Factors Associated With First-Line to Second-Line ART Regimen Switching Identified in the APMR Data Systems in Swaziland

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Systems for Improved Access to Pharmaceuticals and Services
Pharmaceuticals & Health Technologies Group
Management Sciences for Health
4301 North Fairfax Drive, Suite 400
Arlington, VA 22203 USA
Telephone: 703.524.6575
Fax: 703.524.7898
E-mail: siaps@msh.org
Web: www.siapsprogram.org

CONTENTS

ACRONYMS AND ABBREVIATIONS

APMR	Antiretroviral Therapy Patient Monitoring and Reporting [System]
ART	antiretroviral therapy
ATV/r	atazanavir/ritonavir
AZT	zidovudine
CI	confidence interval
DRV/r	darunavir/ritonavir
EFV	efavirenz
ETV	etravirine
HMIS	Health Management Information System [Unit]
3TC	lamivudine
MOH	Ministry of Health
MSH	Management Sciences for Health
NARTIS	nurse-led ART initiation
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NVP	nevirapine
PI	protease inhibitor
RAL	raltegravir
d4T	stavudine
SEC	Scientific and Ethics Committee
SIAPS	System for Improved Access to Pharmaceuticals and Services
SID	Strategic Information Department
SNAP	Swaziland National AIDS Programme
TB	tuberculosis
TDF	tenofovir
WHO	World Health Organization

DEFINITION OF TERMS

First-line antiretroviral therapy (ART): the initial regimen prescribed for HIV patients fulfilling national clinical and laboratory criteria for starting ART. Current World Health Organization (WHO) treatment guidelines recommend two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI) for initial treatment.[1]

Second-line ART: the regimen used immediately after first-line therapy has failed (clinically, immunologically, or virologically). Current WHO treatment guidelines recommend that the protease inhibitor (PI) class be reserved for second-line ART, preferring ritonavir-boosted PIs supported by two agents from the NRTI class.[2]

A switch from first- to second-line regimen: replacement of NNRTIs with PIs in a client's initial regimen.

[1] WHO. ART failure and strategies for switching ART regimens in the WHO European Region: report of the WHO expert consultation, Copenhagen, 7 December 2007. Copenhagen, Denmark: WHO Regional Office for Europe; 2008.
[2] Ibid.

EXECUTIVE SUMMARY

For over eight years, Management Sciences for Health (MSH) has supported the Swaziland Ministry of Health (MOH) to establish and ensure the functioning of the Antiretroviral Therapy Patient Monitoring and Reporting (APMR) and RxSolution data systems for management of patient and logistics data, respectively. During that time, MSH observed a limited use of the data stored in these electronic systems for the purposes of programmatic data analysis and research. Further observations have revealed that approaches employed in using the data were not always comparable, and results of data analysis from these electronic systems have not been adequately incorporated into decision-making processes.

To bridge such gaps, MSH undertook a capacity building initiative to ensure adequate training and demonstration of how the data captured and stored in these electronic data systems could be used for targeted programmatic data analysis and research to improve decision-making. Through engagements with the MOH, a joint decision was taken to implement a study to determine the factors associated with first-line to second-line ART regimen switching identified in the APMR data management systems. The objectives of this study were to:

- Determine the factors associated with first-line to second-line ART regimen switching identified in the APMR data management system
- Determine the rate of first-line to second-line ART regimen switching for ART patients, as recorded in the APMR data management system
- Determine the time taken for t ART patients to switch from first- line to second-line ART regimens
- Document the reasons for switching from first-line to second-line ART regimens, as recorded in the APMR data management system

This study was a retrospective cohort design focusing on a defined cohort of active ART patients between the years 2010 and 2015. The selection of study records involved both convenience and cluster sampling (targeting stand-alone reporting sites and the so-called "mother facilities," the main ART-initiating facilities). Records available in the central national ART database were used to draw the study sample. The sampling frame was a total of 119,404 and the final sample size was 117,586 ART patient records. The study used the Cox regression method, descriptive statistics, and survival analysis (Kaplan-Meier method*)* to address its objectives.

Of the 117,586 ART patient records, 3.6% (n = 4,266) indicated that the regimen was switched from first-line to second-line treatment. The main reason for regimen switching was registered treatment failure (15.3% [652/4,266]). A large proportion of the patients who switched regimens (32.6%) were in the age range of 25 to 44 years. Other reasons for regimen switching were related to adherence (0.6%), clinical reasons (2.7%), drug logistics (0.2%), reason not noted (67.7%), and toxicities (8%).

At a 95% confidence level, all the selected covariates (i.e., WHO clinical staging; age grouping at initiation; geographical region where the patient was receiving treatment; gender)

were found to be significantly associated with regimen switching. Males with a hazard ratio of 1.18 (95% confidence interval [CI]: 1.10-1.27) were found to be associated with a higher hazard of switching from the first- to second-line ART regimen compared to females. Moreover, patients initiating ART between the ages of 15 to 24 years had a higher hazard of switching from first-line to second-line treatment regimen compared to any other age group. ART patients initiated at ages above 45 years were found to have the lowest hazard ratio, at 0.77 (95% CI: 0.68%-0.87%). Patients receiving treatment or initiated at health facilities located in the Hhohho region were found to have a higher hazard of switching from one regimen to the other compared to the other regions in the country. Patients receiving treatment or initiated in a health facility in the Lubombo region were found to have the lowest hazard ratio, at 0.41 (95% CI: 0.36%-0.46%). ART patients initiated in the WHO clinical stage I presented with the lowest hazard of regimen switching compared to the other WHO clinical staging categories. ART patients initiated in the WHO clinical stage II had a hazard ratio of 1.52 (95% CI: 1.39%-1.67%); those initiated in the WHO clinical stage III had a hazard ratio of 1.9 (95% CI: 1.73-2.08); and ART patients initiated in the WHO clinical stage IV had a hazard ratio of 3.55 (95% CI: 3.13%-4.03%).

The median survival time for all ART patients switching from first- to second-line regimens was 607 days (95% CI: 601-613) or 19.5 months. Only 89% of patients initiated on ART in the Hhohho region were likely to remain on the first-line regimen by the end of the five-year follow-up period. In the Manzini and Shiselweni regions, 92% of ART patients initiated by facilities in these regions remained on the first-line regimen at the end of the five-year follow-up period. Lastly, a majority of ART patients (96%) initiated in the Lubombo region remained on the first-line regimen by the end of the five-year follow-up period. ART patients initiated at age 45 and older remained on the first-line regimen for longer periods than other age groups at 93.5%, whereas patients initiated at ages 15 to 24 years seemed to be the most affected by regimen switching during follow-up periods years 1 to 4, but then stabilized to reflect improved survival of 92% by the end of the year 5, surpassing the survival rates for regimen switching among age groups 25-34 and 35-44 years, who had 90% and 91%, respectively, as of the end of the five-year follow-up period. Survival time for males on the first-line regimen was less than that of females, i.e., more females initiated on ART remained on the first-line regimen by the end of the five-year follow-up period compared to males. For patients initiated on ART in the WHO clinical stage IV, only 83% remained on the first-line regimen as of the end of the five-year follow-up period. For patients initiated on ART in the WHO clinical stages II and III, 90% and 91%, respectively, remained on the first-line regimen as of the end of a five-year follow-up period.

Through this study, it became apparent that the following considerations should be taken into account in the design of routine data collection systems:

1. Clinicians and primary users of the systems (i.e., data clerks) should be involved.

2. Logical, built-in data validation rules for each of the systems are needed to avoid data quality issues as a result of poor data capturing.

3. Data quality review sessions should be scheduled to respond to performance indicators and research questions using the data.

Routine data collection systems have huge amounts of useful data that can respond to and help motivate positive changes in the management of patients, thereby improving health

outcomes. Use of these data to address operational research questions needs to be institutionalized in the MOH.

Some of the policy recommendations for the MOH resulting from the study findings are:

- Strengthen systems and develop guidance for the early identification of regimen-switching cases
- Introduce policies or strategies to ensure the early initiation of men on ART
- Introduce strategies for longer retention on first-line ART for younger age groups
- Conduct further studies to provide information on the differences observed in regimen-switching hazards by region

INTRODUCTION

Over the past eight years, MSH has supported the MOH in Swaziland to establish and ensure the functioning of the APMR and RxSolution data systems for the management of patient and logistics data, respectively. In that time, MSH has observed a limited use of the data captured and stored in these electronic systems for the purposes of targeted programmatic data analysis and research. Further observations have revealed that approaches employed in using the data were not always comparable, and results of data analysis from these electronic systems have not been adequately fed into decision-making processes.

Consistent with its health systems strengthening strategy, MSH undertook a capacity building initiative that would ensure adequate training and demonstration of how the data captured and stored in these electronic data systems could be used in targeted programmatic data analysis and research for improved decision-making. This capacity building initiative involved MSH collaborating with the MOH to evaluate the quality, completeness, and potential uses of APMR and RxSolution data in Swaziland. In addition, working with the MOH, MSH developed a list of priority research questions that could potentially be answered using the data stored in the APMR and RxSolution. Through engagements with HIV stakeholders and continuous evaluations of APMR/RxSolution data, a joint decision was made to implement a study to determine the factors associated with first-line to second-line ART regimen switching identified in the APMR and RxSolution data management systems.

During engagements with the MOH, it was learned that there has been limited documentation of the rates of regimen switching in the country. With the scaling up of access to ART, there was a clear need to better understand the factors that may lead to regimen switching among ART patients as well as the distribution of regimen switching among ART patients in the country. Moreover, since the implementation of the HIV treatment program in 2004, anecdotal evidence suggests an increase in regimen switching or substitution.

Earlier assessments have suggested that 6% of all individuals receiving first-line therapy in sub-Saharan Africa needed to switch to second-line regimens in any given year.[3] WHO recommends that patients currently receiving more complicated regimens be switched to a simpler regimen and that efforts should focus on transitioning patients off regimens that contain stavudine (d4T), which has been associated with some severe side effects.

HIV Context and Regimen Switching in Swaziland

Swaziland has an estimated population of 1,119,375,[4] of whom an estimated 210,984[5] are living with HIV infection. HIV prevalence is estimated at 26%, while the incidence rate is 2.4% in the population of 15-49 year olds.[6] The national HIV response was initiated in 1987 through the establishment of the Swaziland National AIDS Programme (SNAP) under the MOH's

[3] Ramadhani, HO, Bartlett, JA, Thielman, NM, et al. (2014). Association of First-Line and Second-Line Antiretroviral Therapy Adherence. Open Forum Infectious Diseases, 1(2), ofu079. http://doi.org/10.1093/ofid/ofu079

[4] Central Statistical Office. Swaziland population projections, 2007-2030: changing shape of the population pyramid. Mbabane: Central Statistics Office; 2010.

[5] The Kingdom of Swaziland, National Emergency Response Council on HIV and AIDS (NERCHA). Swaziland HIV Estimates and Projections Report. Mbabane: NERCHA; 2010.

[6] MOH. Swaziland HIV Incidence Measurement Survey. Mbabane: MOH; 2012.

Directorate for Health Services. The country is using a decentralization strategy, the "wheel and spoke" model whereby the main ART-initiating facilities (referred to as mother facilities) are linked to a group of about five smaller HIV diagnosis and referral facilities (baby facilities). The mother facilities have the full complement of personnel, including pharmacists, doctors, and a data entry officer. The baby facilities have nurses responsible for patient diagnosis, preparation for ART, and routine monitoring. ART initiation was previously done by a medical officer who visited the baby facility on scheduled days. This process changed with the introduction of nurse-led ART initiation (NARTIS). Following the introduction of NARTIS, there has been an increase in ART initiation at the primary health-care level (70%) compared to initiation at hospitals and health centers (30%). There are 170 ART service points throughout the country.[7] ART coverage for adults aged 15 years and above is at 83%, based on the eligibility criteria of CD4 ≤ 350 cells/mmol and is at, 66% according to the 90-90-90 target.

Currently, more than 144,000 patients have been enrolled in ART programs and recorded in Swaziland's APMR and RxSolution databases.[8] Combination ART continues to be the cornerstone for management of patients with HIV infection in the country, and is implemented as per the 2013 WHO HIV treatment guidelines. According to these guidelines, all HIV-infected adults and adolescents with CD4 ≤500 cells/mm^3 should be started on ART. Patients with advanced disease (CD4 ≤ 350 cells/mm^3 or WHO clinical stage III or IV) and those above 50 years of age should be initiated on ART as a matter of urgency**.** Moreover, pregnant women, patients with tuberculosis (TB), patients with hepatitis B virus co-infection, patients with HIV-associated nephropathy, and children under five years of age should be started on ART regardless of CD4 cell count or WHO clinical stage.

Since 2015, the recommended first-line regimen for adults and adolescents in Swaziland is a fixed dose combination of tenofovir (TDF) + lamivudine (3TC) + efavirenz (EFV). The Swaziland Integrated HIV Management Guidelines provide for switching options from the first-line to second- and third-line regimens. Second-line ART for adults and adolescents should consist of two nucleoside reverse-transcriptase inhibitors (NRTI) plus a ritonavir-boosted protease inhibitor (PI); the recommended combination for the third-line regimen is darunavir/ritonavir (DRV/r) 600 mg/100 mg + etravirine (ETV) 200 mg + raltegravir (RAL) 400 mg.[9]

Figure 1 shows the recommended ART regimens for adults.[10]

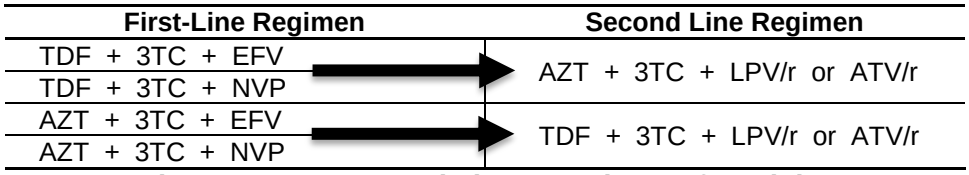

Figure 1. Recommended ART regimens for adults

Regimen change attributed to either substitution or switching has been increasing steadily over the years in Swaziland. As of December 2014, 7% of people registered in the APMR were recorded as having had a change in regimen since enrollment into care.[11]

[7] MOH. Annual HIV Programs Report. Mbabane: MOH; 2015.
[8] MOH. APMR database. Mbabane: MOH; 2015.
[9] MOH. Swaziland Integrated HIV Management Guidelines. Mbabane: MOH; 2015.
[10] MOH. The Swaziland Integrated HIV Management Guidelines, 2015
[11] MOH. ART annual report 2013. Mbabane: MOH; 2014.

OBJECTIVES OF THE STUDY

Primary Objective

- Determine the factors associated with first-line to second-line ART regimen switching identified in the APMR data management system

Secondary Objectives

- Determine the rate of first-line to second-line regimen switching for ART patients, as recorded in the APMR data management system

- Determine the time taken for ART patients to switch from the first-line to second-line ART regimen

- Document the reasons for switching from first-line to second-line ART regimens, as recorded in the APMR data management system

METHODOLOGY

This study is a retrospective cohort design. The selection of study records involved both convenience and cluster sampling (targeting stand-alone reporting sites and mother facilities). Records available in the central ART database were used to draw the study sample. The final sample size was 117,586 ART patient records. This followed a series of data cleaning processes to ensure that the study had a quality sample to respond adequately to the study objectives. The study's criteria were:

Inclusion criteria:

- Active ART patients as of December 31 for each of the years 2010, 2011, 2012, 2013, 2014, and 2015
- Patients aged 15 years and above

Exclusion criteria:

- Currently a pre-ART classified patient
- Patient records with a missing age and date of birth
- Patients lost to follow up or death
- Patients on ART for less than six months

During the data cleaning, the following new variables were created for ease of analysis:

1. Age groups
2. Year of enrollment
3. Period to regimen switch (elapsed time before regimen switching)
4. Number of days on ART

ETHICAL CONSIDERATIONS

This study subscribes to the ethics governing the use of human subject data, which includes the preservation of dignity, anonymity, confidentiality, and nonmaleficence. In observation of these principles and before embarking on the exercise, the research protocol was presented to the Scientific and Ethics Committee (SEC) of the MOH for approval. Permission to use APMR data was obtained from SNAP and the Strategic Information Department's Health Management Information System Unit (SID/HMIS). This study did not use patient names or unique identifiers; rather, a summation of total patients was studied. Data remained the property of and was fully controlled by the SNAP and SID.

DATA ANALYSIS AND DISCUSSION OF RESULTS

Analysis of the study's results was structured to address its four objectives. The study used the following methods to respond to the different objectives:

- Cox regression
- Descriptive statistics
- Survival analysis

Following the data cleaning process and based on the inclusion-exclusion criteria, the total number of ART patient records included in the study was 117,586. Thirty-five percent (35%) of the patients included in the sample were males and 65% were females. Table 1 presents the distribution of the study population by age groups. Figure 2 illustrates the proportional distribution of the age groups among the ART patients included in the study.

Table 1. Number of patient records included in the study, by age groups, 2010 to 2015

Age groups	2010	2011	2012	2013	2014	2015	Total
15-24	2301	1978	2298	2682	3555	4240	17054
25-34	8128	7420	7904	7940	8711	9146	49249
35-44	5469	4855	4986	4848	4917	4861	29936
45+	4491	3503	3580	3565	3274	2934	21347
Total	**20389**	**17756**	**18768**	**19035**	**20457**	**21181**	**117586**

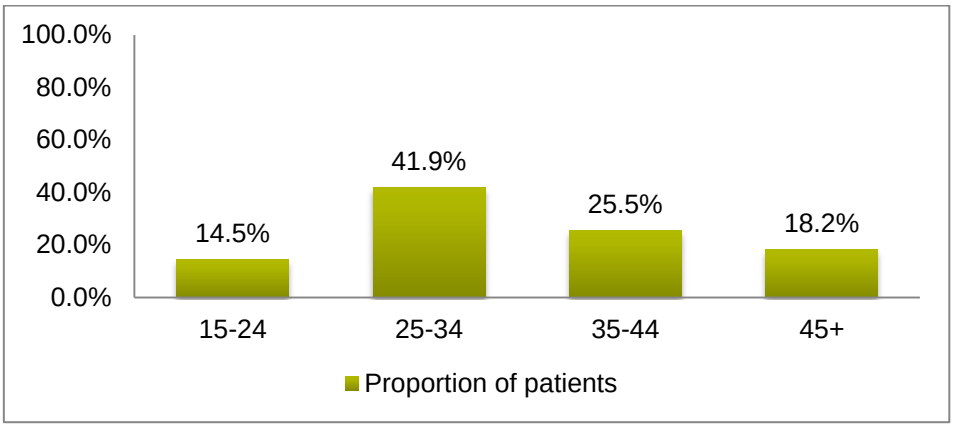

Figure 2. Proportion of patients in the study population, by age group

Switching Rates

One of the secondary objectives of the study was to determine the rate of first-line to second-line ART regimen switching among ART patients, as recorded in the APMR data management system. Of the 117,586 ART patient records included in the study, 3.6% (n = 4266) of the patients switched regimens. Table 2 presents the proportion of active ART patients switching regimens, by year. As seen in this table as well as in figure 3, the proportion of active ART patients who switched from first-line to second-line regimens decreased between 2010 and 2015.

Table 1. Proportion and number of active ART patients switching regimens, by year

Year	2010	2011	2012	2013	2014	2015	Total
Number of ART patients switching regimens	2376	653	524	390	227	96	4266
Proportion of active ART patients switching regimens	11.7%	3.7%	2.8%	2.0%	1.1%	0.5%	3.6%

Figure 3. Proportion of active ART patients switching regimens, by year

Reasons for Switching

Another secondary objective of the study was to document the reasons for switching from first-line to second-line regimens, as recorded in the APMR. The results revealed that for 67.7% of patients who switched, there was no recorded reason for the regimen switching in the APMR. Table 3 shows the distribution of reasons for regimen switching under the following categories: adherence, clinical, drug logistics, guidelines change, reason not entered, other, toxicity, and treatment failure; 15.3% registered treatment failure as the main reason for regimen switching. A large proportion of those patients (32.6%) were in the age range of 25 to 44 years (table 4).

Table 2. Reasons for regimen switching among ART patients switching regimens, by category and age group

Categories for regimen switching	15-24	25-34	35-44	45+	Total
Adherence	8	12	4	0	24
Clinical	16	60	28	13	117
Drug logistics	0	3	2	2	7
Guideline change	0	0	1	0	1
Not entered	312	1152	814	611	2889
Other	36	105	62	31	234
Toxicity	41	141	100	61	343
Treatment failure	72	289	195	95	651
Total	**485**	**1762**	**1206**	**813**	**4266**

Table 3. Proportional distribution of reasons for regimen switching, by category and age group

Categories for regimen switching	15-24 (%)	25-34 (%)	35-44 (%)	45+ (%)	Total (%)
Adherence	1.6	0.7	0.3	0.0	0.6
Clinical	3.3	3.4	2.3	1.6	2.7
Drug logistics	0.0	0.2	0.2	0.2	0.2
Guideline change	0.0	0.0	0.1	0.0	0.0
Not entered	64.3	65.4	67.5	75.2	67.7
Other	7.4	6.0	5.1	3.8	5.5
Toxicity	8.5	8.0	8.3	7.5	8.0
Treatment failure	14.8	16.4	16.2	11.7	15.3

Factors Associated with First-Line to Second-Line ART Regimen Switching

As stated above, the primary objective of the study was to determine the factors associated with first-line to second-line ART regimen switching identified in the APMR data management system. In this study, four covariates were assessed to determine the level of hazard an individual had for switching from the first-line to second-line regimens. At a 95% confidence level, all the selected covariates were found to be significantly associated with regimen switching. The covariates included: sex; WHO clinical staging at initiation of treatment; region where the treatment facility is located; and age at initiation. Table 5 presents the hazard ratios for the different covariates examined.

Table 4. Hazard ratios for the covariates assessed

Variables	Hazard ratio	P-values	95% CI	
Sex				
Females	1.00			
Males	1.18	0.00	1.10	-1.27
Age Group (years)				
15-24	1.00			
25-34	0.93	0.22	0.83	-1.04
35-44	0.89	0.06	0.79	-1.00
45+	0.77	0.00	0.68	-0.87
Region				
Hhohho	1.00			
Lubombo	0.41	0.00	0.36	-0.46
Manzini	0.62	0.00	0.57	-0.67
Shiselweni	0.66	0.00	0.60	-0.73
WHO Clinical Staging				
I	1.00			
II	1.52	0.00	1.39	-1.67
III	1.90	0.00	1.73	-2.08
IV	3.55	0.00	3.13	-4.03

Males with a hazard ratio of 1.18 (95% CI: 1.10-1.27) were found to be associated with a higher hazard of switching from first- to second-line ART regimens compared to females. Moreover, ART patients aged between 15 and 24 at initiation had a higher hazard of switching from one regimen to the other compared to any other age group, i.e., patients initiated later in life. In this study, ART patients in the age group 25-34 were found to have a hazard ratio of 0.93 (95% CI: 0.83%-1.04%). ART patients in the age group 35-44 had a hazard ratio of 0.89 (95% CI: 0.79%-1.00%). Patients at ages above 45 years had a hazard ratio of 0.77 (95% CI: 0.68%-0.87%). The trend among the different age groups assessed was that the risk of regimen switching increased when the age of initiation was later in life. It is worth mentioning, however, that the results for the 25-34 and 35-44 age groups were found to not be statistically significant.

The study revealed that ART patients receiving treatment or initiated at a health facility in the Hhohho region had a higher hazard of switching from one regimen to another compared to ART patients in any of the other three regions of the country (table 5). ART patients receiving treatment or initiated at a health facility in the Lubombo region were found to have a hazard ratio of 0.41 (95% CI: 0.36%-0.46%). ART patients receiving treatment or initiated at a health facility in the Manzini region had a hazard ratio of 0.62 (95% CI: 0.57%-0.67%);

and ART patients receiving treatment or initiated at a health facility in the Shiselweni region had a hazard ratio of 0.66 (95% CI: 0.60%-0.73%).

ART patients were also assessed on their level of hazard or risk of regimen switching based on the WHO clinical staging. The study results indicate that the hazard for regimen switching increased as the WHO staging at initiation progressed from stage I to IV. ART patients initiated in—

- WHO clinical stage I presented with the lowest hazard (1.00) for regimen switching compared to any of the other WHO staging categories (table 5)
- WHO stage II had a hazard ratio of 1.52 (95% CI: 1.39%-1.67%)
- WHO stage III had a hazard ratio of 1.90 (95% CI: 1.73-2.08)
- WHO stage IV had a hazard ratio of 3.55 (95% CI: 3.13%-4.03%)

Survival Time to Switching

Another study objective was to determine the time taken for the selected class of ART patients to switch from first-line to second-line ART regimens. The study statistically investigated, with 95% confidence level, the average amount of time, in years, that a person would take (survive) to eventually switch regimens, from the time he/she began ART. The median survival time for all ART patients switching from first- to second-line regimens was 607 days (95% CI: 601-613) or 19.5 months (data not shown). This statistic can be interpreted to indicate the length of time that a patient can be expected to survive. Comparisons were made to reflect survival time by:

- WHO clinical stages I, II, III, and IV
- Age groups: 15-24, 25-34, 35-44, and 45 years and above
- Regions: Hhohho, Manzini, Lubombo, and Shiselweni
- Sex: male, female

It is worth mentioning that most of the cases did not switch regimens; we call this censoring.[12] The method of analysis selected is the Kaplan-Meier method**.** It was chosen because it is the most appropriate method to use when some of the data are censored. Using this method, we plotted the survival curves showing the probability of surviving to the point of regimen switching. Figures 4, 5, 6 and 7 present the comparisons for the different covariates in this study.

The survival analysis shows that ART patients receiving treatment from facilities in the Hhohho region survived for the shortest period on the first-line ART regimen before switching to the second-line regimen compared to patients in the other three regions of the country (table 6). Table 6 presents the average duration for ART patients on treatment before switching to the second-line regimen, by region over the period 2010 to 2015. The Shiselweni region showed the highest average time for ART patients to switch from the first-line regimen to the second-line regimen. Patients receiving ART in the Shiselweni region were found to survive for longer periods on the first-line ART regimen compared to patients in the other regions. Figure 6 shows that only 89% of ART patients initiated on treatment in the

[12] Lost to follow-up (LTFU) cases are also considered to be censored cases, but they have been excluded from this study.

Hhohho region remained on the first-line ART regimen by the end of the five-year follow-up period. In the Manzini and Shiselweni regions, 92% of ART patients initiated in facilities in these regions remained on the first-line ART regimen by the end of the five-year follow-up period. Lastly, a majority of ART patients (96%) initiated in the Lubombo region remained on the first-line regimen by the end of the five-year follow-up period.

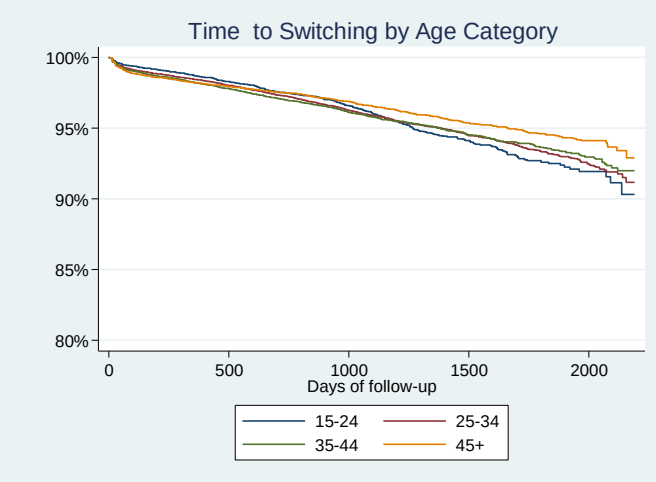

Figure 4. Time to switching by age group

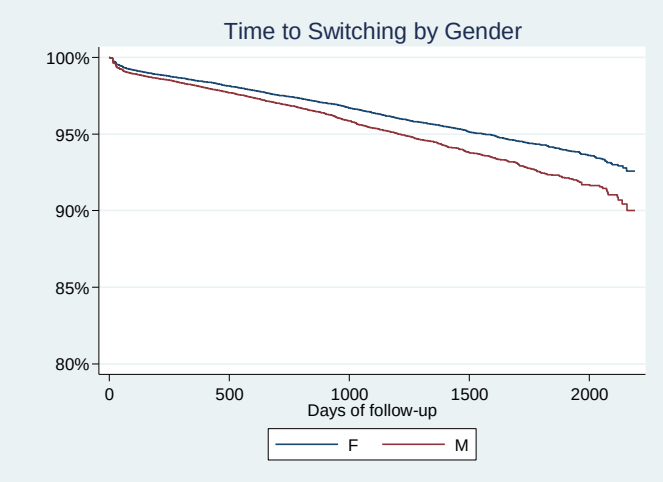

Figure 5.Time to switching by gender

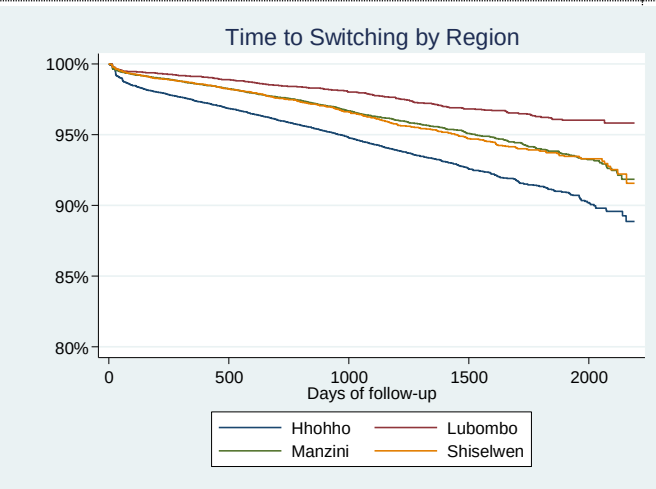

Figure 6. Time to switching by region

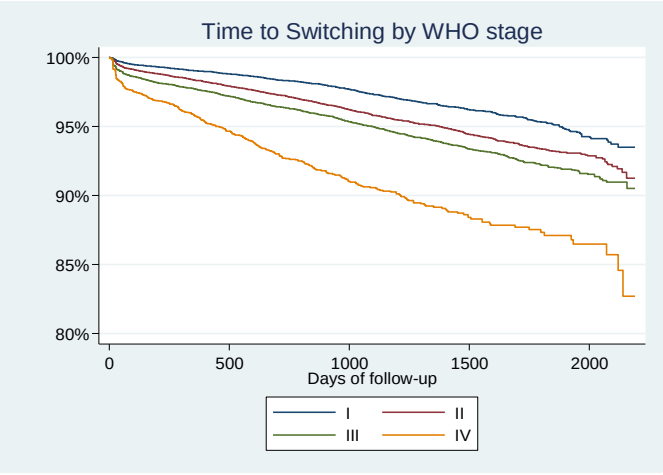

Figure 7. Time to switching by WHO clinical stage

Table 5. Average duration on ART before switching, by region, gender, WHO clinical stage, and age groups, by age at initiation, 2010-2015

	Average duration on ART before switching		
Covariates	**In days**	**In months**	**In years**
Region			
Hhohho	406.8	33.9	1.1
Lubombo	481.8	40.1	1.3
Manzini	476.8	39.7	1.3
Shiselweni	518.3	43.2	1.4
Gender			
F	454.5	37.9	1.2
M	460.0	38.3	1.3
Age groups by age at initiation			
15-24	522.7	43.6	1.4

	Average duration on ART before switching		
Covariates	**In days**	**In months**	**In years**
25-34	475.8	39.7	1.3
35-44	445.6	37.1	1.2
45+	395.1	32.9	1.1
WHO clinical staging			
I	509.5	42.5	1.4
II	517.0	43.1	1.4
III	401.2	33.4	1.1
IV	381	31.8	1.0

Analysis of survival time by WHO clinical staging showed that ART patients initiated on treatment when in WHO stage I had longer survival periods compared to patients starting therapy in WHO clinical stages II, III, and IV (table 6). Patients starting ART in WHO stage IV had the shortest survival times on the first-line regimen compared to the other clinical stages. The analysis showed that the earlier a patient is initiated on treatment, the more likely his or her chances of survival on the first-line regimen as well as a reduction in the chance of switching to the second-line ART regimen. Figure 7 shows that for ART patients initiating in WHO stage IV, only 83% remained on the first-line regimen by the end of the five-year follow-up period. For ART patients initiated in stages II and III, 90% and 91%, respectively, remained on the first-line regimen by the end of the five-year follow-up period.

Figure 5 shows that the survival time for males on the first-line regimen was less than that of females, i.e., more females initiated on ART remained on the first-line regimen by the end of the five-year follow-up period. Figure 6 shows a 90% survival rate for males and 93% survival rate for females. Table 6 shows that during the period 2010 to 2015, the average duration of patients on the first-line regimen before switching to the second-line regimen was slightly greater for males than females.

ART patients initiating treatment at 45 years and above were found to have longer survival periods on the first-line regimen before switching to the second-line regimen (figure 4). Patients initiating at ages 15 to 24 were found to have shorter survival periods on the first-line regimen compared to the other age groups. Figure 4 shows that ART patients initiated at 45 years and older remained on the first-line regimen for longer periods compared to the other age groups, at 93.5%, whereas patients initiated at ages 15 to 24 were the most affected by regimen switching for the periods year 1 to year 4, but then stabilized to reflect improved survival of 92% by the end of the five-year follow-up period, surpassing survival rates for regimen switching in the age groups 25 to 34 and 35 to 44, which had survival rates of 90% and 91%, respectively, by the end of the five-year follow-up period.

Limitations of the Study

There was no interaction with patients in this study for a holistic understanding and perspective on some of the factors that could be influencing regimen change from the perspective of the client, i.e., issues of preference. This is an area for future studies. Furthermore, there was no validation of the secondary patient data. Also, only adults (15+ years) were studied; pediatric patients were excluded. Moreover, the dataset used was limited to 31 facilities that were using the APMR reporting system (annex 1).

POLICY RECOMMENDATIONS

- MOH needs to strengthen systems and guidance for the early identification of regimen-switching cases.

- Further introduce policies or strategies to ensure the early initiation of men on ART.

- Introduce strategies for longer retention on first-line ART for early age groups.

- Conduct further studies to provide information on the differences observed in regimen switching hazards by region.

- Routine data collection systems have huge amounts of useful data that can respond to and help motivate positive change in the management of patients and thereby improve health outcomes. Use of routinely collected data to respond to operational research questions needs to be institutionalized in local ministries.

CONCLUSIONS

Through this study, it became apparent that the following considerations should be taken into account in the design of routine data collection systems:

1. Clinicians and primary users of the systems (i.e., data clerks) should be involved.

2. There need to be logical, built-in data validation rules for APRM and RxSolution systems to avoid data quality issues as a result of poor data capturing.

3. There need to be scheduled data quality review sessions to respond to performance indicators and research questions using the data.

ANNEX 1. CHARACTERISTICS OF FACILITIES FOR POTENTIAL INCLUSION IN THE STUDY

All sites are implementing RxSolution/APMR

Facility #	Name of facility	Description	Patients currently on ART as of December 31, 2014	Patients ever on ART as of December 31, 2014
1.	Mbabane Government Hospital	Mother facility	9575	16518
2.	RFM Hospital		6833	14261
3.	Hlatikhulu Government Hospital		3922	6932
4.	Good Shepherd Hospital		6558	11135
5.	Piggs Peak Government Hospital		4856	7551
6.	Mankayane Government Hospital		3424	6060
7.	Mkhuzweni Health Centre		2950	4534
8.	Sithobela Health Centre		2389	4560
9.	Matsanjeni Health Centre		1723	3655
10.	Nhlangano Health Centre		4104	7815
11.	Dvokolwako Health Centre		2844	4913
12.	King Sobhuza II Clinic	Stand-alone facility	1612	3189
13.	Phocweni Army Barracks Clinic		1719	1812
14.	Wellness Center		375	396
15.	Ka-Mfishane Clinic		639	895
16.	Mashobeni Clinic		480	637
17.	JCI Clinic		864	1148
18.	National TB Hospital		614	818
19.	Sigombeni Red Cross Clinic		692	1199
20.	Ubombo Sugar (Illovo) Clinic		346	355
21.	SAPPI Health Centre		366	2177
22.	Manzini Health Care		2051	2177
23.	Mahwalala Red Cross Clinic		1568	1899
24.	AIDS Healthcare Foundation/ Lamvelase Clinic		9775	11855
25.	Family Life Association Swaziland Clinic – Manzini		752	886
26.	Lulama Health Clinic		510	621
27.	Thembumenzi Clinic		38	50
28.	MSF-Matsapha Clinic		4159	5408
29.	ACTS II		1060	1155
30.	Silele Red Cross Clinic		387	422
31.	Lobamba Clinic		2020	3189

ANNEX 2: LIST OF CONTRIBUTORS

Details	Responsibilities
Principal Investigator Thabo Motsa Monitoring and Evaluation Officer Ministry of Health – Swaziland	• Guides and coordinates development of study protocol and implementation in-country. • Responsible for implementation of study. • Facilitates writing of the report.
Co- Investigators Nxumalo Nkosinathi Humble Monitoring and Evaluation Advisor System for Improved Access to Pharmaceuticals and Services (SIAPS) Program Management Sciences for Health (MSH) Dr. Fortunate Zwane-Shababala Lecturer Faculty of Health Sciences University of Swaziland Mduduzi Shongwe Lecturer University of Swaziland Kidwell Matshotyana Country Project Director SIAPS Program MSH/Swaziland	• Drafts the study protocol. • Gathers necessary quality data for the study. • Coordinates submission and approval process in Swaziland and at the Harvard Pilgrim Health Care Institute. • Supports data analysis and drafting of the report.
Country Support Maheen Malik Principal Technical Advisor Pharmaceuticals and Health Technologies Group MSH Arlington, VA USA Katelyn Payne Project Associate SIAPS Program Management Sciences for Health Arlington, VA USA	• Coordinates development of protocol linking the Swaziland team to the Harvard Pilgrim Health Care Institute and SIAPS headquarters. • Assists with the protocol approval process. • Supports data analysis and drafting of the report.
Consultant Anita Wagner Associate Professor of Population Medicine Department of Population Medicine Harvard Medical School and Harvard Pilgrim Health Care Institute	• Provide guidance on study development and execution as requested by the study team.