Decentralization of antiretroviral treatment in Swaziland: outcome of nurse initiated versus doctor initiated treatment.

By

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Declaration

I, Sikhathele Mazibuko, hereby declare that this report is my own work and that it has not been submitted for any degree or examination in other universities. All the sources that have been used or quoted have been indicated and acknowledged by means of complete references.

Date:

Signature:

Dedication

To my wife Zanele, my son Mvuyelwa and my daughter Zanenhle for their love and support through the various challenges presented by my studies.

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Abbreviations

3TC	Lamuvidine
ABC	Abacavir
aOR	Adjusted Odds Ratio
ART	Antiretroviral Treatment Therapy
ARV	Antiretroviral
AZT	Zidovudine
CBC	Complete Blood Count
CD4	Cluster of Differentiation 4
CI	Confidence Interval
EFV	Efavirenz
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
LPV/r	Ritonavir boosted Lopinavir
NARTIS	Nurse led ART Initiation in Swaziland
NGO	Non-Governmental Organization
NIMART	Nurse Initiated and Managed ART
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
OR	Odds Ratio

PMTCT   Prevention of Mother to Child Transmission of HIV

RCT   Randomised Controlled Trial

TB   Tuberculosis

TDF   Tenofovir Disoproxil Fumarate

USA   United States of America

WHO   World Health Organization

Abstract

Introduction: Decentralization of antiretroviral therapy (ART) services faces decreasing quality when increasing ART coverage. This study compares nurse initiated and managed patients to doctor managed patients under these circumstances, using retention in care as a crude measure of quality of care.

Methods: This was an observational retrospective cohort study. A simple data abstraction tool was used to collect baseline patient data from medical records of HIV positive patients (N=871) initiating ART at Mbabane Government Hospital and four of its outreach clinics, between 1st January and 30th June 2011. Descriptive summary statistics and comparison of the two cohorts using multivariate analysis was done.

Results There was no statistically significant difference in retention rates between the doctors and nurses cohorts at 69.1% and 70.9%, respectively (P was 0.56). After adjusting for sex, haemoglobin, CD4 cell count, weight and WHO stage, the odds of being retained in care were similar between the two groups, adjusted OR: 1.11(95% CI: 0.72, 1.69), with a p value of 0.64. Haemoglobin and weight were positively associated with retention in care, while male sex was negatively associated with retention in care.

Discussion: The similar retention rates between the two cohorts suggest that in terms of retention in care the service provided by the nurses was comparable to that provided by doctors. This is important to ART program managers as they scale-up ART decentralization.

Conclusion: Task-shifting of ART initiation from doctors to nurses is feasible as nurse initiated and managed antiretroviral therapy is comparable to doctor initiated and managed treatment.

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Introduction

1. Background

Swaziland has a generalized HIV epidemic with a prevalence of 41.1% among pregnant women and 26% in the general population (adults aged 15 to 49 years)(1). This is the highest HIV prevalence in the world. The country has an incidence of 2.38%(2) as measured in the Swaziland HIV Incidence Measurement Survey (SHIMS) of 2011. According to projections from the Goals model of EPP/Spectrum®, mathematical modelling software, the country's incidence is on a downward trend since peaking in the late nineties, see **Figure 1** below. These parameters highlight the magnitude of the challenge faced by Swaziland, especially considering the economic and health system challenges currently facing a lot of African countries.

Figure 1: Trends in HIV prevalence and incidence from 1992 to 2010(3). The green graph represents the incidence that was >4% around 1998 but has come down to below 3% in 2010.

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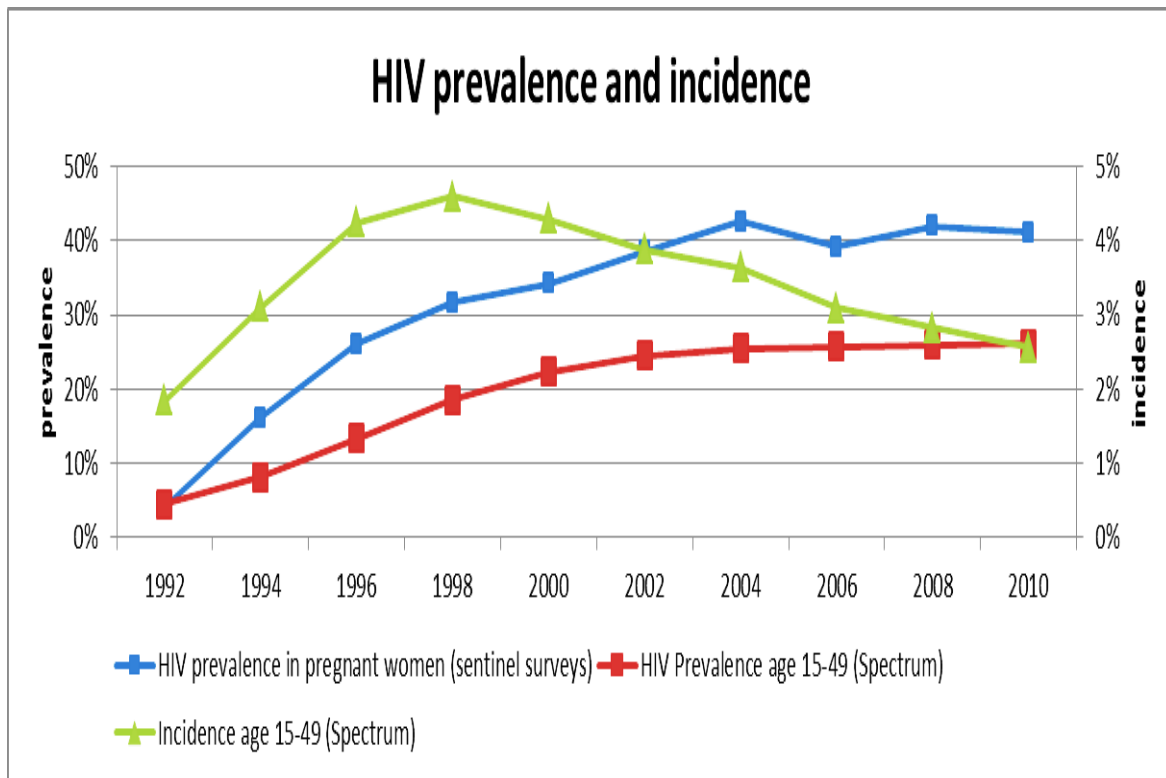
The United Nations Millennium declaration of 2000 had three health related goals that addressed; Child mortality; maternal health and HIV/AIDS, malaria, Tuberculosis and other diseases. To reach the Millennium Development Goals (MDG) related to HIV we have to devise innovative strategies to deliver HIV services. MDG number 6 addresses HIV/AIDS, with sub goal 6(b) specifically looking at achieving universal access to anti-retrovirals. The recommendation is that 80% of the population with advanced HIV disease should have access to anti-retrovirals (ARV). In 2000, these were ambitious goals and progress towards achieving them has been slow. The general consensus is that the MDG target for universal access to antiretroviral therapy for all who need it has been missed, but these goals are still achievable by 2015(3). This is in line with the 2011 United Nations General Assembly Declaration on HIV/AIDS which was adopted with the aim to achieve universal access to HIV prevention, treatment, care and support by 2015.

Looking at the situation in Swaziland, by the end of 2012 the Swaziland National ART Program had 87,524 people on antiretroviral therapy (ART), which translates to a coverage of 91% (4). This was largely due to a successful decentralization program that brought HIV services to the community. Swaziland looks to be well on its way to achieving universal access by 2015.

Decentralization of HIV services therefore is a key step to achieving universal access to ART, however decentralization of ART faces the challenge of a perceived decrease in quality when increasing coverage(5). With improved access to care, greater numbers will seek HIV services and this will invariably test the ability of the health system to handle an increased load, while continuing to deliver quality services with good outcomes. There is a need to strengthen health systems in Sub-Saharan Africa as It is becoming increasingly clear that strong health systems are the key to achieving improved health outcomes (6).

Decentralization of HIV services coupled with capacity building and a structured task shifting program is the strategy chosen by Swaziland to achieve universal access. This is expected to lead to shorter distances for patients to travel, less money spent on travel, wider ART coverage and better patient follow-up and retention in care. In the Swaziland task shifting model, like other countries in the region, nurses in primary health facilities need to be able to initiate and manage ART, treat non-severe opportunistic infections, undertake simple decision making and promote prevention of transmission of HIV (7). Integrated management of adult/adolescent illnesses

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(IMAI) and the Nurse-led ART Initiation in Swaziland (NARTIS), trainings have been used to capacitate nurses in this regard, along with simplified first and second line regimens and standardised, comprehensive data collection tools.

The question on whether, nurse initiated and managed ART is comparable to doctor initiated and managed ART remains to be answered in Swaziland. This study aims to answer this question and to assess the determinants of patient retention in care.

2. Literature review

2.1 The Public Health Approach to Antiretroviral Treatment

Swaziland has adopted the public-health approach to antiretroviral therapy which was proposed by WHO to enable scaling-up access to treatment for HIV-positive people living in developing countries(7). In this approach standardized regimens, data collection tools, simple decision making algorithms and treatment protocols allow for ART services to be decentralized and delivered to large numbers of patients in the public and private sector.

The model used in western countries involves specialist physician management of patients and advanced laboratory monitoring. This model is not feasible in resource limited settings where doctors are scarce (e.g. one per 12500 population in one Ugandan study(8)), laboratory infrastructure and skills are inadequate and the procurement and supply-chain management systems are at best fragile(7). Recognising these limitations, it is imperative to adopt and implement a public health approach, seeing that Swaziland has a high HIV incidence and prevalence in addition to all the challenges mentioned above.

2.2 Benefits of Task-shifting in decentralization

In task-shifting certain tasks are delegated to health workers of lower qualifications or to non-professionals(9, 10) e.g. ART initiation, that was traditionally done by doctors is delegated to the nurse. This is a necessary and critical dimension of decentralising HIV care in resource limited settings. Due to the huge human resource shortage in resource limited settings, task-shifting is promoted as an essential component of ART scale-up programs, to overcome the shortage of doctors and other essential health staff(11, 12).

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This delegation of responsibilities has been proven to be effective(13, 14) and has resulted in increased coverage of HIV services with reasonable outcomes. Other tasks like phlebotomy, weight and height measurements and adherence preparation can be delegated to other cadres in the health sector, to reduce the burden of work on the nursing cadre and allow nurses to focus on their new tasks.

The process of task-shifting requires the cooperation of all stakeholders i.e. Ministry of Health and medical and nursing councils, in the development of standardized protocols. These include simplified clinical guidelines, simplified recording and reporting systems and standardized monitoring and evaluation tools. There is also a need to amend the laws and regulations governing the practice of these cadres, allowing for a widening of their scope of practice. These measures facilitate the decentralization of interventions and care to lower levels of the health system and are associated with improved access, increased national coverage and better geographical equity(10).

Availability of services within the community is expected to reduce travel and indirect costs resulting in improved patient retention. Travel costs have been shown to be associated with a high rate of defaulting from HIV care(15). Other factors associated with poor adherence, though not exhaustive, include large hospitals, financial difficulties and experience of discrimination in the family environment, these have been linked to treatment interruption(16).

Another goal of task shifting is to reduce the cost of health care in low resource settings as roles are delegated to cadres with lesser qualifications and lower salaries; this will save physician and nurse time and costs. Results from a systemic review support this assumption and show that task-shifting from doctors to nurses or from health care professionals to non-professionals resulted in significant savings in costs and physician time(17, 18).

Creating a new cadre with qualifications that are only recognised locally, to fit specific roles in the task-shifting setup is beneficial as these cadres can be retained in rural and hardship areas (10). Expert clients or expert patients are a perfect example. These are HIV positive lay counsellors, with a locally developed training curriculum who provide counselling services that include preparation of patients for ART initiation and follow up of ART and pre-ART patients.

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2.3 Assessing Outcomes of decentralization

The benefit of task-shifting in decentralization demonstrated in some studies relied heavily on intensive training and support from predominantly overseas funded non-governmental organizations (NGOs) and this might not reflect the situation on the ground as these resources may not be readily available especially with changes in guidelines (i.e. increase in CD4 thresholds from 200 to 350 cells/mm^3 for ART initiation) and the need for rapid scale-up of services(19).

Nurse managed treatment has been shown to be comparable to doctor managed care. Chan et al (20) showed that patients managed at lower level health centres had lower mortality (adjusted OR 0.19 (95% C.I. 0.15, 0.25)) and a lower rate of lost to follow up (adjusted OR 0.48 (95% C.I. 0.40, 0.58)). A randomised non-inferiority trial using a composite outcome (Mortality, viral failure, treatment limiting toxic effects, and adherence to treatment schedule) found that nurse monitored ART was not inferior to doctor monitored ART.

Retention in care is a commonly used outcome measure in evaluating decentralization, or its converse, attrition. Patients are considered retained in care if they are alive and on treatment at the time of assessment. Patients who are transferred out are technically not lost to the system but since this study is looking at only one mother-baby cluster, outcomes of patients transferred out of the cluster cannot be determined hence they are considered lost to the cluster and are counted under attrition.

Improved Retention in care and decreased HIV related mortality are the main goals of decentralization and many studies have tried to demonstrate that nurse managed ART is comparable to doctor managed treatment using these measures. An evaluation of a pilot study in Rwanda on nurse centred ART initiation between 2005 and 2008, was impressive and showed retention on ART of 90% and mortality of 7%(9) at the end of the study period. In Mozambique an MSF led study used community ART groups to distribute ARVs in one health zone. This was in an effort to improve adherence and retention in care. The outcomes were excellent with retention in care after 12 months of 97.5%, mortality 2% and lost to follow up of 0.2%(5).

Low Cd4 count, anaemia and patient decentralization/down referral have been shown to be positively associated with retention in care, with a reciprocal decrease in mortality (9, 21, 22).

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Low weight for age and younger age were associated with adverse outcomes in a cohort of children managed in primary health care clinics(21). Other factors like tuberculosis co-infection and reported adverse events need to be investigated further.

2.4 Challenges facing decentralization and task-shifting

Remuneration is one of the biggest challenges to task-shifting and decentralization of ART services. Health workers continue to emigrate from Sub-Saharan countries to western countries and one of the main reasons cited for this migration is poor salaries(23). This could be worsened by increasing their scope of practice and introducing new tasks without additional compensation. It has been shown that nurses may resist taking on doctors' roles without commensurate salary increases to match their new skills (10, 24). Tasks need to be defined with clear job descriptions and establishment of appropriate remuneration packages to avoid possible exploitation of vulnerable workers who may continue to be paid only for work for which they are qualified.

Does task-shifting affect the quality of care delivered? This is a valid question. A study in Malawi(18) found that community health workers were poor at identifying patients eligible for ART compared to clinicians, highlighting the limit to which tasks can be shifted. Clearly there is a need to define what tasks can be shifted and to whom. Capacity building programs and supervision for these cadres who are recipients of these tasks should be robust enough to ensure provision of services of comparable quality to those provided by the usual officers.

2.5 The Swaziland model of decentralization

The Swaziland model of decentralization of HIV care, in which nurses initiate ART and doctors supervise them and manage complex cases is similar the one used in Malawi (10) and a similar model is promoted by WHO (25).

Primary health care clinics in Swaziland are largely manned by nurses and nursing assistants. Doctors are not stationed in these facilities, but a doctor is generally scheduled to visit the clinics and assist in the management of challenging cases. Most primary healthcare clinics have two registered nurses, with at least one of them being a midwife and at least one nursing assistant. The number of nurses stationed at the facility varies based on the volume of patients seen, and the number of services provided by the facility. Additional staff at the clinic may also include orderlies, a phlebotomist, lay counsellors and a night watchman.

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The first step in the decentralization exercise was the revision of the nursing scope of practice to allow nurses to prescribe ARVs. Training of nurses and nursing assistants working at the primary health care level in HIV testing and Counselling (HTC) and Integrated management of Adult and Adolescent illness (IMAI) followed.

Clinics that could provide ART refill services were identified and accredited by the National ART Program. The accreditation process was the responsibility of the National ART program. It looked at staffing levels, capacity of staff to provide refills, sound infrastructure, secure space to house the ARVs and adequate and well ventilated waiting areas. The ability of the clinic to store and manage drug stocks and to report timely was also assessed. Once accredited the clinics (commonly referred to as baby clinics), began refills on stable patients, down referred from the central hospitals (referred to as the mother facility).

NARTIS (Nurse led ART Initiation in Swaziland), also known as Nurse Initiated and Managed ART (NIMART) refers to the program of equipping nurses with ART management skills. Before nurses are trained in NARTIS they are required to have completed a basic IMAI course and should have been refilling ART for at least six months prior to undergoing the NARTIS training. Nurses undergo a one week didactic course covering history taking, examination, diagnosis, and management of non-severe opportunistic infections, selection of appropriate ART regimens and management of side effects. This is followed by a week-long clinical attachment at a major ART site. The participants are attached to a doctor and practice ART initiation and patient management during this attachment. Participants are expected to write up five cases for presentation at the end of the attachment period.

Successful participants receive a certificate of competence. These nurses then go on to initiate and manage ART in their facilities with constant supervision by a team of experienced clinicians from the mother facilities and Ministry of Health mentors and implementing partners.

Figure 2 and 3 below illustrate how decentralization has progressed since 2010. It is clear that a lot of the facilities shaded in blue in the 2010 map (refill sites) have transitioned to ART initiating sites (Shaded in green in the 2012 map). In light of the new recommendations from the WHO Consolidated guidelines released in June 2013(26), were ART is recommended for all pregnant women regardless of their CD4 cell count, all facilities that provide PMTCT will have

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to become ART sites to successfully provide this service. Therefore all sites currently providing PMTCT services will have to transition to ART initiation sites in the next year. This will be a big challenge for the ART program and will require in big investment in the capacity building of nurses and also ensuring there is adequate supervision.
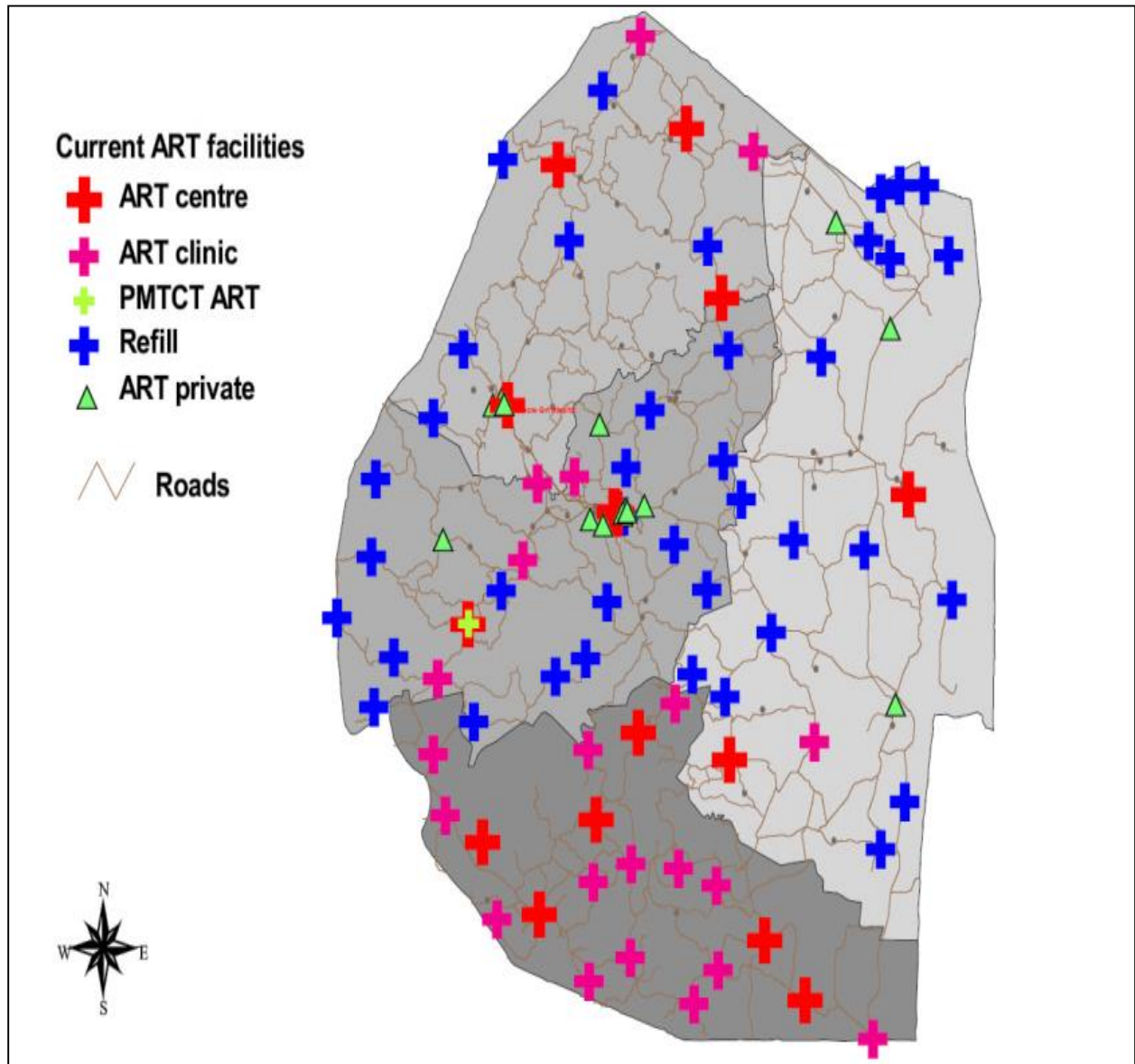
Figure 2: Map showing health facilities providing ART services (2010). Refill facilities are in blue; Initiating facilities are pink and ART centres are red. (Annual ART Report 2010)

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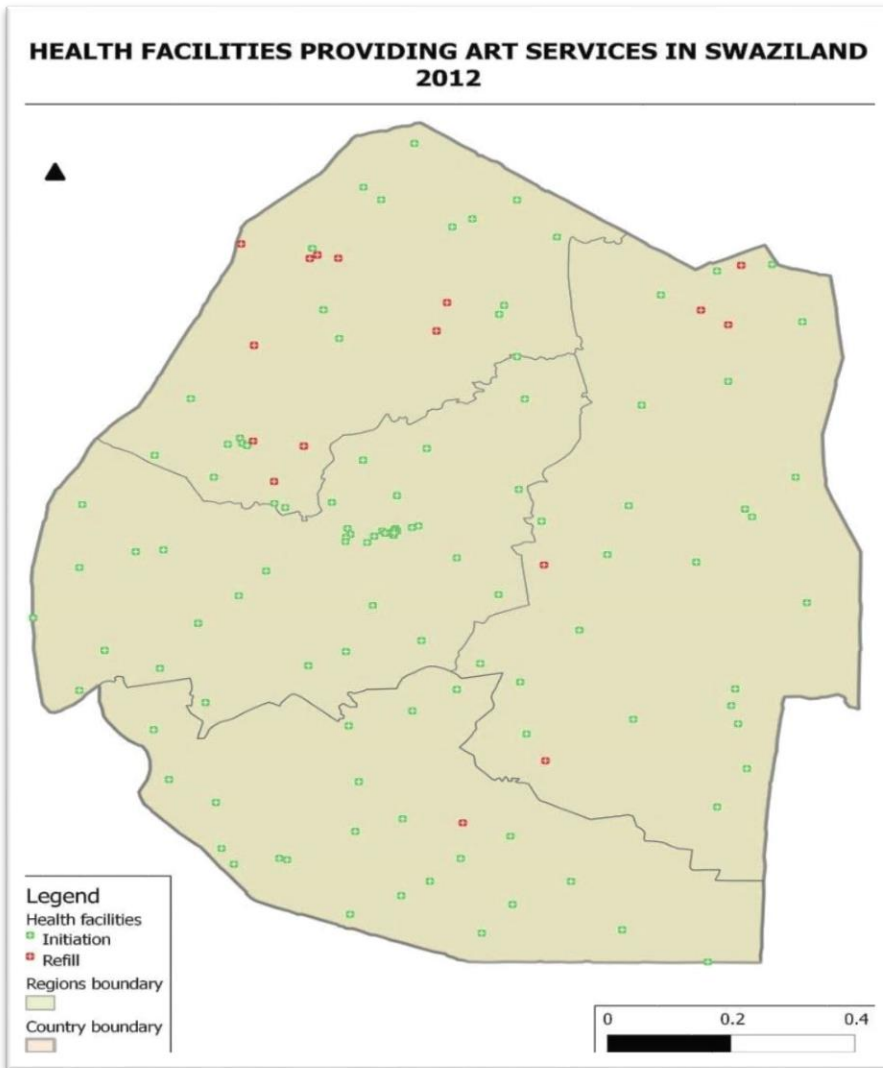
Figure 3: Map Showing Health Facilities Providing HIV Services in Swaziland (2012). Refill facilities are in red and ART initiation facilities are in green(4).

Table 1 below shows the distribution of facilities providing ART services by region and also stratifies then by whether they are public or private facilities. It is clear from this table that the majority of sites providing ART are public sites with very few private facilities providing comprehensive ART services. There is still room for expansion, as we have only reached about 48% of earmarked sites. It should be noted that the all hospitals, health centres and the majority of public primary health facilities are providing comprehensive ART services and the outstanding sites are mostly small private clinics that can provide services for only a specific section of the population.

REGION	Total Facilities (earmarked for ART)	Public Facilities (Govt, Mission, NGO)	Private and Industrial Facilities	ART Initiation Public	ART Initiation Private	ART Refill Public	ART Refill Private	TOTAL ART SITES
HHOHHO	68	44	20	22	1	29	1	30
LUBOMBO	55	37	18	16	3	26	5	31
MANZINI	112	60	46	32	7	33	7	40
SHISELWENI	36	30	6	23	0	23	0	23
TOTAL	261	171	90	93	11	111	13	124

Figure 4: Distribution of facilities providing comprehensive ART services, by region(4).

2.6 Rationale for this study

Although this not the first study to compare nurse managed ART to doctor managed ART, it was important for it to be conducted as the comparisons are not always unbiased and the findings cannot be easily generalised. It has been stated earlier that in some of the studies the patients managed by nurses were down referred patients who were stable on referral and were therefore always going to have better outcomes in comparison to hospital managed patients who tend to have complicated presentations and a poorer prognosis.

Pre-service training programs may vary from country to country. The specific trainings to capacitate nurses in ART initiation, though similar in their goals may have curriculums that differ significantly, as do the requirements prior to embarking on this training. In addition the level of supervision differs and this should have an impact on the practice of the nurses and

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patient outcomes. Different cadres are used in different countries, with some countries using clinical officers or physician's assistants. These are nurses with clinical training beyond the nursing curriculum and therefore make the transition to managing ART patients simpler as they are already carrying out similar tasks.

This study attempted to give a "real world" comparison of doctor and nurse managed patients.

Aims and objectives

1. Aim

The aim of this study is to compare **retention in care** for patients initiated and managed by nurses versus those initiated and managed by doctors at a referral hospital in Swaziland.

2. Objectives

- Determine factors associated with retention in care.
- Compare the retention rates amongst the two cohorts adjusting for confounders.
- To describe the cohorts and their outcomes.

3. Hypothesis

3.1.1 Null Hypothesis

There is no difference in retention rates of patients managed by nurses, compared to those managed by doctors.

3.1.2 Alternate hypothesis

Patients managed by nurses in primary health care clinics have better retention rates compared to those managed by doctors.

Methods

1. Study design

The study was a retrospective observational cohort analysis using routine data from standard Ministry of Health monitoring tools. Data sources used were the patient file and the electronic patient management database. Data was primarily collected from the patient file and cross referenced with data from the electronic patient management database for completeness. Mbabane government hospital ART clinic has been piloting a real time data entry system, with electronic and paper based records used simultaneously, therefore some of the records are not complete and cross referencing is essential. Outcomes were compared between patients initiated and managed on ART by doctors at a tertiary hospital and patients initiated and managed on ART by nurses at the peripheral clinics supported by that hospital. The cohorts consisted of patients enrolled on ART from the 1st of January 2011 to 30th of June 2011 and they were followed up for a period of 12 months.

2. Setting

The study setting was the HIV treatment and care clinic at the Mbabane Government Hospital, Swaziland and its outreach clinics, namely Lobamba clinic, Motshane clinic, Sigangeni clinic and the TB clinic at the Mbabane Government Hospital. Mbabane Government Hospital has been providing ART services since 2003 and is the largest ART facility in the country. The nurse managed patients were in the primary health care clinic, while the doctor managed patients were at the hospital.

This study took place soon after the change in guidelines as recommended by WHO, which changed the threshold for ART initiation from ≤ 200 cells/ mm^3 to ≤ 350 cell/mm^3. Participants in the study were patients who were initiated on therapy based on the Swaziland National ART and Care Guidelines (2010). Patients with a CD4+ count of ≤ 350 cell/mm^3, or WHO stage III or IV were eligible for ART initiation. Patients with co-morbid conditions like renal failure (HIV associated nephropathy), Hepatitis B virus co-infection and a confirmed tuberculosis infection were eligible for antiretroviral treatment regardless of their CD4 cell count. The preferred first line regime was tenofovir (TDF) + lamuvidine (3TC) + efavirenz (EFV). Zidovudine (AZT) and abacavir (ABC) are the preferred alternative Nucleoside Reverse Transcriptase Inhibitors (NRTI)

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and can replace TDF for patients were TDF is contraindicated, while nevirapine can replace EFV, when it is contraindicated. Preparation for ART comprises a minimum of three adherence counselling sessions, of which, at least one should be an individual (one on one) counselling session. Patients are encouraged to disclose to someone who can assist them with their treatment (Treatment Supporter).

Once initiated patients are reviewed after two weeks. On this visit bloods are taken and a clinical consultation is done. The health worker assesses the patient for adverse effects, complications and adherence challenges. There after the patient is seen monthly for a clinical review, with follow up blood work done every three months. Stable patients have their CD4 cell count done every six months. Viral load is done on targeted patients i.e. where treatment failure is suspected.

3. Patient Selection

3.1. Inclusion Criteria
- Confirmed HIV positive status
- Age ≥ 18 years
- Initiating first line HAART at one of the selected facilities

3.2. Exclusion criteria
- HIV negative
- Age less than 18 years
- Previous experience with ART (Excluding Prevention of Mother to Child Transmission (PMTCT))

4. Definitions
- **Dead**: patient is deceased. This can be reported by the patient's relatives or confirmed on patient follow up for a missed appointment/ loss to follow up.
- **Lost to follow-up (LTFU)**: this is a patient who has not attended the facility for more than three months since their last appointment. Patients who are lost to follow up during the study and return to the clinic and are active at the time of assessment will be counted as active as they are a result of defaulter tracing activities in the program and contribute to retention in care.

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- **Transfer out**: Patient has been transferred to a facility outside the cluster being studied.
- **Stopped**: Patient has stopped taking treatment on a health worker's instructions

5. Measurements

5.1. Outcome variable:

Retention in care at 12 months: This is defined as the patient being alive and on treatment at the assessment time at 12 months. If the patient is not retained then they can be classified as Lost to follow up (LTFU), Transferred out, Dead or Stopped treatment.

5.2. Demographic Variables:

- Sex
- Age
- Unique patient Identifier (ART Number)

5.3. Clinical variables:

- Nurse or Doctor managed
- Weight at initiation
- Clinical stage at initiation
- ART regimen prescribed at initiation
- Active TB at initiation
- Cd4 cell count at initiation
- Haemoglobin at initiation

6. Data Collection and Management

6.1. Data collection

The data collectors in the study were the Data Manager and the three data clerks who work at the Mbabane government ART clinic and manage the data for the whole cluster. They were the obvious choice because they were already familiar with the electronic database and patient file and they and participated in previous data abstractions for program evaluations. The orientation

period was short and we did a pilot data collection using the data abstraction tool on a small sample of patients initiating treatment in 2010.

The sampling frame was a list of all patients generated from the electronic database, who initiated ART in the chosen facilities during the period 1st of January to 30th June 2011. Patients who did not meet the initiation criteria were removed from this list. These included children under 18 years of age, patients transferred in from other facilities with an initiation date that fell within the study period and those that attended the clinic for Post exposure prophylaxis (PEP) during the study period. Data abstraction forms were printed and were used to collect information from the patient file. This information was later transferred to an excel spread sheet and cross-referenced with the electronic patient database for verification and completeness. Where there were discrepancies with the data, we relied on the paper record (i.e. the patient file) as this was the primary data source and is regarded as the most reliable by the facility and the National ART program. The data was imported to STATA® for analysis

6.2. Data cleaning process

Graphic displays of the data and the use of the filter function in the excel spread sheet were used to isolate outliers and verify if they were true outliers or the result of a data capture error. This also identified entries that did not fit into the chosen categories. Suspicious variables were manually verified i.e. relevant files were retrieved and compared to the electronic record and the excel data capture sheet. All patients with missing data had their files retrieved for verification.

6.3. Sample Size Calculation

The following considerations where made when calculating the sample size:

- Approximately 60% of ART patients are initiated at the central hospital and approximately 66% of patients on ART in Swaziland are women.
- A 10% difference in retention at 12 months between the two cohorts is clinically significant and may require programmatic intervention. Assuming retention at 12 months for patients at the central hospital is 75% (27), while among patients in the primary health care clinics is 85%, a total sample size of 660 patients (330 patients per cohort) achieves power of 80% at 0.05 significance level, to detect 10% difference between 12 month retention proportions. Calculations for sample size were done using STATA®.

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7. Data Management and Analysis

7.1. Descriptive Variables

Clinic ID; Sex; age (years); weight (Kg); CD4 (Cells/mL); Haemoglobin (g/dL); TB at initiation; Nurse versus Doctor managed; PMTCT exposure; ART regimen and WHO clinical stage were the variables used to describe the sample. Summary measures were calculated and used to describe the sample and to compare the cohorts. The numerical variables were not normally distributed, therefore, medians and inter quartile ranges were calculated and Mann-Whitney-Wilcoxon test was used to compare the medians. Chi Square test was used to compare proportions of categorical variables. We compared retention in care and LTFU between the doctor and nurse managed cohorts. Transferred out and dead were not compared as the number of events in each cohort was very small.

Multivariate analysis was used to evaluate the main exposure (retention in care) while adjusting for known confounders and possible interactions. It was noted that, the prevalence of HIV differed significantly by sex, with women being affected more than men(1). CD4 and WHO stage at presentation also differ by sex(4) and this made sex a likely confounder in this analysis. Low CD4, Anaemia and WHO stage have been found to be associated with retention in care in other studies, therefore they were considered for inclusion in the multivariate model(9, 22). Variables with a p value <0.25 in the univariate analysis were selected and the Allen-Cady modified backward method of selecting variables was followed(28). All variables with a univariate p value <0.25 were included in the multivariate analysis. The variable with the highest p value were dropped from the analysis until only variables with a p value <0.05 remained.

8. Ethical considerations

The study protocol was approved by the University of Pretoria Academic Committee, Ethics committee, and the Swaziland Ethics and Scientific Committee. Permission was obtained from the Swaziland National ART program to access patient records and information. Since the study used routinely collected patient data, there was no need for a written consent from the patients. Patients records used in this study were treated with utmost confidentiality. This involved the use

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of security measures to protect patient information such as the use of unique study identifiers instead of patient names, passwords for computers and lockable cupboards for hard copies.

Results

This study reports the findings of a retrospective cohort comparing doctor managed versus nurse managed patients. The main outcome of the study was retention in care and was defined as the proportion of patients who are alive and on ART at the time of assessment (12 months after ART initiation).

1. Baseline characteristics

Table 2 shows the baseline characteristics of the study sample. Mbabane government hospital contributed the most patients at 517(69.4%). These patients also made up the cohort managed by doctors in the study. The majority of patients in the study were female (511(58.4%)). The age of patients participating in the study ranged from 18 to 78 years, with a median age of 33 years (IQR; 28, 41 years). Median CD4 was 172 cells/mm3 (IQR 82 to 261cells/mm^3), median weight was 61 kg (IQR 55, 70 kg), and median haemoglobin was 11.7 g/dl (IQR 9.9, 13.1 g/dl). The majority of patients (70%) were in WHO stage I or II. Eighty two Patients (9.4%) had active Tuberculosis at initiation, and only 21(2.5%) had documented exposure to PMTCT at initiation.

Table 1: Description of the baseline demographic and clinical characteristics of the sample (N=871)

Variables	n (%)	Median	IQR
N	871(100)		
Clinic ID			
Mbabane ART Clinic	517(59.4)		
Lobamba Clinic	136(15.6)		
Motshane Clinic	144(16.5)		
Sigangeni Clinic	35(4.0)		
Mbabane TB Clinic	36(4.5)		
Sex			
Female	511(58.7)		
Male	360(41.3)		
Age (years)		33	28, 41
CD4 (cells/mm^3)		172	82, 261
WHO Stage			

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Variables	n (%)	Median	IQR
I	185(21.3)		
II	431(49.5)		
III	187(21.5)		
IV	67(7.7)		
Weight (kg)		61	55, 70
Haemoglobin (g/dl)		11.7	9.9, 13.1
Active Tuberculosis Infection	82(9.4)		
PMTCT	21(2.5)		
Nurse managed	354(40.6)		
Doctor managed	517(59.4)		

2. Comparison of Doctor and Nurse Managed Patients

2.1 A comparison of baseline demographic, clinical characteristics

Table 3 shows a comparison of doctor and nurse managed patients. The nurse managed group had a larger proportion of females (227(64.1%)) compared to the doctor managed group (284(54.9%)) and this difference was statistically significant, with a p-value of 0.007. The nurse managed group also had a significantly higher proportion of patients with TB at baseline, 44(12.5%) compared to 38(7.4%) in the doctor managed group, *P* was 0.011. WHO stage distribution, differed significantly between the two groups, with a *P* value of 0.019. Median CD4 at initiation was similar between the two groups (*P* value was 0.06). There was a significant difference in the median age, which was lower in the nurse managed group (32 years) compared to the doctor managed group (34 years), with a *P* value of 0.02. Median Haemoglobin and weight were similar between the two groups.

Figure 5 is a graphical representation of the median CD4, median Age and median haemoglobin, by nurse or doctor managed. In both cohorts the median CD4 cell count at initiation is below 200cell/mm^3. **Figure 6** shows the distribution of CD4 cells by category for all patients at ART initiation. It highlights the fact that the majority of patients in the study had a Cd4 <200 cells/mm^3. **Figure 7** shows the distribution of CD4 cell count at baseline by whether patients were nurse or doctor managed. **Figure 8** is a comparison of median CD4, median age and median haemoglobin by facility. This highlight the much lower median CD4 at the Mbabane TB Clinic.

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Table 2: Baseline comparison of the demographic and clinical characteristics of the cohort managed by nurses and the cohort managed by doctors

Characteristic	Doctor Managed (n=517)	Nurse Managed (n=354)	p-value
	n (%)	n (%)	
Female	284(54.9)	227(64.1)	0.007
TB	38(7.4)	44(12.5)	0.011
PMTCT	9(1.7)	12(3.5)	0.098
WHO Stage			**0.019**
I	108(20.9)	77(21.8)	
II	266(51.6)	165(46.6)	
III	95(18.4)	92(26.0)	
IV	47(9.1)	20(5.7)	
	Median(IQR)	Median(IQR)	p-value
CD4 (cells/mm^3)	169(77-260)	176(103-264)	0.06
Age (years)	34(28–41)	32(28-39)	0.02
Weight (kg)	61(55–69.3)	61.5(55–70)	0.79
Haemoglobin (g/dl)	11.4(9.8–13.1)	12(10–13.2)	0.22
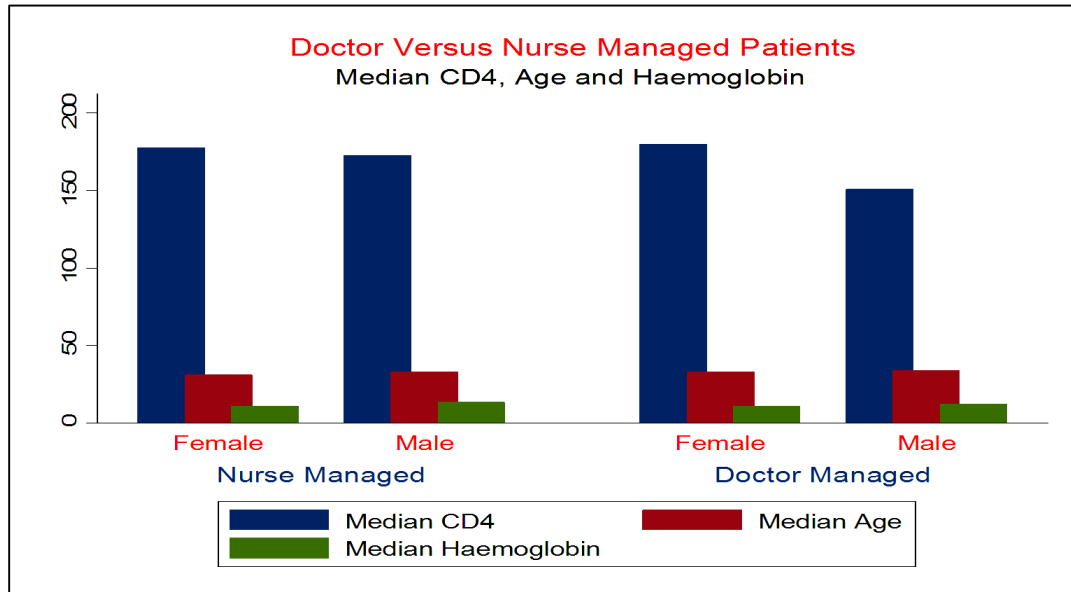
Figure 5: Comparison of CD4, Age and Haemoglobin Medians, by Sex in Patients Managed by Nurses and Doctors.
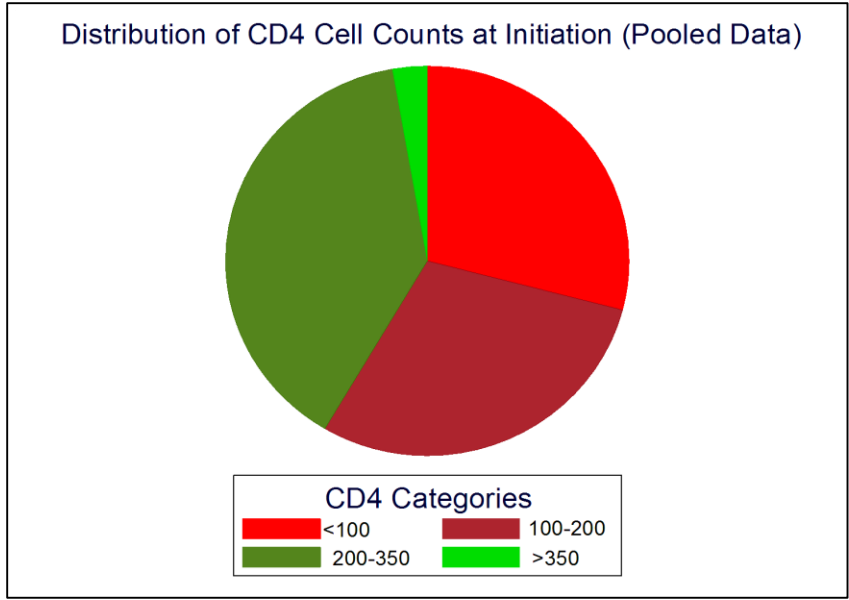
Figure 6: Distribution of CD4 cell counts by category among patients initiating ART at Mbabane government hospital and its outreach clinics.
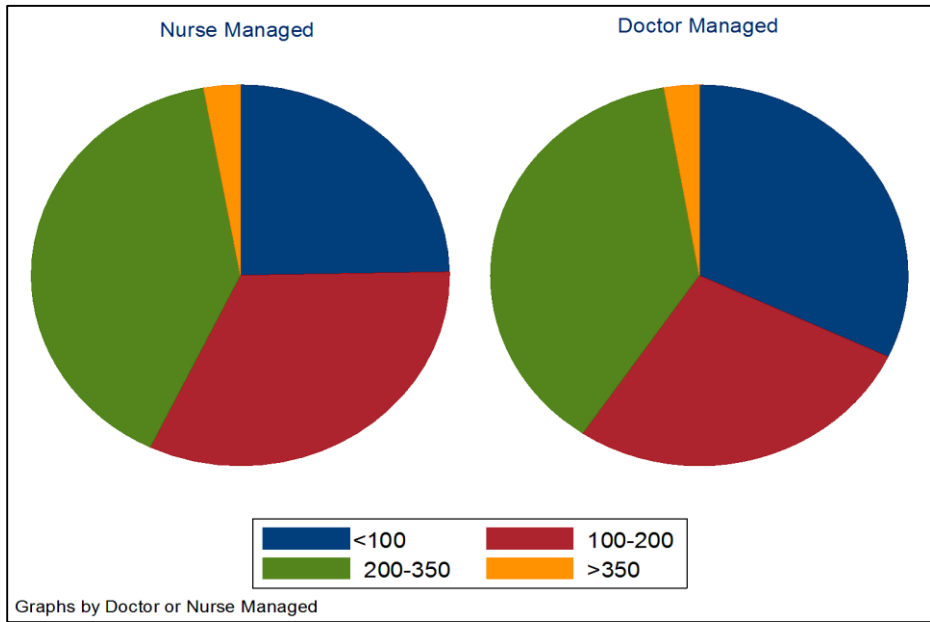
Figure 7: Distribution of CD4, by Doctor or Nurse Managed
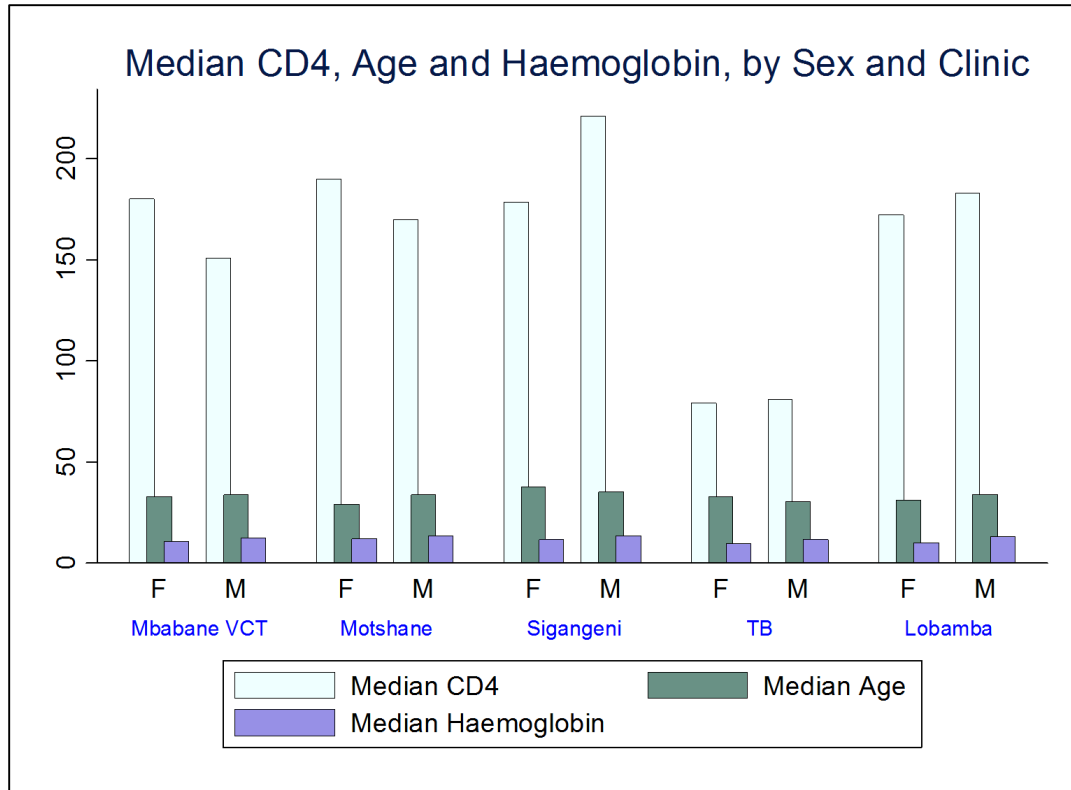
Figure 8: Comparison median CD4, median age and median haemoglobin, by sex and clinic for patients at ART initiation.

2.2 Comparison of Outcomes

The key outcome was retention in care. Comparing the retention in the doctor and the nurse cohorts, we see that retention in care was similar between the cohorts, 69.1% and 70.9%, respectively, *P* was 0.56. Patients that were not retained in care were classified as LTFU, transferred out, dead or stopped. A comparison of lost to follow up, showed no statistical difference between the 2 groups, with a loss to follow up of 30.6% and 25.4% in the doctors and nurses cohorts respectively, *P* was 0.099. The group managed by doctors did not have any recorded deaths while the nurse cohort had four recorded deaths. No patients stopped treatment in either cohort during the study period. **Figure 6,** shows the retention in the two cohorts and compares it to the regional average retention rate in the Sub-Saharan region, represented by the red horizontal line in the graph below.

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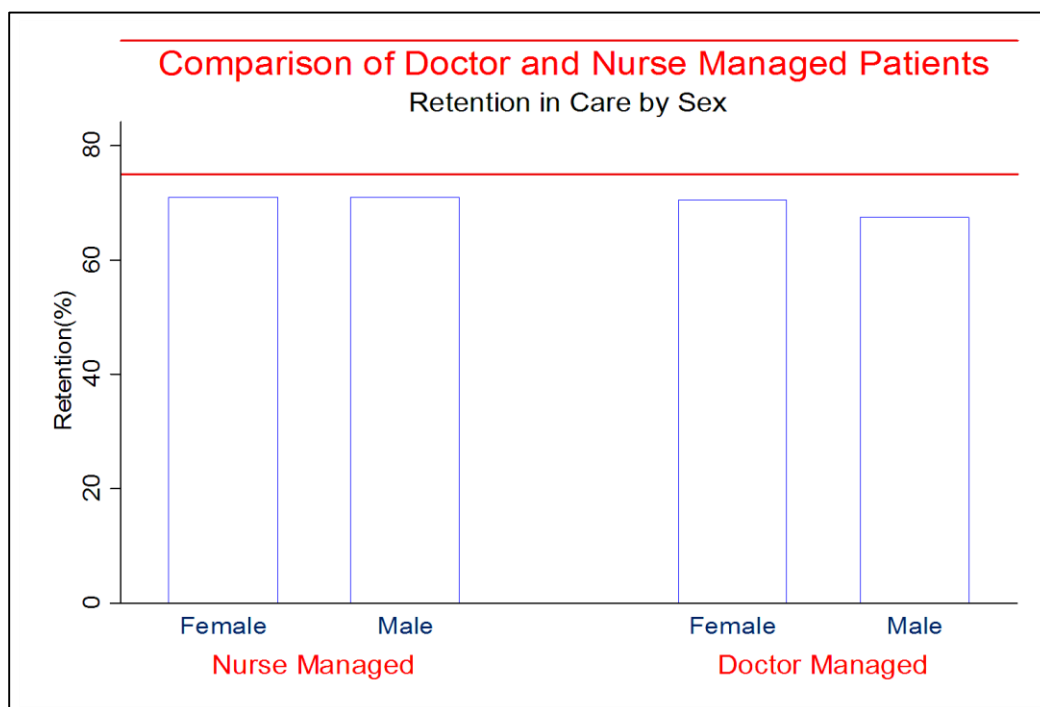
Figure 9: Retention in Care a Comparison of Patients Managed by Doctors and Nurses, by Sex. The Horizontal line at 75% represents the Average Retention rate found in a Meta-analysis in South Africa published in 2007(27).

2.3   ART Regimens prescribed at Initiation

Table 4 shows the distribution of ART regimens prescribed at initiation in the study. The majority of patients were on TDF/3TC/EFV, 606(69.6%) and 132 (15.2%) were on AZT/3TC/NVP. There were only 2(0.2%) patients not on a standard first line regimen. These patients were on AZT/3TC/LPV/r and were in the doctors' cohort. Therefore 99.8% of patients in the study were prescribed a standard first line regimen. No patients were prescribed d4T+3TC+NVP and only 16(1.8%) were prescribed d4T+3TC+EFV, with only 3(0.9%) of these on the nurses group.

Table 3: ARV Regimens prescribed at ART initiation. Comparison of doctor and nurse managed patients using Fisher's exact test yielded a p <0.001.

ART Regimen	Total	Doctor Managed	Nurse Managed
	n(%)	n(%)	n(%)
TDF/3TC/EFV	606(69.6)	359(69.4)	247(69.8)
TDF/3TC/NVP	63(7.2)	50(9.7)	13(3.7)

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ART Regimen	Total	Doctor Managed	Nurse Managed
	n(%)	n(%)	n(%)
AZT/3TC/NVP	132(15.2)	62(12.0)	70(19.8)
AZT/3TC/EFV	44(5.1)	24(4.6)	20(5.7)
d4T/3TC/NVP	0(0.0)	0(0.0)	0(0.0)
d4T/3TC/EFV	16(1.8)	13(2.5)	3(0.9)
ABC/3TC/EFV	2(0.2)	2(0.4)	0(0.0)
ABC/3TC/NVP	6(0.7)	5(1.0)	1(0.3)
Other	2(0.2)	2(0.4)	0(0.0)

3. Univariate Associations

The results listed below in **Table 5** are the univariate association of the different explanatory variables and the main outcome variable (Retention in care). Whether the patient was managed by a doctor or a nurse was the main exposure being investigated. The variable doctor or nurse managed had an unadjusted Odds Ratio (OR) of 0.92(95% CI: 0.68, 1.23) and p value of 0.56. Sex had an unadjusted OR of 0.91(95% CI 0.68, 1.22) and a *P* was 0.52. The following were the univariate associations with significant *P* values: CD4: unadjusted OR: 1.23(95% CI: 1.04, 1.45), *P* was 0.014; weight; unadjusted OR: 1.87(95% CI: 1.39, 2.52), *P* was <0.001; WHO stage: unadjusted OR: 0.81(95% CI: 0.68, 0.96), *P* was 0.014; haemoglobin had an unadjusted OR: 1.40(95% CI: 1.20, 1.62), *P* was <0.001 and Active tuberculosis infection at ART initiation had an unadjusted OR: 0.57(95% CI: 0.36, 0.82), *P* was 0.020. There were no variables with a *P* value that fell between >0.05 and <0.25. The rest of the variables had *P* values >0.25 and therefore were not included in the multivariate analysis.

Table 4: Univariate associations of retention in care and explanatory variables

Covariate	Number of observations	Unadjusted Odds Ratio(OR)	95% Confidence Interval	P-values
Clinic ID	871	1.05	0.95, 1.16	0.37
Sex	871	0.91	0.68, 1.22	0.52
Age (Years)	867	1.01	0.99, 1.02	0.32
CD4 (cells/mm^3)	867	1.00	1.00, 1.00	0.041
Weight (kg)	650	1.03	1.01, 1.04	<0.001

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Covariate	Number of observations	Unadjusted Odds Ratio(OR)	95% Confidence Interval	P-values
WHO Stage	870	0.81	0.68, 0.96	0.014
Haemoglobin (g/dl)	723	1.17	1.09, 1.25	<0.001
Regimen	871	0.94	0.84, 1.05	0.28
Tuberculosis at Initiation	870	0.57	0.36, 0.92	0.020
History of PMTCT	857	1.83	0.61, 5.50	0.28
Doctor/Nurse managed	871	0.92	0.68, 1.23	0.56

4. Multivariate Analysis

Table 6 shows the adjusted Odds Ratios (aOR) for factors associated with retention in care. The main exposure was Doctor or nurse managed. There was no association between retention in care and whether patients were managed by a doctor or a nurse with all other factors kept constant. After adjusting for sex, haemoglobin, CD4 cell count, weight and WHO stage, the odds of being retained in care were similar between the two groups, aOR: 1.11(95% CI: 0.72, 1.69), with a *P* value of 0.64. Male patients had an aOR of 0.63 (95%CI: 0.45, 0.95) of being retained, *P* was 0.026. The odds of being retained increased by 3% for every one kg increase in weight, while keeping all other factors constant, aOR: 1.03 (95%CI: 1.01,1.05), *P* was 0.001. The odds of being retained increased by 17% for every one g/dl increase in haemoglobin, aOR: 1.17 (95% CI: 1.07, 1.28), p<0.001.

Table 5: Best multivariate model showing adjusted Odds ratios and p values for variables associated of retention in care

Variables	Adjusted Odds Ratio	95% CI	P-Value
Doctor or Nurse Managed	1.11	0.72, 1.69	0.64
Sex	0.63	0.45, 0.95	0.026
Weight (kg)	1.03	1.01, 1.05	0.001
Haemoglobin (g/dl)	1.17	1.07, 1.28	<0.001

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Study Limitations

1. This was an observational study and therefore lacked the rigour of a Randomised Control Trial (RCT). There is need for randomised controlled trials to show the benefits of task shifting ART initiation to nurses.

2. The study used retrospective data and was therefore limited by the quality of data available. A prospective study, preferably with randomization can improve this aspect of the study and enhance the generalizability of the findings.

3. The study setting was a limitation as well. Doctor managed patients were all based at the hospital while nurse managed patients were all at the primary health care clinics. The differences in these settings and the fact that the patients attending these facilities may differ make the comparison very difficult and may introduce confounding.

4. The study was not nationally representative, and this should be considered when we generalize these findings.

5. The study documented mortality but its use in the analysis was limited due to the constraints of collecting mortality data in Swaziland. The defaulter tracing component of the ART program recently started using cellular phones to track patients and this has overtime seen an improvement in the quality and reliability of mortality data.

6. The investigators were not able to collect data on side effects. This was due to the fact that data clerks were used for data abstraction; a nurse would have been the ideal cadre to collect this information on side effects, as it is difficult to extract this information from the patient file due to the way it is recorded.

Discussion

1. Key Results

Retention is similar amongst the doctor and nurse managed patients. Lost to follow up rates were comparable between doctor and nurse managed patients. It was found that weight and haemoglobin are positively associated with retention in care, while male sex is negatively associated with retention in care. A significantly larger proportion of women are initiated on treatment compared to men. The majority of patients in this study presented late for treatment as evidenced by the low median CD4 cell count at ART initiation.

2. Decentralization of HIV services and retention in care

In this study the main outcome was retention in care. Patients were considered retained in care if they were active and on treatment at the time of assessment. Patients who were not retained in care were classified as lost to follow-up, transferred out, dead or stopped. Patients who are transferred out were technically not lost to the program but since their outcomes cannot be determined in this study they were classified as not retained as they were considered lost to the cluster. Deaths were recorded and reported but their use was limited as they are not always reliably documented. This was due to the challenges in collecting and documenting information on deaths prior to the availability of cellular phones for patient follow-up. The strengthening of the defaulter tracing program in Swaziland has led to an improvement in the reporting and documentation of deaths. This aspect of the ART program has improved over time and the mortality statistics are now very reliable.

It is very likely that in this study a good number of deaths fell into the lost to follow up category. An unpublished evaluation of loss to follow-up amongst patients on ART done by the Swaziland National ART program and WHO in 2010 found that 35% of patients originally classified as lost to follow-up were eventually confirmed to be dead(29).

Decentralisation of ART services to the primary healthcare level, using a nurse led program is feasible and safe as the retention and lost to follow up rates between doctor and nurse managed patients were comparable in this study. Retention rates were found to be similar between the two

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cohorts. Since the p value was >0.05 and we were unable to reject the null hypothesis and concluded that there was no difference in retention between doctor and nurse managed patients. This is comparable to findings in similar studies in the region (9, 21, 22, 30). The retention rates at 12 months however were lower than the average retention rate in the region of 75% (27). **See figure 9** above. It is clear from this graph that in both cohorts the retention rate was below the regional average of 75%. This can be explained by the fact that it was early in the decentralization program and it followed a change in the threshold for ART initiation. It is possible that the program was still adjusting to these changes and should stabilize over time with a concomitant increases in retention rates.

This study adds to the current evidence on nurse initiated and managed ART. It is important to look at patients who start treatment at the primary health facility and are largely managed by nurses at that facility and compare them to patients managed by doctors at larger facilities, rather than comparing stable, down-referred patients who invariable will have better outcomes compared to patients managed in hospitals(20). The fact that these patients are selected for down-referral because they are stable on treatment introduces bias and makes it difficult to make a fair comparison, but for a long time we did not have studies that compared patients who were initiated and managed at the primary health level by nurses to compare to doctor managed patients.

3. Men, women and access to HIV services

Generally there are more women than men accessing HIV services in Swaziland. In this study majority of patients were women at 58.4% of the study population, the nurse managed cohort had a much larger proportion of women (64.1%) and this was significantly higher than in the doctor managed cohort. Though HIV is known to affect women more than men(2, 31), women exhibit better health seeking behaviours compared to men, hence more women present to treatment and care facilities, resulting in more women being initiated on ART.

Males were 37% more likely not to be retained compared to women, adjusted OR: 0.63 (95% CI: 0.45, 0.95), *P* was 0.026. As seen previously man present late for treatment, with advanced disease (evidenced by lower median CD4 count at initiation compared to women), patients who present late are likely to have severe opportunistic infections, liver and/ or kidney dysfunction,

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and are likely to be initiated on more complex regimens and possibly have a greater likelihood of developing complications.

4. Baseline parameters and their impact on retention in care

The median weight was 61 kg, IQR: 55, 70 kg. There was no difference in the median weight between the two groups of patients. Body mass index (BMI) was not calculated as data on height was not collected in this study. Height was not routinely documented in the patient file as the calculation of BMI was not critical for the prescription of ARVs; this has changed with the advent of the "food by prescription" program, which was introduced late in 2011. In this program patients with BMI <18.5 kg/m^2 are enrolled into outpatient a nutritional rehabilitation program or an inpatient program for those who were severely malnourished. This has necessitated routine collection of patient heights in the clinical management of ART patients. There was a positive association between weight and retention in care, aOR: 1.03(IQR: 1.01, 1.05), *P* was 0.001, suggesting that an increase in weight plays a role in the retention of patients in care.

The median CD4 is 172 (IQR: 82, 261) which is in keeping with the fact that the majority of patients present late for treatment, and are found to have low CD4 cell counts at ART initiation. A large proportion of patients in this study (557(58.5%)) had a CD4 cell count below 200 cells/mm^3, with a further 29.1% with a CD4 cell count below 100 cell/mm^3. This is illustrated in **figure 7** above. Although the majority of patients had low CD4 cell counts and initiation, 70% of patients initiated on ART had a WHO stage of I or II. This suggests that, though patients in Swaziland present late for treatment in terms of CD4 cell count criteria, a lot of them would not have experienced a major opportunistic infection prior to ART initiation and were still in reasonably good health.

In this study CD4 cell count and WHO stage at baseline were not associated with retention in care. Low Cd4 cell count has been positively associated with retention in care in similar studies in Sub-Saharan Africa(9, 22). The fact that the majority of patients had a low WHO stage despite the low CD4 cell count in this study may explain this difference as patients who are well are less likely to die and therefore are less likely to be lost to the cohort.

With a median haemoglobin of 11.7 g/dl, IQR: 9.9-13.1, at least 50% of patients in the study were anaemic. The normal haemoglobin reference range is 11.5-16 g/dl for women and 13-18 g/dl for men(32). The median haemoglobin levels were comparable between the two groups.

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Regarding haemoglobin, healthier patients (i.e. those with higher haemoglobin) were more likely to be retained in care. Haemoglobin had a positive associated with retention in care, aOR: 1.17(95% CI: 1.07, 1.28), p <0.001. This can be interpreted to mean that for every 1 g/dl increase in haemoglobin the odds are 17% better that the patient will be retained in care. Like weight above we can draw the conclusion that healthier subjects are more likely to be retained in care as evidenced by the adjusted odds ratios for weight and haemoglobin. **Figure 8** above**,** shows the median CD4, age and Haemoglobin by clinic. The TB clinic in Mbabane had the lowest median Cd4 (<100 cell/mm^3). This should be expected as all patients seen in this clinic had advanced disease, because they had active tuberculosis infection at initiation and were classified as WHO stage III.

5. Challenges in the comparison of literature from different decentralization programs

The challenge with comparing literature or findings from decentralization programs in Africa is that there may be a number of important differences in the ART programs that may influence patient outcomes. Capacity building programs, designed to facilitate nurse initiation of ART in the different programmes may have different curricula and hence any comparison or generalization we make needs to take this into account.

The cadres involved in task shifting may also differ from country to country as some countries have nurses with a diploma, while other countries have degreed nurses while in some countries they have clinical officers who receive additional training in medical diagnosis and treatment over and above the standard nursing training curriculum. These different health professional will handle the additional tasks handed to them differently, with the transition being much simpler for some.

In Swaziland, specific HIV management modules have recently been introduced into the nurses' pre-service training. The amount of HIV medicine covered in the pre-service training may differ from country to country, as does the practical exposure nurses get prior to qualification.

The level of supervision and mentoring that the nurses receive will also differ as different programs have diverse decentralisation strategies and different resources available to support these programs.

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These differences make it challenging to compare findings form different program setting as the program set up has a significant influence on outcomes. Despite all these challenges we attempt to make the most of the evidence available and try to improve treatment programs and patient outcomes.

A strength of this study is that it was an evaluation of a real world situation where nurses were initiating and managing patients on ART, and producing comparable outcomes, albeit under the supervision of doctors. In this model of decentralisation, doctors from the mother facility visited the outreach clinic once every two weeks and nurses were able to contact doctors per phone to consult or seek advice on difficult cases when they needed to. This is a model that can be implemented in low resource settings such as Swaziland.

Conclusion and Recommendations

It can be concluded that task shifting is feasible and safe in Swaziland as retention in care of nurse initiated and managed ART are similar to those of doctors. It should be noted though that retention only represents one aspect of quality of care and can therefore not be used to compare the total quality of care provided by doctors to that provided by nurses. This supports findings from other studies that compared nurse and doctor managed patients or looked at the expansion of the role of nurses to include ART initiation(30,33).

These findings can be generalized to similar populations with similar epidemic levels, socio-economic and health system challenges in the region.

Healthier patients (using findings on weight and haemoglobin in this study) appear to have better outcomes in terms of retention in care; this supports the recommendations from WHO to start patients' on treatment earlier.

Further research is needed to show the benefits or pitfalls of task shifting. A randomised Controlled trial to answer other aspects of quality of care like mortality, side effects, adherence levels, viral load suppression, management of co-morbidities and a comparison of the decision making of both cadres.

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Appendices

Appendix 1: Data Abstraction Tool

ID	Clinic Name	ART Number	Sex	Age	Wt	WHO Stage	CD4	Hb	Nurse/ Doctor Initated	Regimen	Active Tuberculosis	PMTCT	Outcome

Appendix 2: Ethical Approval