years, 10–14 years) from 2010 to 2015 on the EDT database in Namibia was conducted from July to September 2016.

Data on pediatric ART patients in 50 main public health ART sites in all 14 regions of Namibia, as captured in the EDT, was extracted into a Microsoft Excel database; anonymized; cleaned; and analyzed using Stata v11 and Excel to generate percentages and survival/failure as well as determine associations between/among variables. Data was anonymized and no personally identifiable information (PII) was included in the analysis or results. The results are presented in the form of tables, graphs, and summarized text. The study was approved by the Permanent Secretary of MoHSS, Namibia.

Key Findings

A total of 5,476 children aged 0–14 years were enrolled for ART from 2010 to 2015. The number of children starting ART decreased over the years. The most enrolled age group in 2010-2015 was the 1–4-year group. The Omusati, Ohangwena, and Kavango regions recorded the highest enrollment in the study period. Older children (10–14 years) enrolled more in 2014 and 2015 as compared to other age groups, which likely attributed to ART policy changes in 2014; 8% of the 5,476 children enrolled in ART from 2010–2015 switched from first- to second-line ART regimens. Most switches were observed among males (61%, log-rank test: p=0.000) and the 10–14-year categories. The rate of switching from first- to second-line ART regimens increased after at least 12 months of treatment. The rate of switching after two years was approximately 4% and increased to approximately 12% after five years. Over 16% (16.2%) of the 5,476 children enrolled in ART from 2010–2015 were lost to follow-up (LTFU) in the study period. Most (87%) of the 888 children on ART recorded as LTFU were started on ART at hospitals. Younger children (0–4 yrs) (59%) were more LTFU than older ones. The most documented reason for switching from first-line to second-line treatment was virological failure.

Conclusions

Pediatric ART enrollment has been decreasing over the years. Most switches from first- to second-line ART regimens were observed among males and the 10–14-year groups. The rate of switching to second-line treatment was lower, at approximately 4% after two years, but increased to approximately 12% after five years. Younger children (0–4 years) tended to be more LTFU than older children. The majority of switches were justified if the documented reason for change was virological failure.

Recommendations

It is recommended that a study be conducted to explore factors contributing to reduced number of children enrolled for ART (e.g., could it be that there are fewer children in need of ART due to prevention of mother-to-child transmission [PMTCT] success?). Early enrollment of children, especially male children and the 10–14-year group, is highly recommended. Late ART initiation and co-morbidities in the 10-14-year group may be associated with the higher regimen switches. MoHSS should strengthen interventions (e.g., treat all/test and treat) for increased enrollment of this group. A study should be conducted to explore factors associated with patients switching from first to second line and those LTFU so that enhanced clinical monitoring can be done for patients with similar characteristics to avoid switching and further LTFU. The MoHSS Treatment Technical Working Group should identify interventions for improving pediatric patients' management to minimize LTFU that could lead to treatment failure, HIV drug resistance, and the need for regimen switches. Side effects of second-line treatment may be a possible cause of LTFU, and further studies are needed on causal factors/predictors. Similar analysis is recommended for adult patients on ART. Other reasons for switching that could be significant but were missed in the EDT need to be documented accurately in the future.

INTRODUCTION

Background

Namibia has a population of 2.18 million people (National Planning Commission, 2011) in an area of more than 825,000 square kilometers, making it one of the world's most sparsely populated nations, with approximately two persons per square kilometre.[1] Such a low population density presents challenges for staffing, training of health care workers, and logistics for health care service delivery. Public health service delivery is complemented by the private sector. The public health sector is structured in a three-tier hierarchy with central, regional, and district levels. The central level has devolved authority to 14 MoHSS regional directorates and 34 districts.[2]

The first case of HIV in Namibia was reported in 1986. With an estimated antenatal HIV prevalence rate of 16.9% as of 2014, Namibia has one of the highest HIV prevalence rates in the world. The total population of people living with HIV (PLHIV) aged 15 years and above is estimated at 260,000. Revised 2015 estimates project that the number of PLHIV will increase to over 273,000 in 2017, and over 296,000 by 2020.[3]

HIV and AIDS is among the top 10 causes of death among children under five years in Namibia.[4] According to a report by the Joint United Nations Programme on HIV/AIDS (UNAIDS), in 2014 it was estimated that there were approximately 16,000–17,000 children aged 0 to 14 years living with HIV in Namibia. There is a 6.3 higher chance of death for an infant born to an HIV-positive mother, if no treatment is provided. The Child Health Epidemiology Estimation Group estimates that, globally, up to 17% of all under-five deaths are caused by HIV and AIDS. The MoHSS data from the Health Management Information System (HMIS) shows that between 2008 and 2012, HIV and AIDS caused up to 3% of under-five mortality and was the tenth cause of under-five mortality.[5]

ART is known to prolong and improve the quality of life of people living with HIV and AIDS and to reduce mortality among these patients. This therapy has been available in the private sector in Namibia since 1997.[6] The national ART programme was launched in June 2003 with funding from PEPFAR and the Global Fund to Fight AIDS, Tuberculosis, and Malaria. As of July 2015, there were 50 main public health facilities offering ART services in Namibia. By the end of 2013, the World Health Organization (WHO) reported that Namibia had achieved 80% coverage under the WHO 2010 treatment guidelines, which recommends initiating ART at CD4 ≤350 cells/mm3 or clinical stages III or IV.[7] As of March 2015, an estimated 240,000 Namibians were living with HIV, and, of these, approximately 136,000 patients were receiving ART in the public sector, of which 8% (10,578) were pediatric patients.[8]

Children may be infected with HIV during pregnancy, delivery, or postnatally (through breastfeeding). Left untreated, the mortality rate from HIV and AIDS is approximately 30% by age 1, 50% by age 2, and 60% by age 3. The mortality rate from untreated HIV and AIDS is highest for those less than 18 months of age.[9] The immunological response to ART in children with HIV is better than in adults. Children restore their CD4 cell counts and percentages better and more rapidly than adults, even in late stages of HIV-1 infection. Moreover, normalization of CD4 cell count in HIV-1-infected children taking ART is age-

independent. In Namibia, all children and adolescents under 15 years are eligible for ART and should be initiated on ART, irrespective of CD4 count and clinical stage.[8, 10]

Dispensing of ARVs to all patients in the public health sector is captured in real time through the EDT, which is available at all ART pharmacies, and the mobile EDT (mEDT), which is a hand-held device used to dispense ART to patients at outreach sites.[11] Data from the mEDT is seamlessly transferred to the main ART site EDT database via a cradle connection upon return to the main ART site. The EDT captures information on appointment keeping, pill count, changes in regimen, and full dispensing data per patient per visit. The system also allows for monitoring of consumption of ARVs at each facility. The national database, consisting of data from all EDTs at facilities in the country, is situated at the Pharmaceutical Services Division at MoHSS headquarters. The Central Medical Stores, a sub-division of the Pharmaceutical Services Division, handles all public sector ARV procurement, including that supported by PEPFAR and the Global Fund.

In 2008, the Intermediate Hospital Oshakati, the main referral hospital in the northern part of Namibia, was faced with many challenges in the management of pharmaceutical supplies. Coupled with high patient overload and associated long wait times at the pharmacy, the hospital needed a more efficient way of managing and handling the pharmaceutical products and patients presenting at the pharmacy. Through the Oshana regional directorate and Permanent Secretary of MoHSS, the hospital management requested support from the USAID-funded Strengthening Pharmaceutical Systems program, implemented by Management Sciences for Health (MSH). RxSolution was implemented at the hospital starting in 2009–2010 to help alleviate the challenges associated with the management of non-ART products and patients.[12]

In Namibia, electronic tools for dispensing ARVs at the point of care have been in use for over five years.[13] The EDT has been used to ensure that the correct medicines for the management of HIV and AIDS and opportunistic infections have been dispensed and to ensure the availability of vital data used in monitoring patients, medicines, facilities, and program-level performance. The EDT helps the dispenser carefully monitor the patients' adherence, response, and possible side effects, while allowing a health facility to compile service statistics needed to support management decisions. The routine patient-level data collected through EDT at the point of care represent great potential resources for conducting operational, clinical, epidemiological, and health systems research to inform decision-making.

A recent literature review from Fox and Rosen (2015) found a lack of evidence about the level of adherence to ART in children, with some data suggesting that it is probably no better than in adults. The authors found "39 reports of retention in 45 patient [children] cohorts and 55,904 patients [children] in 23 countries. Among them, 37% of patients not retained in care were known to have died and 63% were lost to follow-up. Unweighted averages of reported retention were 85, 81, and 81% at 12, 24, and 36 months after ART initiation. From life-table analysis, [the authors] estimated retention at 12, 24, and 36 months at 88, 72, and 67%. [The authors] estimated 36-month retention at 66% in Africa."[14]

Determinants of pediatric adherence to ART are complex. As in adults, adherence behavior is influenced by many factors, which may be categorized as characteristics of the child, the caregiver(s) and family, the regimen, and society and culture.[14–16] Moreover, adherence to treatment in children is highly affected by the knowledge, attitude, and practice of the

caregiver toward HIV treatment. There is a direct relationship between adherence to treatment and desired treatment outcomes, primarily viral load suppression. This assessment utilized existing EDT data to quantify patterns of ART treatment in children and examined variations by region, clinic, and child characteristics.[17,18] The focus of this evaluation was on ART uptake, treatment adherence, regimen switches, and retention in care by pediatric patients in Namibia. Conclusions drawn from the discussion of the data presented in this assessment will be influential in preparing for future study of the determinants of treatment adherence among pediatric patients, which will help inform improvements in health service delivery targeted at pediatrics in Namibia.

Problem Statement

In Namibia, a preliminary review of EDT records suggests that children form a small proportion of the patients accessing ART in any given setting, nationally composing 8% of the patients on ART in the MoHSS facilities.[7] Over the years, managing children has been complicated with formulations that have not been friendly for children, complicated regimens, and occasional stock-outs of pediatric ARVs. These challenges have been compounded by the increasing need to optimize pediatric ART regimens; high dependency of children on parents (who are often HIV positive) and guardians for picking up ARV refills; and, most importantly, adherence to treatment, which has rendered pediatric patients subject to a high risk of mismanagement and missed opportunities of identification and continuity of care.[14,19–23]

These challenges may increase the number of children that might receive suboptimal care, including delayed or no interventions in face of poor adherence, ultimately leading to suboptimal response to treatment. This can then increase the risk of HIV drug resistance and leads to short survival of HIV-infected children. Additionally, compared to adults, children are expected to have a longer treatment duration.[24, 25]

Findings from this assessment will provide much needed evidence on trends in pediatric HIV treatment uptake, levels of adherence, and retention among those on treatment. Ultimately, the evidence generated will support MoHSS policy makers and leaders in modifying and strengthening interventions aimed at enhancing treatment uptake, adherence, retention, and viral load suppression among HIV-infected children in Namibia. The problem statement is summarized in a conceptual model (figure 1).

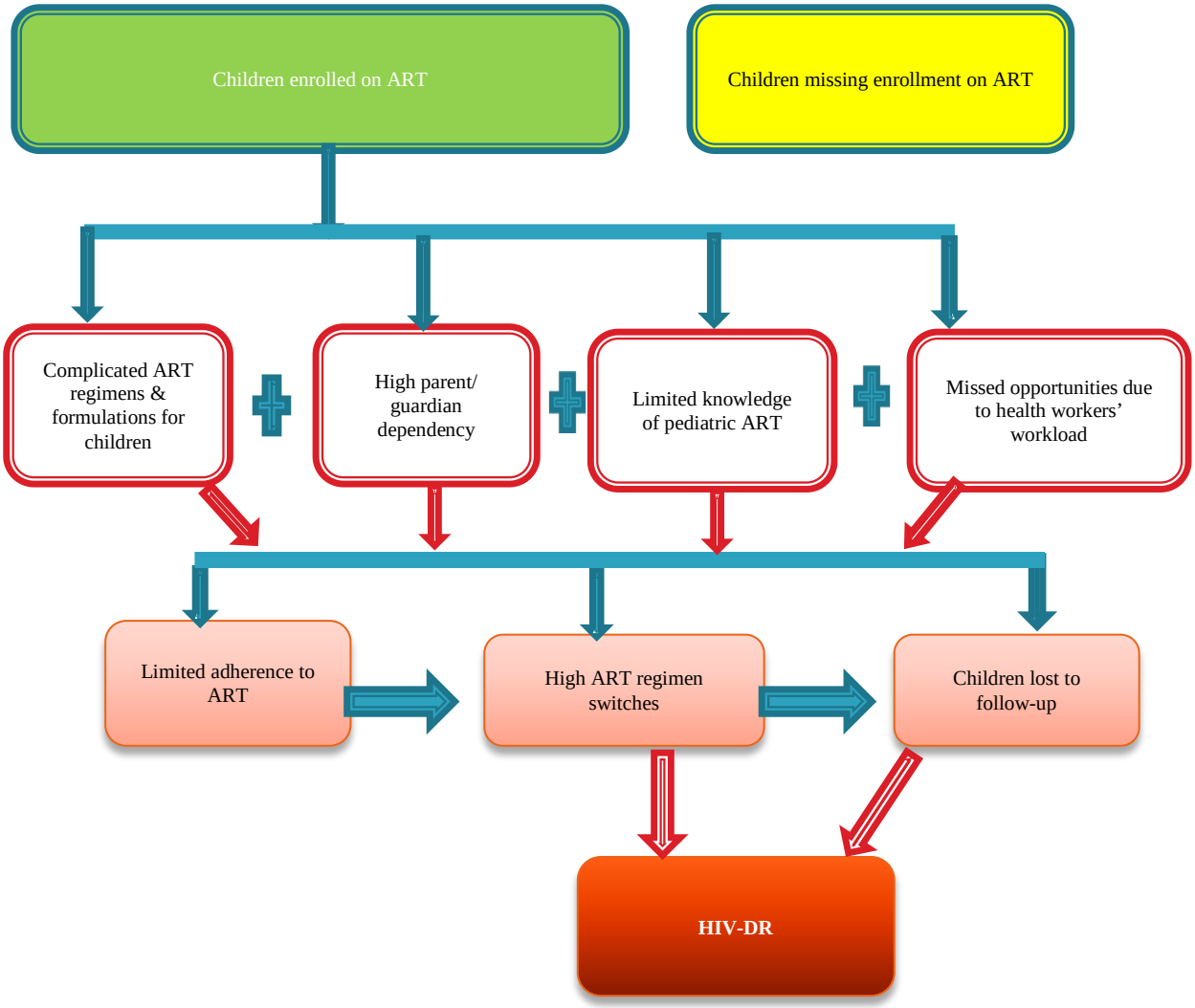

Figure 1: Problem statement – conceptual model

METHODOLOGY

Objectives of the Assessment

Broad Objective

The broad objective was to conduct a programmatic and policy-relevant longitudinal analysis of routinely collected pediatric data (<1 year, 1–4 years, 5–9 years, 10–14 years) from 2010 to 2015 on the EDT database in Namibia. Specifically, we assessed trends in HIV treatment uptake, retention in care, and switches from first to second line ART regimens among HIV-infected children in Namibia between 2010 and 2015.

Specific Objectives

To determine the trends over time in the:

- Number of children starting ART
- Proportion of children on ART not accessing treatment on time (on-time pill pickup)
- Proportion of children on ART having inadequate medicine coverage and LTFU
- Proportion of children switched from first line to second line ART regimens

Additional objectives included documenting and describing the reasons for ART regimen switches in children and facility compliance with ART national guidelines.

Assessment Design

This was an observational study based on the retrospective review of EDT records to calculate pediatric ART trends over the past five years for variables of interest. Namibia has experience using a centralized EDT database where primary data have been validated before. A defined cohort of pediatric patients enrolled in ART care and treatment from all ART sites in Namibia for the period of July 2010 to June 2015 was selected for the assessment to provide a national picture.

Population and Sample

The assessment in Namibia involved all public ART sites where an estimated 8% are pediatric patients enrolled on ART.[7] Sites that had started providing HIV treatment services in July 2010 were included in the assessment. The assessment population included all pediatric patients who were initiated on ART treatment from July 2010 to June 2015. This included pediatric patients who were on both first- and second-line ART regimens. Figure 2 below shows the algorithm that was used for the selection of assessment sample and data flow.

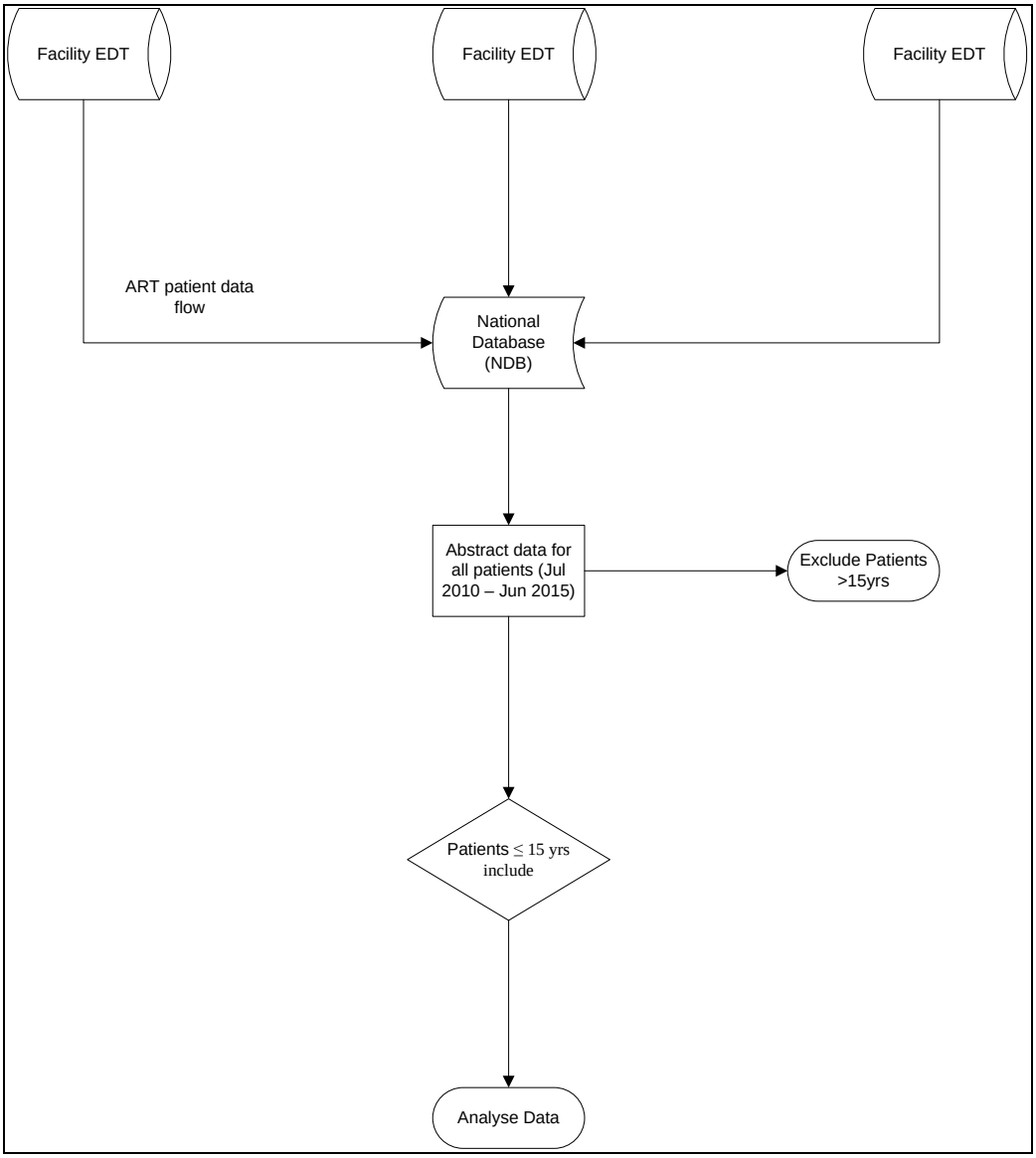

Figure 2: Algorithm for sample selection and data flow

Sampling of Health Facilities for the Assessment

All 34 districts were included in the assessment. Data sets from all 50 public main ART health facilities in Namibia (35 hospitals, 9 health centers, and 6 clinics) that were equipped with EDT and provided pediatric ART services between July 2010 and June 2015 were used. The target population was stratified by age (<1 year, 1–4 years, 5–14 years) at the time of ART enrollment.

Data Extraction

Data extraction was done by special scripts on the selected databases. The data extraction was limited and focused on assessment objectives and scope and was anonymized. No PII was extracted. Name—such as full name, maiden name, mother's maiden name, or alias—was not extracted. The extracted data from the EDT review provided characteristics such as percent (%) medicine coverage, patients' appointment keeping, and patient retention on ART without

any patient-specific information. Context of use of the extracted data was only for aggregated analysis.

Data Management and Analysis

This assessment utilized existing data for patients in the public health sector in the centralized EDT. The EDT captures information on all variables of interest for this assessment, such as appointment keeping, pill count, changes in regimen, and full dispensing data per patient per visit. The system also monitors consumption of each ARV at each facility. The national database, consisting of data from all EDTs at ART main facilities in the country, is situated at the Division of Pharmaceutical Services at MoHSS headquarters. To validate the extracted data, an initial manual check for data completeness was carried out so that the auto-population of the data extraction template would reflect a true data set. This helped to eliminate any double counting of patients (based on definitions). Duplicate data was cleaned and up-to-date records were used in this assessment.

Data on pediatric ART patients in 50 main public health ART sites in all 14 regions of Namibia, as captured in the EDT, was extracted into a Microsoft Excel database; anonymized; cleaned; and analyzed using Stata v11 and Excel to generate percentages and survival/failure as well as determine associations between/among variables. The results are presented in the form of tables, graphs, and summarized text.

Ethical Considerations

The study was approved by the Permanent Secretary of MoHSS, Namibia. Data was anonymized and no PII was included in the analysis or results. Data extraction from the EDT database and its anonymization was conducted by selected assessment team members who already had authorized access to the database.

Safety to Assessment Participants

The assessment was based on existing data in the EDT database and thus did not incur any physical, psychological, or social harm to the assessment participants. No patient interviews were done and PII was neither extracted nor used anywhere during analysis or presentation of results.

Confidentiality of Patient Information

Data was anonymized during extraction from the EDT. No PII was extracted. Name—such as full name, maiden name, mother's maiden name, or alias—was not extracted. The extracted data from the EDT review did not yield any patient-specific information. Only assessment team members responsible for data extraction and analysis had access to the data.

IMPLICATION FOR ASSESSMENT FINDINGS AND DISSEMINATION PLAN

To ensure continuity of this type of analysis and to incorporate lessons learned from this assessment for the future, the collaborating institutions included the Division of Pharmaceutical Services within MoHSS; National HIV/AIDS Control Program, working through the Directorate of Special Programs; Namibia University of Science and Technology, with their enhanced capacity for data analysis; University of Namibia's School of Pharmacy, spearheading the work with their capacity for supporting MoHSS with analyses of public health and ART data; and technical support from SIAPS, implemented by MSH, and Harvard Pilgrim Health Care Institute in defining/refining the assessment question(s), identifying data needed to address priority questions and establish a data management process that included a description of resources and skills needed, and assisting in the execution of the assessment and compilation of the technical report and policy brief for MoHSS managers. MoHSS will spearhead dissemination of results and recommendations with stakeholders and a wider audience through various mediums, including publication of this work in reputable journals, after approval from MoHSS.

Although currently children make up a small proportion of all patients accessing ART in public health facilities (estimated at 8%), pediatric ART management is complex and will continue to be so for the foreseeable future.

Sound programmatic, policy, and guideline decision-making can improve pediatric ART care and treatment when guided by useful information obtained from routinely collected data, such as those in the EDT database. The results from this assessment will be shared among MoHSS, the Directorate of Special Programs, National HIV/AIDS Control Program, Directorate of Tertiary Health Care and Clinical Support Services, Division of Pharmaceutical Services, and MoHSS partners in health service delivery. MoHSS will utilize the findings to make decisions that will improve pediatric ART care in Namibia. Also, SIAPS is supporting the MoHSS to develop a data management process (template) that includes a description of resources and skills needed to conduct similar data analyses in the future to ensure this level of programmatic use of existing data becomes routine. With MoHSS leadership, the findings and recommendations will be widely disseminated through different technical and professional forums, as well as published in peer-reviewed journals.

RESULTS

Description of Facilities, Visits, Patients

The analyzed data came from 51 health facilities and involved 5,476 pediatric patients enrolled for ART in public health facilities in Namibia in the period 2010 to 2015.

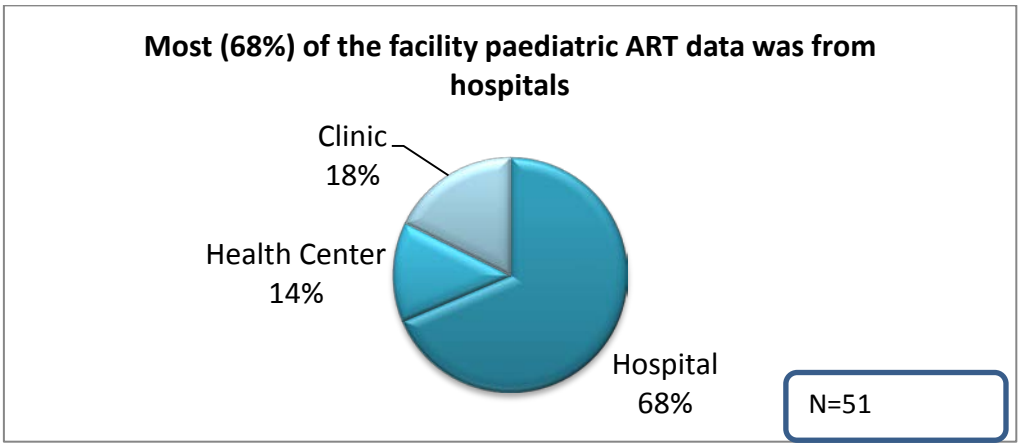

Figure 3: Proportion of health facilities, by level, involved in the assessment

Number of Children Starting ART from 2010 to 2015 (N=5,476)

Figures 4, 5, 6, and 7 show the number of children starting ART from 2010 to 2015. The number of children starting ART decreased over the years. The most enrolled age group in 2010–2015 was the 1–4-year age group. The Omusati, Ohangwena, and Kavango regions recorded the highest enrollment in the study period. Older children (10–14 years) enrolled more in 2014 and 2015 compared to other age groups.

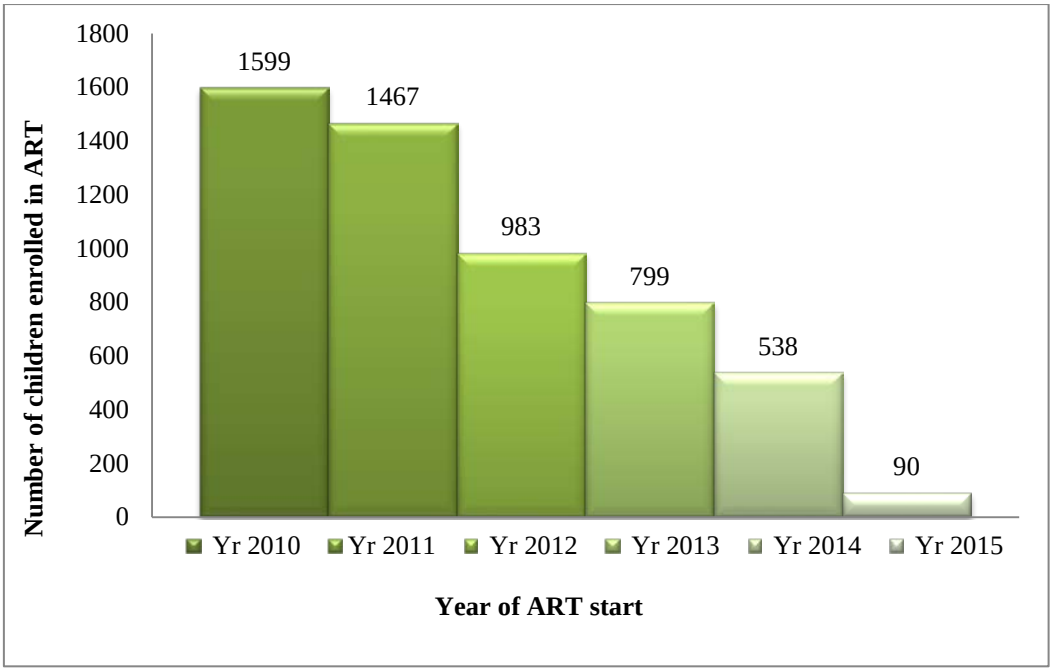

Figure 4: Number of children enrolled in ART reduced over time from 2010–2015

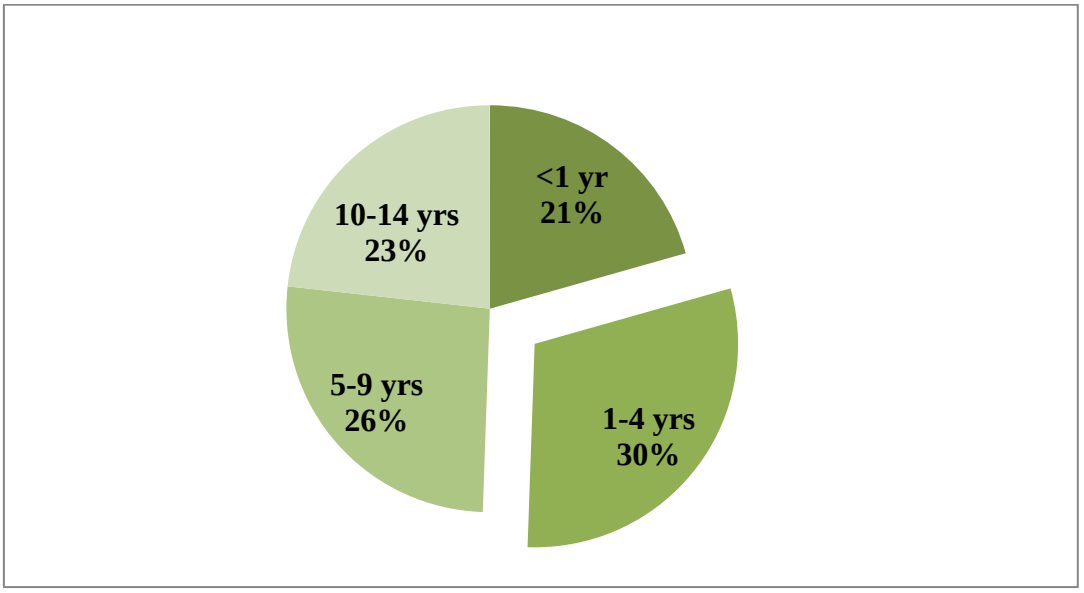

Figure 5: The 1–4-year group most enrolled age group for ART in 2010–2015

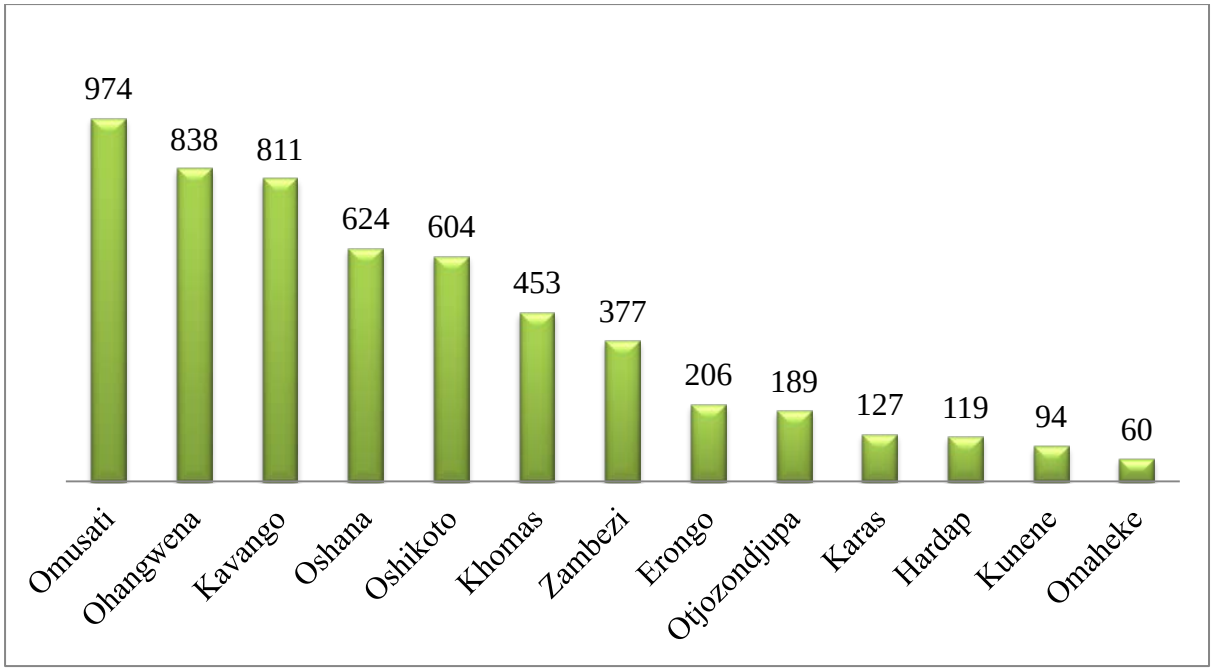

Figure 6: Number of children by region starting ART in 2010–2015

In the Omusati, Ohangwena, and Kavango regions, most pediatric patients were enrolled in 2010 and 2011.

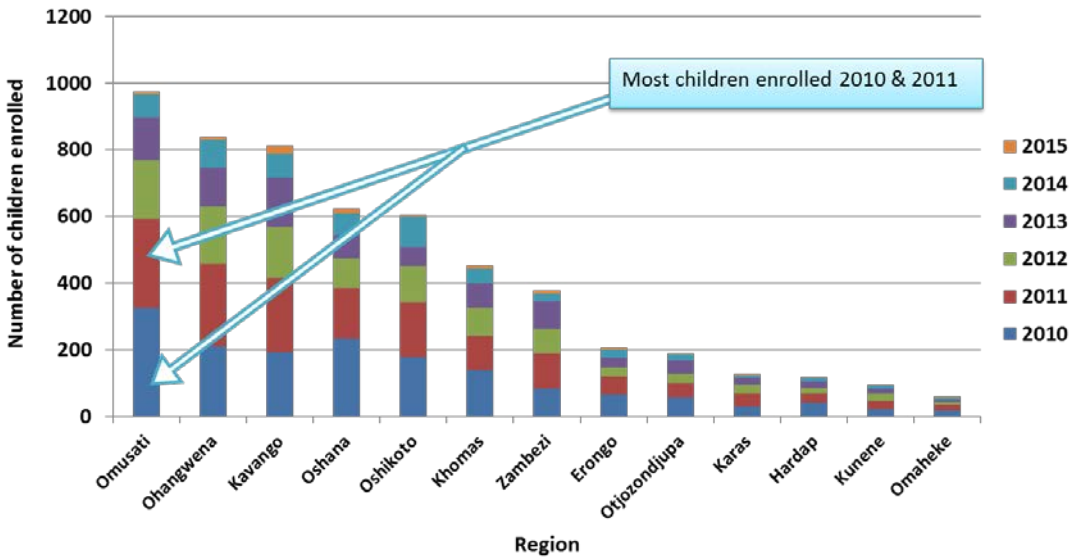

Figure 7: Number of children enrolled in ART by region and year of enrollment

Proportion of Children on ART Not Accessing Treatment on Time (On-Time Pill Pickup)

Table 2 shows the proportion of children picking up their ARVs on time from 2009–2015. Patients picking up their ARVs within three days of the pharmacy appointment were considered to be on time. On average, the percentage of patients picking up their ARVs on time in this period was 73.89%.

Table 2: Proportion of children on ART accessing treatment on time (on-time pill pickup)

Year	On-time pill pickup	Late pill pickup	(Missing days late)	Total
2009	1,616 76.12%	418 19.69%	89 4.19%	2,123 100%
2010	1,326 71.44%	478 25.75%	52 2.8%	1,856 100%
2011	1,398 75.81%	390 21.15%	56 3.04%	1,844 100%
2012	876 71.86%	301 24.69%	42 3.45%	1,219 100%
2013	714 70%	264 25.88%	42 4.12%	1,020 100%
2014	1,363 73.92%	426 23.1%	55 2.98%	1,844 100%
2015	531 77.75%	98 14.35%	54 7.91%	683 100%
Total	**7,824** **73.89%**	**2,375** **22.43%**	**390** **3.68%**	**10,589** **100%**

Proportion of Children on ART Having Inadequate Medicine Coverage and LTFU (2010–2015) (N=888)

A total of 888 children were LTFU between 2010 and 2015. This figure is likely to be overstated as some patients may have transferred out to other health facilities (and were therefore retained on ART) but did not inform their health facility staff. These patients end up being flagged as LTFU. Children within the 1–4-year age group (30%) and <1-year age group (29%) were more likely LTFU compared to older age groups. Figure 9 shows that a majority of the children who were LTFU were registered at the hospital level.

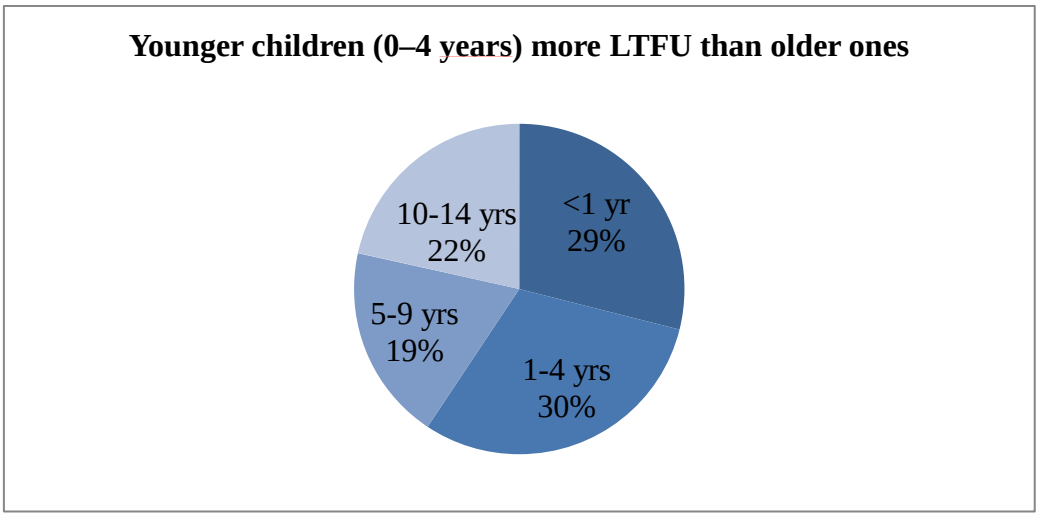

Figure 8: Proportion of children on ART who were LTFU, by age category

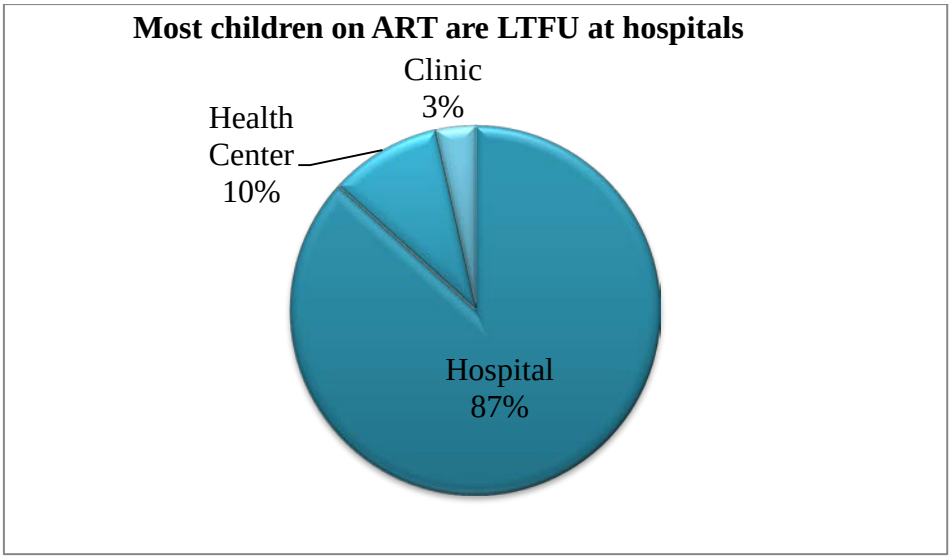

Figure 9: Proportion of children LTFU by facility level

Proportion of Children Switched from First-Line to Second-Line ART Regimens (N=5,476)

Figures 10, 11, and 12 show that 8% of children enrolled in ART from 2010–2015 switched from first- to second-line ART regimens. Switching was more prevalent in older and male children.

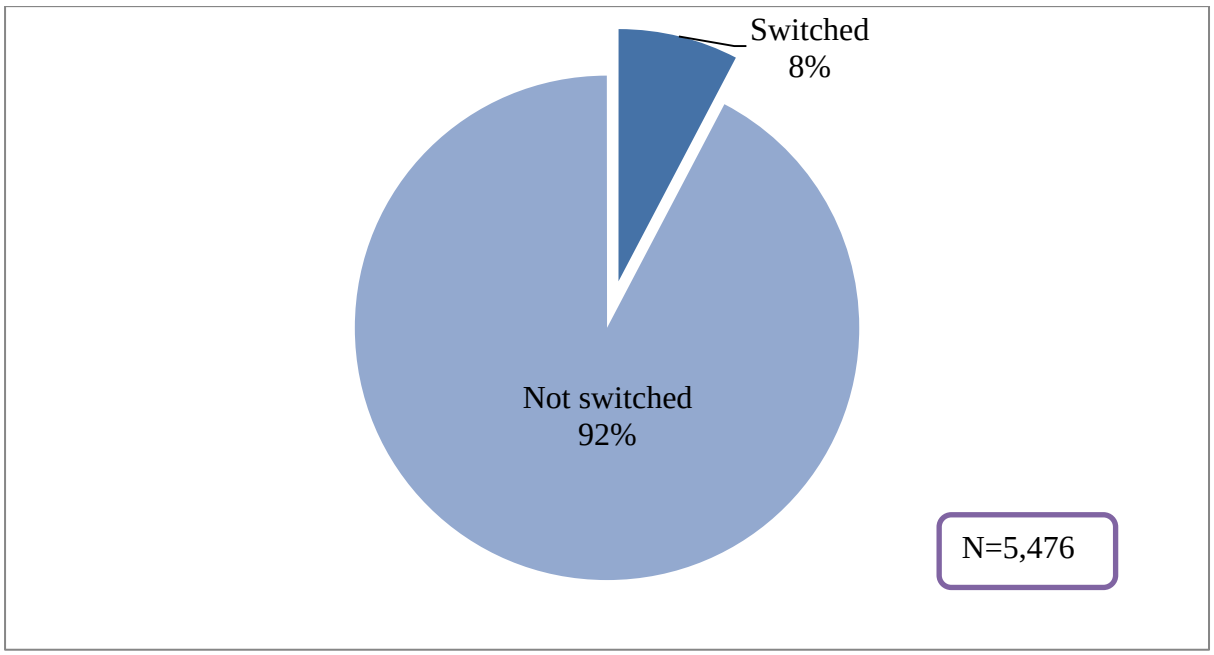

Figure 10: The proportion of children switched from first line to second line ART regimens in 2010–2015

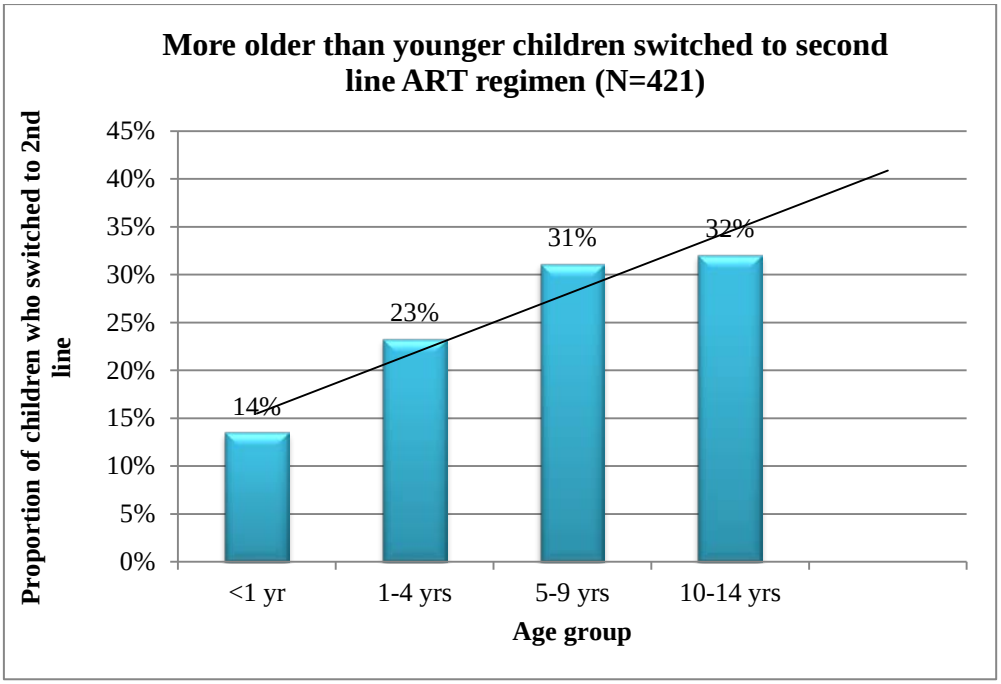

Figure 11: Proportion of children who switched from first- to second-line ART regimens in 2010–2015

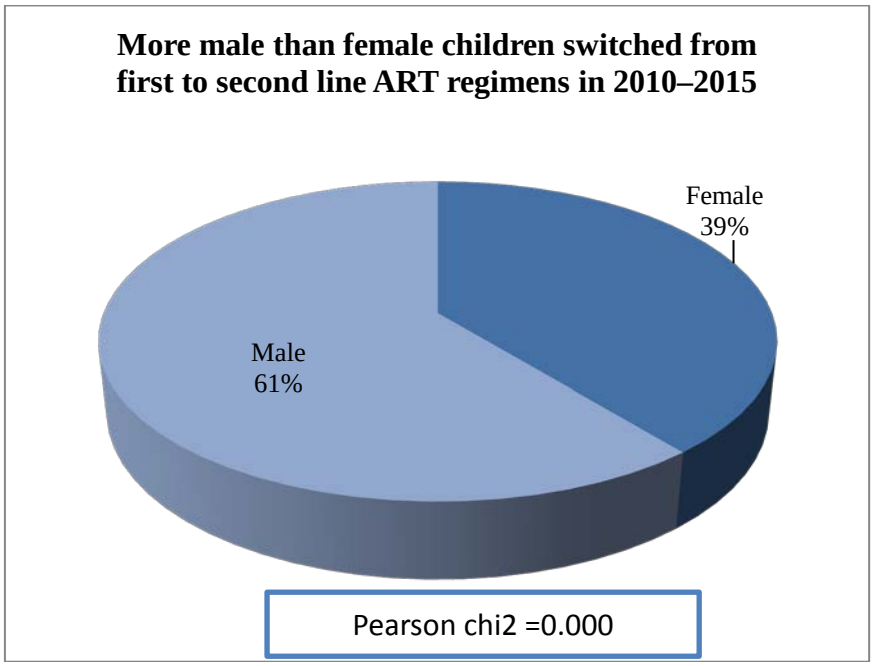

Figure 12: Children switched from first- to second-line ART regimens in 2010–2015, by gender

More switches from a first- to a second-line ART regimen happened after 12 months and were higher among males (N=421).

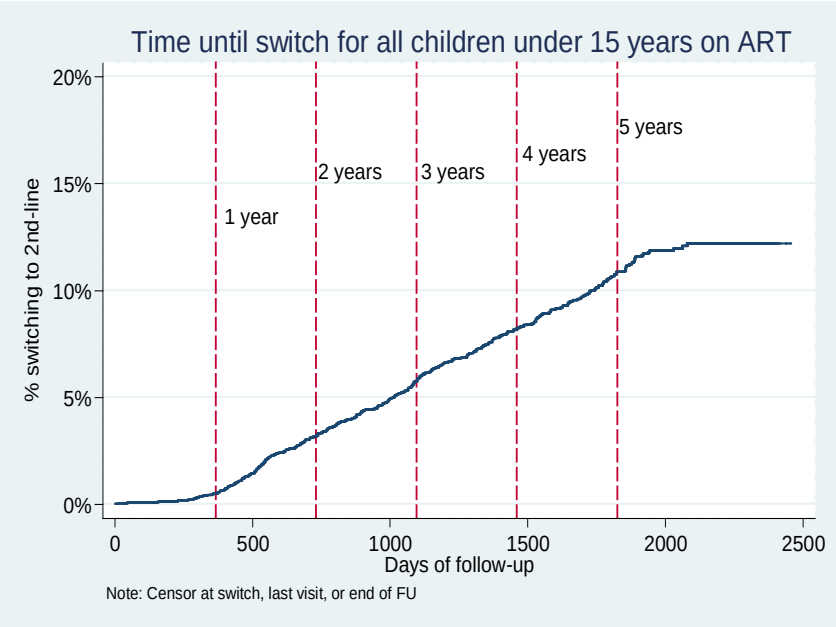

Figure 13: Time until switch from first- to second-line ART regimen for all children under 15 years on ART

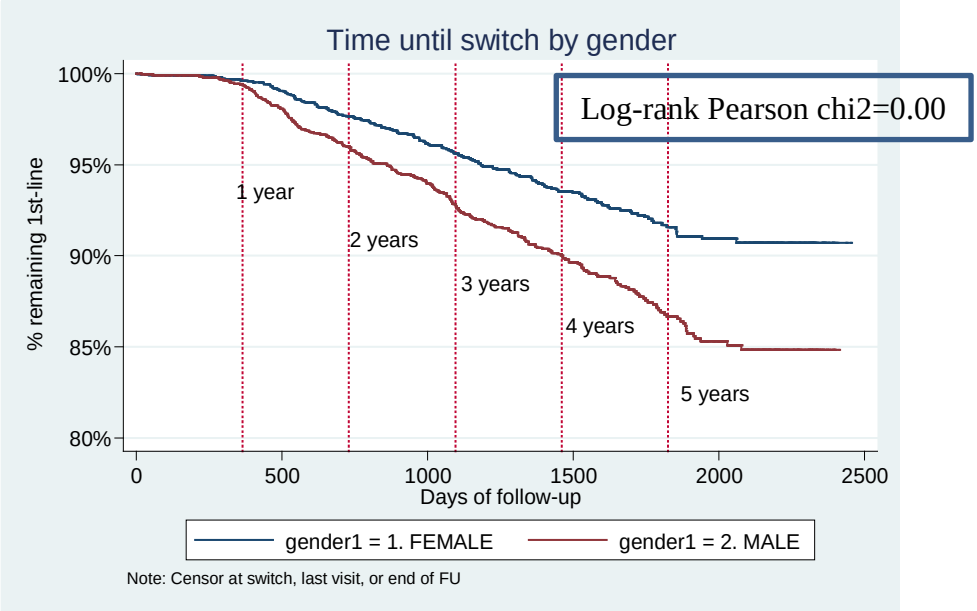

Figure 14: Time of switch to second-line ART regimen, by gender

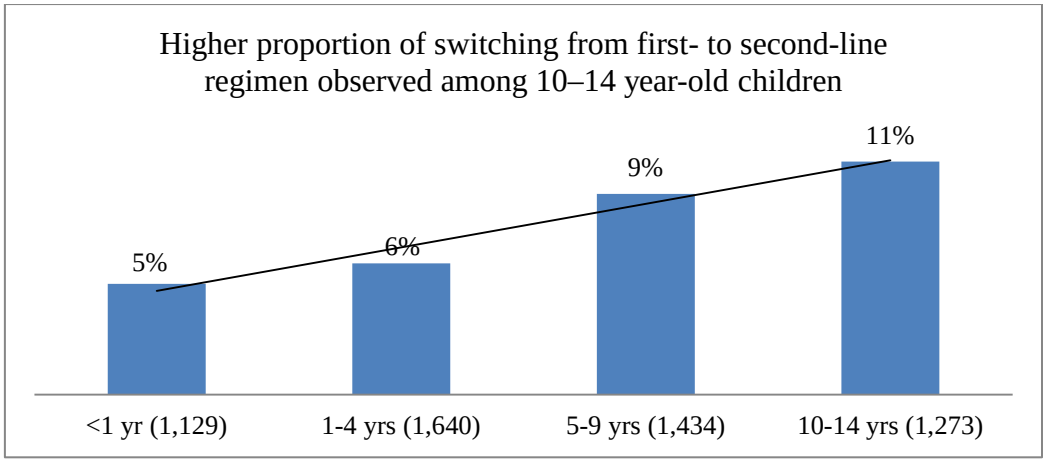

Figure 15: Proportion of children who switched from first- to second-line regimens in 2010–2015 within age group

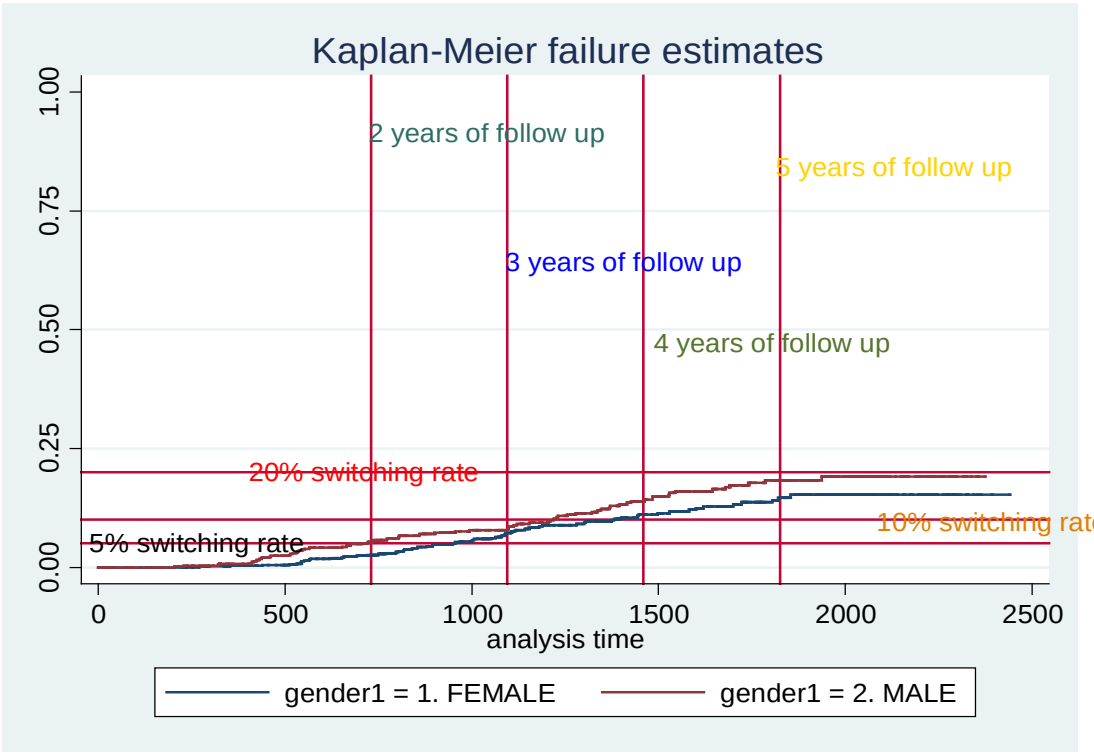

Figure 16: Rate of switch to second line ART regimen among 10–14-year children

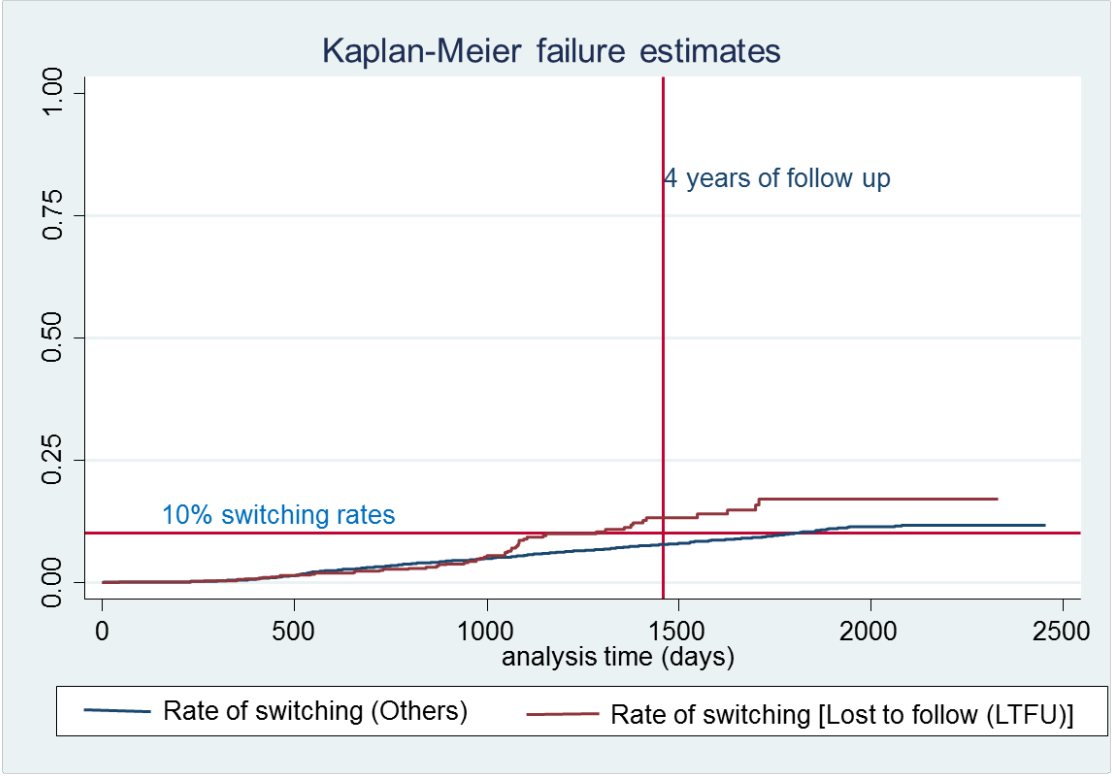

Figure 17: Rate of switch to second line ART regimen among 10–14-year children who were LTFU

Documented Reasons for ART Regimen Switches in Children and Facility Compliance with ART National Guidelines

The EDT captures reasons for switching from first-line to second-line regimens. Virological failure was the predominant reason for switching among children.

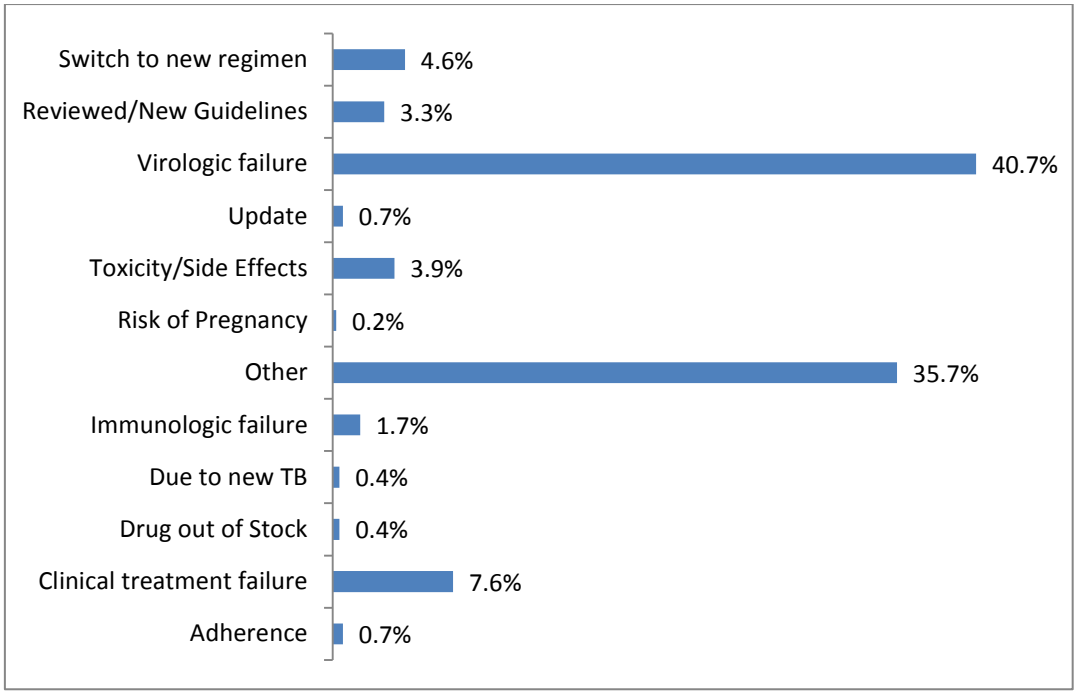

Figure 18: Documented reasons for switching from first- to second-line regimen in children

DISCUSSION OF FINDINGS

Results from the data analysis of the EDT on pediatric patients are discussed in this section. The results presented show insights into some pediatric statics that have not been previously captured in routine MoHSS reports.

Based on the EDT data analyzed from 50 health facilities, 5,476 pediatric patients were enrolled for ART in public health facilities in Namibia in the period 2010 to 2015. This finding corresponds with routine reports such as the ART-Pharmaceutical Management Information System reports and the 2011 annual analysis of ARV therapy regimens report.[26] A large number of children were started on treatment in 2010 and 2011, with the likely reason being the revision of CD4 criteria and early infant diagnosis using DNA PCR testing in the 2010 guidelines, which led to more children in need of ART being identified and put into care early.[27] However, there was an unexplained and progressive decline in the number of children starting ART from 2010 to 2015. The majority of children started on ART were in the age group 1–4 years. The Omusati, Ohangwena, and Kavango regions recorded the highest enrollment in the study period. These are generally high-burden peripheral regions in Namibia, with a large rural-based population.

On-time pill pickup is an important measure of patient adherence that is associated with loss to follow up, HIV drug resistance, virological failure, and increased mortality.[27] Patients picking up their ARVs within three days of the pharmacy appointment were considered to be on time. Over 73% of pediatric patients achieved this stringent criterion of on-time pill pickup. This criterion is set by WHO as an early warning indicator for HIV drug resistance. There was no significant difference in the year-to-year analysis of on-time pill pickup.

In the period 2010–2015, a total of 888 (16%) children were registered as LTFU. This figure is likely to be overstated as some patients may have transferred out to other health facilities (and were therefore retained on ART) but did not inform their health facility staff. Namibia is distinguished by a decentralized model of ART care, and HIV treatment is offered at lower level health facilities, such as clinics. These patients end up being flagged as LTFU. Nevertheless, LTFU patients are at high risk for experiencing treatment interruptions and developing HIV drug resistance.[28]

Eight percent (8%) of children enrolled in ART from 2010–2015 switched from first- to second-line ART regimens. Switching was more prevalent in older and male children. In this study, a switch is defined as the change from a first-line to a second-line ART regimen and is consequent on the failure of first-line therapy, as defined by the national ART guidelines. More switches occur after 12 months of therapy and were mostly observed in male children.

The current study found that in patients with treatment failure, virological failure and clinical failure were the most common reasons cited, with a proportion of patients indicating toxicity, immunological failure, and stockouts as reasons for switching. Our findings demonstrate that the reasons for switching are not routinely documented, even though the EDT is capable of capturing this information.

CONCLUSIONS AND RECOMMENDATIONS

Overall, the number of children starting ART decreased over the years. The most enrolled age group in 2010–2015 was 1–4 years old. The Omusati, Ohangwena, and Kavango regions recorded the highest enrollment in the study period. Older children (10–14 years) enrolled more in 2014 and 2015 compared to other age groups, which was likely attributable to ART policy changes in 2014.

- A study should be conducted to explore factors contributing to reduced number of children enrolled for ART (e.g., could it be that there are fewer children in need of ART due to PMTCT success?).

- Early enrollment of children, especially male children and the 10–14-year group, is highly recommended. Late ART initiation and co-morbidities in the 10–14-year group may be associated with higher regimen switches. MoHSS should strengthen interventions (e.g., treat all/test and treat) for increased enrollment of this group.

Eight percent (8%) of the 5,476 children enrolled in ART from 2010–2015 switched from first- to second-line ART regimens. Most switches were observed among males (61%, log-rank test: p=0.000) and the 10–14-year age categories. The rate of switching from first to second-line ART regimens increased after at least 12 months of treatment. Rate of switching after two years was approximately 4% and increased to approximately 12% after five years.

- A study should be conducted to explore factors associated with patients switching from first to second line and those LTFU so that enhanced clinical monitoring is done for patients with similar characteristics to avoid switching and loss to follow-up.

Approximately 16.2% of the 5,476 children enrolled in ART from 2010–2015 were LTFU in the study period. Most (87%) of the 888 children on ART recorded as LTFU were started on ART at hospitals. Younger children (0–4 years) (59%) were more LTFU than older ones.

- The MoHSS Treatment Technical Working Group should identify interventions for improving pediatric patients' management to minimize loss to follow-up, which could lead to treatment failure, HIV drug resistance, and the need for regimen switches.

- Side effects of second-line regimens may be a possible cause of loss to follow-up. Further studies are needed on causal factors/predictors.

- A similar analysis is recommended for adult patients on ART.

LIMITATIONS OF THE ASSESSMENT

The analysis and conclusions were limited by available data in the EDT data set that was used. The data gaps limited further analysis that was desired to explore possible factors associated with the findings, but could answer the study questions in the approved protocol. The following data gaps were identified:

- Clinical data (e.g., viral load, clinical stage, and CD4 count at ART initiation) were missing in the data set as it is not captured in the EDT; such data could be linked to some of the outcomes.

- The date of first switch was not available in the data set. The analysis was based on the date of switch to second line, but the patient may have switched to other regimens prior to this.

- Missing data for "re-activated/re-started" patients showing status "active" at the time of data extraction that may explain some of the switches from first to second line were not available in the EDT database that was used in the study.

- The date of clinician switch may not be the date of ART regimen switch captured in the database. This may have presented gaps in the time between clinician recommendation to the actual date of ART regimen switch captured in the EDT database.

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ANNEX A. ASSESSMENT TEAM

Name	Institution	Role on the Team
Dr. Ndapewa Hamunime	MoHSS Namibia	Principal Investigator
Ms. Francina Tjituka-Kaindje	MoHSS Namibia	Associate Principal Investigator
Mr. Lazarus Indongo	MoHSS Namibia	Co-Investigator
Mr. Evans Sagwa	SIAPS Namibia	Co-Investigator
Mr. Nicholus Mutenda	MoHSS Namibia	Associate Principal Investigator
Dr. Assegid Mengistu	MoHSS Namibia	Technical Advisor
Mr. Greatjoy Mazibuko	SIAPS Namibia	Technical Advisor
Mr. Samson Mwinga	SIAPS Namibia	Technical Advisor
Ms. Harriet R. Kagoya	SIAPS Namibia	Technical Advisor
Mr. Nasser Mbaziira	SIAPS Namibia	Technical Advisor
Mr. Innocent Maposa	Namibia University of Science and Technology	Technical Advisor, Statistician
Dr. Tadesse Mekonen	MoHSS Namibia	Technical Advisor
Mr. Kennedy Kambyambya	MoHSS Namibia	Technical Advisor
Ms. Naita Nghishekwa	MoHSS Namibia	Technical Advisor
Dr. David Mabirizi	SIAPS Arlington	Technical Advisor
Mr. Dan Kibuule	University of Namibia, School of Pharmacy	Technical Advisor
Prof. Timothy Rennie	University of Namibia, School of Pharmacy	Technical Advisor
Dr. Vialle-Valentin	Harvard Medical School	Technical Advisor
Dr. Dennis Ross-Degman	Harvard Pilgrim Health Care Institute	Technical Advisor
Mr. Salomo Natanael	MoHSS Namibia	Technical Advisor
Dr. Maheen Malik	SIAPS Arlington	Technical Advisor
Ms. Katelyn Payne	SIAPS Arlington	Technical Advisor
Ms. Rosalia Indongo	USAID Namibia	Technical Advisor
Ms. Dinah Tjipura	SIAPS Arlington	Technical Advisor

ANNEX B. EDT MAIN SITES

No.	Region	Facility Name	Facility Type
1.	Zambezi	Katima Mulilo	Hospital
2.	Erongo	Omaruru	Hospital
3.		Swakopmund	
4.		Usakos	
5.		Walvis Bay	
6.	Hardap	Aranos	Health center
7.		Mariental	Hospital
8.		Rehoboth	
9.	Karas	Karasburg	Hospital
10.		Keetmanshoop	
11.		Luderitz	
12.		Rosh Pinah	Clinic
13.	Kavango	Andara	Hospital
14.		Nankudu	
15.		Nkurenkuru	Health center
16.		Nyangana	Hospital
17.		Rundu	
18.	Khomas	Katutura HC	Health center
19.		Katutura IH	Hospital
20.		Khomasdal	Clinic
21.		Okuryangava	
22.		Otjomuise	
23.		Robert Mugabe	
24.		Windhoek CH	Hospital
25.	Kunene	Khorixas	Hospital
26.		Opuwo	
27.		Outjo	
28.	Ohangwena	Eenhana	Hospital
29.		Engela	
30.		Odibo	Health center
31.		Okongo	Hospital
32.		Ongha	Health center
33.	Omaheke	Gobabis	Hospital
34.	Omusati	Okahao	Hospital
35.		Okalongo	Health center
36.		Onesi	Clinic
37.		Oshikuku	Hospital
38.		Outapi	
39.		Tsandi	
40.	Oshana	Ondangwa	Health center
41.		Ongwediva	
42.		Oshakati	Hospital
43.	Oshikoto	Omuthiya	Hospital
44.		Onandjokwe	
45.		Oshivelo	Clinic
46.		Tsumeb	Hospital
47.	Otjozondjupa	Grootfontein	Hospital
48.		Okahandja	
49.		Okakarara	
50.		Otjiwarongo	