Acceptability and effectiveness of rapid ART initiation: Patients' and healthcare workers' perspectives.

BY

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A thesis by manuscript submitted in fulfilment of the requirements for the degree of Doctor of Philosophy Discipline of Public Health Medicine, School of Nursing and Public Health, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa

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June 2022

DECLARATION 1: PLAGIARISM

I, Sabina Govere declare that:

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DECLARATION 2: PUBLICATIONS AND MANUSCRIPTS

The publications (in print, in press and submitted) that constitute this thesis and the contribution I made to each of the manuscript are presented here.

Publication 1

Sabina M. Govere, Moses J. Chimbari. 2020.The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa: A scoping review. *Southern African Journal of HIV Medicine | Vol 21, No 1 | a1103.*

Authors' contributions

S.M.G. and M.J.C. conceptualized the study. S.M.G. did literature searches, analysis, writing and compilation of manuscript. M.J.C. supervised the processes, reading all versions. Both authors have read and approved the final article

Publication 2

Sabina M. Govere, Chester Kalinda & Moses J. Chimbari. 2021. Factors Influencing Rapid Antiretroviral Therapy Initiation at Four eThekwini Clinics, KwaZulu-Natal, South Africa. *AIDS and Behavior 308*

Authors' Contributions

Sabina M. Govere and Moses J. Chimbari conceptualised the study. Moses J. Chimbari supervised the study processes. Sabina M. Govere wrote the main manuscript text. Chester Kalinda and Sabina M. Govere conducted the analysis. Moses J. Chimbari and Chester Kalinda reviewed the paper and approved the final manuscript.

Publication 3

Sabina M. Govere, Tawanda Manyangadze, Chester Kalinda, Moses J. Chimbari. 2021. An assessment on the implementation of Same Day Antiretroviral Therapy initiation in eThekwini clinics, KwaZulu-Natal, South Africa. JPHIA - Journal of Public Health in Africa. *paper 2179*

Authors Contributions

Sabina M. Govere and Moses J. Chimbari conceptualized the study. Moses J. Chimbari supervised the study processes. Sabina M. Govere wrote the main manuscript text. Chester Kalinda, Tawanda Manyangadze and Sabina M. Govere conducted the analysis. Moses J. Chimbari, Tawanda Manyangadze and Chester Kalinda reviewed the paper and approved the final manuscript.

Manuscript 4

Sabina M. Govere, Tinashe Mutero & Moses J. Chimbari 2021. Experiences, knowledge and observations influencing implementation of same day ART initiation in four eThekwini clinics: healthcare worker's perspective. *The Qualitative Report. Under review.*

Authors' Contributions

Sabina M. Govere and Moses J. Chimbari conceptualised the study. Moses J. Chimbari supervised the study processes. Sabina M. Govere wrote the main manuscript text. Tinashe Mutero and Sabina M. Govere conducted the analysis. Moses J. Chimbari and Tinashe Mutero reviewed the paper and approved the final manuscript.

Manuscript 5

Sabina M. Govere, Chester Kalinda & Moses J. Chimbari 2022. The impact of Same-day Antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa. *BMC Global Health Research and Policy. Under review*.

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[redacted] 27 June 2022

Sabina Govere Date:

DEDICATION

Special dedication goes to my late parents; I know they are proud of me for this achievement which I believe they would have loved to witness.

1. Ms H. Kazingizi who passed a few months before my Ordinary Level examinations and sacrificed all she had to provide the best foundation for my education.

2. Mr W.B. Govere who passed on a few weeks before my undergraduate degree graduation.

3. My adorable daughter Claire for her unending love in filling the void and always being my pillar of strength.

ACKNOWLEDGEMENTS

I would like to express my heartfelt gratitude to my supervisor Professor Moses J. Chimbari for his guidance, endless patience, support, encouragement and constructive criticisms throughout this study. Without your undeniable assistance, this work could not have been successful. Much appreciated.

Many thanks to Dr Chester Kalinda who acted as a mentor throughout the PhD process and assisted in the statistical data analysis. I am also grateful to my boss at work Dr I. V. Bassett for allowing and supporting me to pursue my studies and guide me in my research skills.

I am thankful to Prof S. Duma, Dr T Manyangadze, Dr E. Ojewole, Dr T. Mutero and Dr T. Mindu for their invaluable guidance and support. I am thankful to the College of Health Sciences, University of KwaZulu-Natal who financially supported the study.

Special thank you goes to my adorable daughter Claire Anesu for the sacrifices, tolerance, understanding, endless encouragement when I felt weak to continue and unconditional love they have shown throughout my study; I'm forever grateful. Thank you to all my friends in my social life and academia for encouraging and believing in me; all your words kept me going. I also appreciate all the patients who participated in the study as well as clinic management and staff from the four health institutions for granting us permission to enrol patients in their facilities.

Finally, this study could have never been possible without the grace of the Almighty God who gave me the breath, strength and wisdom to complete this doctoral research project.

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ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome
HIV	Human Immunodeficiency Virus
ART	Antiretroviral Therapy
PLWHIV	People living with HIV
UTT	Universal Test and Treat
WHO	World Health Organization
UN	United Nations
KZN	KwaZulu Natal
SPSS	Statistical Package for the Social Sciences
ARV	Antiretroviral
UNAIDS	United Nations Programme on HIV and AIDS
CD4	Cluster Difference 4
TROA	Total Number of People on ART.
VL	Viral load
HTS	HIV Testing Services
SDGs	Sustainable Development Goals
SDI	Same day ART initiation
PHC	Primary Healthcare

ABSTRACT

The Joint United Nations Programme on HIV/AIDS is leading the global effort to end AIDS as a public health threat by 2030. In achieving these goals, emphasis has been on the 95–95–95 targets that by 2030, 95% of people living with HIV know their HIV status. However, the focus is on achieving the second 95 and third 95; having 95% of people diagnosed with HIV initiating on treatment within the expected timeframe and 95% of those on treatment obtaining a suppressed viral load. Commendable efforts have been made in increasing HIV testing numbers however, same day initiation on treatment and achieving viral load suppression remains a challenge. According to the WHO recommendations; same day (ART) initiation should be offered to all people living with HIV following a confirmed diagnosis. This study determined the factors influencing the acceptability and implementation of Universal Test and Treat by both patients and healthcare workers. Universal Test and Treat is a prevention strategy encourages that if a person tests HIV positive, irrespective of the persons CD4 count and clinical staging at the time of testing they will have to begin treatment immediately. Furthermore, patient's clinical outcomes following test and treat in eThekwini municipality in KwaZulu-Natal were determined.

This study was cross-sectional and used prospective - mixed methodology to collect data from 403 patients who either accepted or deferred same day ART initiation from June 2020 to May 2021. A structured questionnaire was used to collect demographic information, sexual behaviour, acceptance of same day ART initiation and knowledge of Universal Test and Treat on the day of HIV diagnosis. Key informant in-depth interviews were conducted with healthcare workers and patients were followed up at 6 months after HIV diagnosis to determine clinical outcomes for both groups, rapid and deferred ART initiators using medical charts and electronic databases.

Two different analysis univariate and multivariate logistic regression were performed to examine associations between same day ART initiation and several explanatory factors. Logistic regression was performed to examine associations between same day ART initiation and several explanatory factors, retention in care, clinical outcomes and facility related factors. Thematic analysis was used to assess experiences, knowledge and observations of healthcare workers in implementing the Universal Test and Treat policy. Among the 403 participants same-day initiation was 69.2% (n=279). In an adjusted analysis (age, gender, level of education were adjusted at 0.5 significance level in univariate level) number of sexual partners (aOR: 0.35; 95% CI: 0.15-0.81), HIV status of

the partner (aOR: 5.03; 95% CI: 2.74-9.26), knowledge of universal test and treat (aOR: 1.97; 95% CI: 1.34-2.90), support from non-governmental organizations (chi-square = 10.18; p-value= 0.015 and provision of clinic staff (chi-square = 7.51; p value = 0.006) were identified as major factors influencing uptake of same-day ART initiation. In the bivariate analysis; gender (OR: 1.672; 95% CI: 1.002–2.791), number of sexual partners (OR: 2.092; 95% CI: 1.07–4.061), age (OR: 0.941; 95% CI: 0.734–2.791), ART start date (OR: 0.078; 95% CI: 0.042–0.141) and partner HIV status (OR: 0.621; 95% CI: 0.387–0.995) were significantly associated with viral load detection and retention in care. (All variables that were significant at e.g. 0.5 level in univariate).

Our results suggest a steady increase in uptake of same day ART initiation with poor retention in care. The results also emphasise a vital need to not only streamline processes to increase immediate ART uptake further but also ensure retention in care in order to meet the 95-95-95 targets. The findings of the study contribute to knowledge useful for strengthening rapid ART initiation implementation by considering individual patient factors, healthcare workers' perspectives and facility level factors. The qualitative findings revealed variations in UTT knowledge, experiences and observations among diverse healthcare workers from the four clinics in different geographical settings. While training on UTT and SDI of ART initiation was conducted at the inception of the implementation phase, the understanding and interpretation varied especially between clinicians and non-clinical healthcare providers. Denial, feeling healthy, fear of disclosure, limited knowledge about ART, fear of ART side effects, fear of stigma and discrimination were some of the factors HCW observed as hindering uptake of SDI. These findings relate to some of the reasons given by patients with fear of disclosure frequently mentioned by those who deferred SDI of ART.

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OUTLINE OF THE DISSERTATION

This dissertation has preliminary sections followed by Chapter 1 comprising of the introduction and literature review. Chapters 2, 3, 4 and 5 are data chapters while Chapter 6, the final chapter, provides an overall discussion and synthesis of the thesis. The data chapters are presented in accordance with the format of the journals to which they were submitted or published.

Chapter 1: Introduction and literature review

This chapter contextualises the study and provides a general overview of the literature that informed the study. The literature review is presented in the form of a scoping review titled: Sabina M. Govere, Moses J. Chimbari. 2020.**The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa: A scoping review.** *Southern African Journal of HIV Medicine | Vol 21, No 1 | a1103.* The manuscript is published.

Chapter 2: Factors Influencing Rapid Antiretroviral Therapy Initiation at Four eThekwini Clinics, KwaZulu-Natal, South Africa.

This was a cross-sectional study aimed to investigating individual factors of patients that could influence the uptake of same day ART initiation in eThekwini municipality area. The manuscript is published: Sabina M. Govere, Chester Kalinda & Moses J. Chimbari. 2021. *Factors Influencing Rapid Antiretroviral Therapy Initiation at Four eThekwini Clinics, KwaZulu-Natal, South Africa. AIDS and Behavior 308*

Chapter 3: Experiences, knowledge and observations influencing implementation of same day ART initiation in four eThekwini clinics: healthcare worker's perspective.

The study was cross-sectional and qualitative exploring the experiences, knowledge and observations among a diverse group of healthcare workers on the implementation of Universal-Test-and-Treat (UTT) particularly same day ART initiation to strengthen and improve the policy implementation. *The manuscript is under review in The Qualitative Report journal.*

Chapter 4: An assessment on the implementation of Same Day Antiretroviral Therapy initiation in eThekwini clinics, KwaZulu-Natal, South Africa.

The study presented in this chapter was longitudinal aimed at assessing the clinic level implementation of same day ART initiation policy.

The manuscript has been accepted in Journal of Public Health in Africa

Chapter 5: The impact of Same-day Antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa.

This was an observational prospective cohort study aimed at evaluating retention in care, and clinical outcomes 6 months after HIV diagnosis with the cohort comprising of Same-Day-Initiation (SDI) and delayed ART initiators.

The manuscript is under review in BMC Global Health Research and Policy.

Chapter 6: Synthesis of the dissertation

This last chapter gives a summary consolidating findings from all chapters demonstrating their interconnectedness and relevance to thesis objectives. It also provides the general conclusion and highlights of the study. Furthermore, it provides policy implications of the study findings and makes recommendations for further studies and policy strengthening.

CHAPTER 1:
GENERAL INTRODUCTION, REVIEW PAPER, RESEARCH PROBLEM, QUESTIONS, OBJECTIVES AND THESIS STRUCTURE

1.1 Introduction

The Joint United Nations Programme on HIV/AIDS (UNAIDS) describes Human Immunodeficiency Syndrome (HIV) and Acquired Immune-Deficiency Syndrome (AIDS) as a public health burden (1). Several published reports between 2016 and 2020, revealed that recent global annual HIV incidences account for 2.8 million and AIDS-related deaths at 1.8 million people (2). Significant progress in expanding HIV programs and access to treatment worldwide, requires radical ways to meet the increasing demands on public health care providers (3). The World Health organization (WHO) introduced the Universal Test and Treat (UTT) policy recommending same day initiation of Antiretroviral therapy (ART) on the same day of HIV diagnosis. However complex barriers and facilitators to the implementation and uptake throughout the UTT cascade can be anticipated (4).

UNAIDS's 95-95-95 target by 2030 in low and middle income countries requires inventive solutions to meet the increasing strain placed on public healthcare system(5). The 95-95-95 target is to have 95% of people living with HIV (PLHIV) know their status, 95% of people who know their HIV-positive status are initiated on treatment and 95% of people on treatment have suppressed viral loads which means having an undetectable HIV viral copies in the blood (3). Attaining the 2030 target will set the world on course to ending the AIDS epidemic by 2030 in line with the Sustainable Development Goals (1). As of 2020, an estimated 27.5 million people, globally, were receiving antiretroviral therapy (ART) (7). This was an increase from 21.7 million people over the number receiving such treatment in 2017 (6).

Universal Test and Treat (UTT) is a policy in which all HIV infected individuals receive treatment immediately after diagnosis regardless of Cluster of differentiation 4 (CD4) count or disease stage (7). Based on (WHO) modelling, it is predicted that UTT will reduce HIV transmission globally (8). In a "test-and-treat" strategy, individuals are routinely tested for HIV, and those found positive for HIV are put on antiretroviral therapy (ART) immediately, irrespective of their stage of disease, to reduce their plasma viral load and thereby reduce their likelihood of transmitting the infection (9). In line with the WHO recommendations, the Department of Health in South Africa introduced the Universal Test and Treat (UTT) policy in September 2016 (10).

Evidence has shown increase in testing. However, the level of community acceptability of the HIV "test-and-treat" strategy is not known. Furthermore, clinical outcomes on patients and operational feasibility have led to vigorous debate in the global HIV community.

In order to reach the 95-95-95 targets by 2030, it is not only important to test large numbers of people for HIV but to rapidly initiate those found positive onto ART and have their viral load suppressed as the intended outcome (11). Viral load suppression of people living with HIV (PLWHIV) in a large population will lead to reduction of new infections. We evaluated the acceptability, effectiveness and implementation levels of rapid ART initiation in the era of UTT on the patients and healthcare workers as service providers. Through this study we anticipated informing policy makers and government in strengthening the UTT policy implementation processes and reaching the 95-95-95 target. We also aimed at identifying gaps in implementing same day ART initiation which will assist in benchmarking rapid ART initiation processes in other facilities.

1.2 Literature review

The literature review in this thesis is made up of a narrative review and a scoping review. The following sections constitute the narrative review and the scoping review is pasted after the narrative review in the format in which it was published. A section with overall conclusion of the literature review is placed after the scoping review.

Since the introduction of the HIV "Universal Test-and-Treat" (UTT) approach, its clinical rationale, operational feasibility, and effectiveness have become a subject of vigorous debate in the global HIV community (8). Progress has been made globally and locally to reach the 95-95-95 target by Joint United Nations Program on HIV and AIDS (UNAIDS) in pursuit of ending the AIDS pandemic BY 2030 (1). The ART program in South Africa underwent a series of developments to improve access to ART leading to the introduction of the Universal Test and Treat (UTT) strategy (7, 9). The evolving ART program brought about changes to the ART eligibility criteria and timeliness to ART uptake (12). This literature review provides an overview of literature globally and in the South African context on the following: evolving of ART guidelines over the years; Universal Test and Treat strategy; Delayed and early ART initiation in relation to patient outcomes, 95-95-95 strategy, ART adherence, retention to care and burden of rapid ART initiation on health providers.

Evolving of ART initiation guidelines

The first version of ART treatment guidelines became available in 2004 with the primary goal of decreasing HIV-related morbidity and mortality at that time and reduction in HIV incidence as a secondary goal (6) . The guidelines have been broadened through a series of changes over the years with the latest version focusing on reducing incidence of HIV, prolonging life expectancy and improving quality of life of PLHIV among other goals (13).

The CD4+ threshold was raised to <350 cells/μL from the initial <200 cells/μL on the 1st of December 2009. In 2013, a fixed dose combination (FDC) pill made up of tenofovir 300mg, emtricitabine 200mg and efavirenz 600mg was introduced to promote adherence and retention in care (14). In January 2015, the rise in CD4+ threshold to <500 cells/μL came into effect; and finally the Universal Test and Treat (UTT) strategy was introduced in September 2016 (15). All

these efforts increased access to ART and aimed to reduce the burden of disease. Currently 56% of the estimated 7.1 million people living with HIV in the country are receiving ART (16).

Universal Test and Treat Policy (UTT)

The World Health Organisation (WHO) released guidelines recommending all people to be offered ART soon after diagnosis, regardless of CD4 count or clinical staging in 2015 (15). Same day uptake of anti-retroviral therapy (ART) is crucial in ensuring the success of Universal Test and Treat (UTT) approach for preventing HIV transmission in high-prevalence settings (7). This strategy is in accordance with the National Development Plan and the UNAIDS 95-95-95 targets of 2030 (17). Current recommendations for the scale-up of universal ART initiation requires novel studies focusing on individual and healthcare service providers to understand the barriers in resource-limited settings.

In September 2016 Dr Aaron Motsoaledi, Minister of Health in South Africa announced that the UTT in HIV management was to be implemented as per the WHO guidelines (18). Consequently, current South African HIV management guidelines recommend that every person who is HIV positive, irrespective of the CD4 count at the time of testing, should be encouraged to get on ART immediately. Cluster of differentiation 4 (CD4) count was removed as an eligibility criterion for ART initiation. Prevention interventions alone or in combination with other strategies, might significantly decrease HIV incidence. The model suggests that only universal voluntary HIV testing and same day initiation of ART could reduce transmission to the point where elimination might be feasible by 2030 for a generalised epidemic, such as that in South Africa (20).

Strategies of rapid ART initiation

Regular voluntary universal HIV testing followed by same day initiation (SDI) of anti-retroviral therapy (ART) for individuals with a positive diagnosis regardless of CD4 count and clinical staging would diminish HIV incidences in severe epidemics from 20 in 1,000 people to 1 in 1,000 in a period of 10 years (18). This is based to a mathematical model developed by specialists from the WHO predictions (19). The strategy may have public health benefits, including decreasing incidence of tuberculosis and reductions in the transmission of HIV from mother-to-child (20). The model also envisages that there might be a substantial drop of HIV-related morbidity and mortality in resource-limited countries with high HIV epidemics (21).

Delayed and early ART initiation

Due to lack of resources and worries regarding adherence; previously eligible patients went through intensive psychosocial sessions before being initiated into care, which could take weeks to months, but the final decision to treat still depended on the team at the ART centres (22). This is the exact opposite of the new guidelines; where readiness is briefly assessed and patient is initiated into care as soon as possible (18). These changes in policy and eligibility criteria were a result of evidence showing the benefits of starting treatment early (WHO) (21).

One of the most critical concerns about test and treat is whether the long-term benefit of early ART initiation as a prevention measure outweighs the potential risks to the individual of long-term health effects, such as drug toxicities and earlier treatment failure (23). Because rigorously derived data answering these questions are not anticipated for another few years, implementation efforts should first be focused on achieving universal testing and treatment according to current WHO guidelines for the initiation of ART (24). According to WHO there will be an increase in people eligible for treatment from 28 to 37 million worldwide, under the new guidelines (16). Research has shown that intensifying UTT to reach all HIV infected people has its own challenges. In low-and-middle income countries, it is a huge task requiring more human resources than currently available in most healthcare facilities (25). There is need to double the capacity of personnel in the public sector in order to provide services to the increased number of people on ART. Literature shows that there is a need to ensure that drugs are available in sufficient quantities in health facilities to avoid drug shortage (26).

Joint United Nations Programme on HIV/AIDS

UNAIDS indicates that achieving the 2030 milestones will yield numerous major benefits in reducing HIV incidences globally (13). Impressive advances by 2030 in health science, accrued implementation practices, public engagement, advances in human rights and global solidarity have presented a remarkable opportunity to end the AIDS epidemic as a public health threat by 2030 (1). The Fast-Track approach is an agenda for speeding up the pace of ART initiation implementation at the global, regional, country, province, district and local community level (27). It entails setting ambitious goals and quickening the provision of high-impact HIV prevention and treatment services. It involves using novel strategies to expand services in addressing community needs and focusing on the settings as well as populations with the highest HIV burden (11, 28).

Implementing directed, high-impact prevention strategies involving fast-tracked HIV testing, increased early treatment initiation and retention in care together with anti-discrimination programs led to reduced number of adults acquiring HIV infection from 2.1 million in 2010 to fewer than 500 000 in 2020 and fewer than 200 000 in 2030 (1). These interventions may mark the end of the AIDS epidemic as a public health threat by 2030.

Early Treatment initiation as Prevention

Treatment as prevention (or TasP) refers to methods in which HIV treatment can be used to lower the risk of HIV transmission (29). For PLHIV, one of the benefits of taking ARVs is that the drugs can lower the viral load thus making the blood, vaginal fluids, breast milk, and semen unlikely to transmit HIV to negative partners(30).

Despite several studies showing the potential preventative effect of HIV drugs, these benefits are not being realized extensively for several reasons including delayed ART initiation until the disease has progressed due to stigma, discrimination and other human rights violations daunt people from seeking early treatment and compromises their ability to adhere to ART (19). Furthermore, individuals may fail to access test and treat services shortly after being infected, when viral load levels are high, meaning they are most probably going to transmit HIV even if they get treated at a later stage (24). There are concerns that the use of ARVs, at population level, as an HIV prevention measure could lead to a significant increase in levels of HIV drug resistance (HIVDR), due to poor adherence and treatment interruptions (16). Poor health systems, limited access to viral load testing and inadequate resources for more expensive treatments which are characteristic of many low- and middle-income countries, including sub-Saharan Africa, could compromise the benefits of a test and treat strategy.(6) Increasing uptake of HIV testing, offering early treatment and linking people in care decreases population level rates of HIV transmission with treatment now considered as a prevention measure for changing the global response to HIV (31).

The benefits of UTT extend beyond the individual, as a high percentage of viral suppression will result in reduction of disease transmission. Achieving this would be a way-forward to the HIV epidemic in every country but particularly so in resource-limited contexts in sub-Saharan Africa (12). As the ART program expands and guidelines evolve, there is need to invest in evaluating the impact of the policies on individuals, service providers and at population level. With the

inconsistent evidence of benefits of rapid ART initiation on adherence found in previous studies and uncertain impact of policy level changes, it is important to evaluate the effect of changes in ART eligibility criteria on patient clinical outcomes. This has the potential to strengthen the certainty of studies conducted in South Africa to determine the impact of policy changes on rapid ART initiation; but might also highlight hidden gaps in acceptance, adherence, retention in care and clinical outcomes.

Available literature has revealed the different evolution phases of ART initiation. Additionally, the need for implementation of policies that advocate for rapid ART initiation in all health facilities has also been identified. To my knowledge there is limited published evidence on acceptability and effectiveness of same day ART initiation for both patients and healthcare providers; and the undefined impact of policy level changes on clinical outcomes. This has the potential to provide strategies in strengthening the UTT policy especially same day ART initiation and also highlight gaps in determinants of SDI and delayed ART initiators, retention in care, clinical outcomes for both early and delayed ART initiators and healthcare provider's perspective.

Conclusion

The ART initiation program is transforming the overall HIV prevention, treatment and care strategy globally. Universal Test and Treat (UTT) represents a combination prevention tool comprising of testing, linkage to care and early initiation to treatment. Swift expansion of HIV programs without assuring acceptability and impact from the recipients can undermine their effectiveness, waste resources and contribute to negative public health outcomes. Rapid uptake of ART with religious retention in care and adherence to achieve high rates of viral suppression, could lead to steep reductions in HIV incidence and potentially to the long-term elimination of HIV as a public health problem.

In order to fully understand the factors affecting ART initiation policy implementation, we assessed the facilitators, barriers and country level timely implementation of ART initiation changes in SSA. This work has been published and is presented here as published.

Sabina M. Govere, Moses J. Chimbari. 2020.The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa: A scoping review. Southern African Journal of HIV Medicine | Vol 21, No 1 | a1103

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa: A scoping review

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Dates:
Received: 06 May 2020
Accepted: 26 July 2020
Published: 30 Sept. 2020

How to cite this article:
Govere SM, Chimbari MJ. The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa: A scoping review. S Afr J HIV Med. 2020;21(1), a1103. https://doi.org/10.4102/sajhivmed.v21i1.1103

Background: Despite past and present global interventions, the human immunodeficiency virus (HIV) pandemic remains a public health problem in low- and middle-income countries (LMICs). The World Health Organization (WHO) has assisted these countries by providing antiretroviral therapy (ART) policies for adoption and adaptation to local needs.

Objectives: This article describes the response of countries in sub-Saharan Africa (SSA), to the WHO's changing CD4-threshold ART-initiation recommendations of the past two decades.

Methods: Relevant articles published in international peer-reviewed journals were accessed via the following search engines: PubMed, Google Scholar, Cochrane, Embase and EBSCOhost. The study's inclusion criteria were articles published in the English language between 2000 and 2019 that highlighted changes to the CD4 ART-initiation threshold and that focused on the WHO's 'commencement of ART' policy guidelines. Sixteen studies (n = 16) from SSA were identified and included in this review: four are cross-sectional, four deal with cost-effectiveness, four are retrospective, one is a randomised trial and three are observational studies. Only studies conducted in SSA were assessed.

Results: Four themes emerged: (1) adoption of the WHO CD4-ART-initiation policy by SSA countries, (2) timely implementation of the changing guideline initiation policy in the region, (3) barriers and facilitators encountered in the implementation of the changing guidelines and (4) description of similarities in policy implementation at country level from 2002 to 2019. Regional studies – cross-sectional, observational, retrospective, cost-effectiveness and randomised have described greater access to ART in SSA. However, barriers remain. The most common barriers to the timely implementation of 'new' ART-initiation guidelines were economic constraints, drug stock-outs, delays in obtaining baseline blood-test results and staff shortages.

Conclusion: Although countries in SSA have adopted the WHO-ART-CD4 initiation-threshold policy guidelines, implementation has seldom occurred in a timely manner. Barriers have been identified. Whilst a small number of countries have implemented recommendations promptly, for many, the barriers still require to be overcome.

Keywords: ART initiation; WHO-ART guidelines adoption; implementation of ART guidelines in sub-Saharan Africa; CD4; human immunodeficiency virus.

Background

The first cases of the acquired immunodeficiency syndrome (AIDS) were reported in 1981. Since then, infection with human immunodeficiency virus (HIV) has spread globally and caused an estimated 74.9 million infections and 32 million AIDS-related illnesses.[1] In its first 15 years no treatment could control the infection or halt its spread.[2] By 2018, the African region was home to approximately 25.7 million people living with HIV (PLWH)[1] and in that year alone, Africa experienced approximately 1.1 million new infections.[1] Almost two-thirds of all new global infections occur in sub-Saharan Africa (SSA).[1]

The World Health Organization's (WHO's) antiretroviral therapy (ART) initiation-guidelines have changed substantially over the last two decades.[2] The guidelines were first published in 2002.[3] These (2002/2003) recommended starting ART in those with AIDS-related conditions and/or at a CD4 of ≤ 200 cells/mm. The available treatment at that time was expensive and toxic. Delaying ART until the CD4 reached levels < 200 c/mm^3 was intended to minimise these drawbacks.[4] Continued deaths from AIDS and success with ART prompted a CD4 increase in 2006

200 to 350 cells/mm³. In addition, all pregnant women and persons with Stage 3 and 4 infection were offered ART.[3] In 2010, the threshold was raised to CD4 < 350 c/mm³ for all irrespective of clinical stage.[4,5] By June 2013, the threshold was further increased to CD4 < 500/cells/mm³ for all children > 5 years and adults irrespective of stage/symptoms.[6] In 2015, the WHO and numerous international organisations removed the CD4 threshold and recommended ART to all regardless of CD4 cell count and clinical stage.[7] Data from two highly influential randomised controlled clinical trials, the START and TEMPRANO studies, underpinned this decision. Both demonstrated survival advantage to those on ART irrespective of clinical stage or CD4 count.[8,9] This led to the introduction by all international agencies, including the WHO, of the policy of 'universal test and treat (UTT)'. The WHO estimates that if these recommendations are adopted globally, 21 million deaths and 28 million new infections could be prevented by 2030.[10]

The rate at which countries have aligned their national ART programmes and implemented WHO guidelines since 2002 has varied. Most SSA countries took ± 2 years to implement the WHO's 2010 ART guidelines.[5] From December 2015 to May 2017, Rwanda, Kenya, Uganda, Botswana, Malawi, Zimbabwe and South Africa revised national ART eligibility guidelines to align with the WHO's 2015 guidelines.[11] On average, this integration took 12 months (range, 6–23 months).[11] The implementation of the WHO guidelines in resource-constrained countries is complex. Consequently, it has not always been possible to implement the guidelines timeously where ART is most needed and where access to health services is limited.[2] In this review, we sought to determine how different SSA countries adapted to the WHO's ART-initiating CD4-threshold changes over time and how WHO guidelines have impacted ART in the region.

Methods

Search strategy and selection criteria

We carried out a systematic electronic literature search on PubMed, Google Scholar, Cochrane, Embase and EBSCO host for the period, 2000–2019 (Figure 1). The databases were selected based on our inclusion criteria and the availability of free full-text articles and papers. In this review, we used the preferred reporting items for systematic reviews and meta-analysis (PRISMA) as described by Moher et al., to identify an evidence-based dataset and to provide transparency in the selection process of the articles.[12]

The search was based on the combination of the following terms and Boolean operators: WHO-ART guidelines or ART-initiation guidelines and changes in CD4-initiation guidelines and implementation of WHO guidelines or adoption of WHO-ART guidelines. We also applied a manual country filter to limit our search to SSA. Articles published in a language other than English and articles focusing on ART regimen-change were excluded. The study included articles that focused on CD4-threshold changes and were published between 2000 and 2019. The following articles were not included: duplicates, articles not centered on the WHO and ART initiation guidelines or their adoption and implementation. Exclusion was based on the screening of the title and abstract.

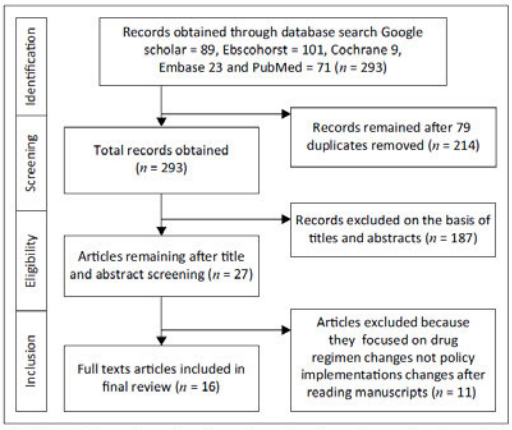

FIGURE 1: Preferred reporting items for systematic reviews and meta-analysis flow diagram showing the process of selecting articles included in the review.

The search process is illustrated in Figure 1. Seventy-nine (79) duplicate articles were removed, which were identical in Google Scholar and PubMed. Fewer articles dealt with the topic in Cochrane and Embase. The articles in PubMed were more detailed, easier to search and free to access. We also excluded 187 articles because they did not specifically address implementation based on CD4-threshold changes. Another 11 were excluded because they focused on only regimen change. Only 16 articles remained. These covered quantitative and qualitative synthesis of how SSA countries adopted the WHO and ART initiation guidelines between 2000 and 2019 and its impact on the management of HIV.

Data extraction and synthesis

The following information was extracted from selected studies using a template: publication details, country of study, objective(s) of the study, study design, summary of findings and theme (Table 1). Two review authors independently assessed the eligibility of the studies identified in the search. Articles with different study designs and objectives were selected to reduce the risk of bias. We used different high-impact databases to search for articles and global authors. The study designs were divided into five groups: cross sectional, cost-effectiveness, retrospective, randomised trial and observational studies. We did not subject the reviewed articles to this quality process because this is a scoping review. For synthesis, extracted information was grouped into themes derived from the articles in line with the review objectives and different study designs. The themes identified were: how different SSA countries adopted WHO and ART initiation policy guidelines at country level, timely implementation levels of the policies by different SSA

TABLE 1: Summary of studies.

Author and year	Guidelines year	Theme identified	Study objectives	Type of study	Study focus	Study location	Major outcomes of study	Strength/weakness of design
Ambia et al.[13] 2017 Paper 1	2013	Timely implementation of WHO and ART initiation policy guidelines at country level. Adoption of WHO and ART initiation policy guidelines at country level Barriers and facilitators to WHO-policy implementation	The study assessed the uptake of the 2013 WHO recommendations related to the eligibility threshold for ART-initiation, the availability of first-line ART- regimens, and recommendations to improve retention.	Cross-sectional survey	Inclusion of the 2013 WHO HIV treatment recommendations	Kenya, Malawi, South Africa, Tanzania, Uganda and Zimbabwe	Although expansion of ART access was explicitly stated in all countries' policies, most lacked policies that enhanced retention. The proportion of facilities that initiated ART at CD4 counts of 500 or less cells/mm³ increased from 12% to 68%. Treatment stock-outs affected increase in ART enrolment. Facilities initiating patients onto 2013 WHO recommended ART-regimen increased from 42% to 87%.	To their knowledge this was the first study to use two sequential cross-sectional surveys to compare implementation of policies on ART access and retention across six African countries with a generalised HIV epidemic. The conceptual framework that underpinned this study was developed prior to the first facility survey round and was based on a review of literature and policy in circulation up to 2015. Whilst comprehensive at the time, the provision of HIV care and treatment is a rapidly evolving field and it is possible that additional indicators would now be included.
Burrage et al.[14] 2018 Paper 2	2013	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at country level Barriers and facilitators to WHO-policy implementation	To understand the lag between guideline development and implementation, as well as the ART coverage gap, CDC assessed national HIV-guidelines and analysed Joint United Nations Programme on HIV and AIDS. Timeliness of WHO-ART guideline adoption varied by country.	Cross-sectional survey	The study analysed the levels of WHO guidelines implementation of ART initiation and how countries timeously changed and adopted country guidelines.	Angola, Botswana, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe	This report highlights the continuing gaps in ART coverage in PEPFAR-supported SSA countries with high HIV burden, despite expanded ART eligibility criteria. SSA countries are failing to implement WHO guidelines timeously. As of 2015, all 20 PEPFAR-supported sub-Saharan African countries included in this analysis had adopted the 2013 WHO guidelines for ART eligibility. However, adoption of the 2013 guidelines in some countries did not occur until 2 years later, that is, in 2015.	A robust data collection methodology was employed using self-reports and medical charts from both patients and healthcare workers. The limitation of the study was that it was conducted at only two treatment centres, hence the results cannot be generalised to the entire country, although we believe patients attending these two clinics are typical of those attending public health clinics throughout South Africa.
Plazy et al.[15] 2015 Paper 3	2010 and 2013	Adoption of WHO and ART initiation policy guidelines at country level Timely implementation of WHO and ART initiation policy guidelines at country level	To describe the changes in ART initiation based on the changes on CD4 threshold changes.	Cross-sectional study.	The study aimed at describing ART initiation percentages in a large HIV programme according to the temporal changes of country ART eligibility guidelines from 2007 to 2012.	Rural KwaZulu Natal, South Africa	As temporal changes of guidelines were occurring, percentages of ART initiations significantly increased in newly ART eligible people and did not decrease in those with very low CD4 counts. It will be crucial to continue to verify the evolution of these percentages of ART initiations with future recommendations reaching near-to-universal access to ART, to ensure that individuals most in need of ART receive it on time.	The study was based on data of a large HIV treatment and care programme allowing unbiased findings and giving an accurate representation of the entire population. Some individuals may have initiated ART outside the programme, which may have led to an underestimation of the ART initiation percentages. However, this bias is likely to be limited as the Hlabisa HIV programme is decentralised in primary healthcare clinics with relatively easy access and this area is rural and poor, making it difficult for people to access ART somewhere else. Another limitation is that amongst included participants, some people may have failed to return to the clinic to receive their CD4 count result after HIV testing and thus were unaware of their status regarding ART eligibility, however we cannot provide a precise figure as this information was not collected in the database.

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TABLE 1 (Continues...): Summary of studies.

Author and year	Guidelines year	Theme identified	Study objectives	Type of study	Study focus	Study location	Major outcomes of study	Strength/weakness of design
Hsieh et al.[6] 2014 Paper 4	2013	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The study assessed adaptation and implementation of the 2013 WHO guidelines at country level and suggests how to optimise community engagement to inform future guidelines.	Cross-sectional e-survey and e-forum discussion, FGDs	The study focused on evaluating community and HCW values and preferences on key topics to inform the development of the 2013 WHO consolidated guidelines for antiretroviral therapy in low- and middle-income countries.	Malawi and Uganda.	The findings of these community consultations have reinforced the importance of community representation, involvement, and participation in normative guidelines development. For the effective scale-up of ART programmes, it is critical to have a nuanced appreciation for the different ways in which people interact with certain services, and the role of communities and civil society in service delivery.	The data were collected from various field experts, comprising HIV clinicians, researchers, country HIV programme managers, guideline methodologists, partners from the United Nations or other development agencies and nominated representatives of civil society and/or networks of people living with HIV (selected on the basis of four criteria: technical knowledge, constituency and regional representation, previous experience with guidelines development). We ensured a balance of representation by country and sex, however, there were more females from Uganda.
Song et al.[16] 2018 Paper 5	2015	Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The study assessed differences in clinical benefits between individuals starting treatment at CD4 counts ≥ 500 cells/mm^3 (early initiation) as compared with < 500 cells/mm^3 (deferred initiation).	Observational Study	Clinical outcomes and benefits of early ART initiation at CD4 cell count 500 and below.	South Africa, Zambia, Angola, Kenya, Uganda, Lesotho and Nigeria	Mortality risk and risk for AIDS appear to be reduced amongst people living with HIV with early initiation of ART, based on current WHO guidelines, as compared with those with deferred initiation of ART (< 500 cells/mm^3).	The study used a large sample size from all the countries and tried to identify facilities with similar structures and resources. Observational studies inherently are limited because they may provide a relatively lower quality of evidence than randomised controlled clinical trials. Furthermore, it is possible that the data density such as frequency of follow-up visits and clinical assessment between these periods may have affected our results.
Beck et al.[3] 2006 Paper 6	2002	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level	The study investigated the existence of national ART guidelines in SSA-countries by the WHO and compared their content with the 2002 WHO-ART guidelines.	Observational Study	Questionnaires were sent to countries identified by WHO as requiring special attention for developing HIV-therapeutic and preventive health services, because of their high HIV-burden or because of their strategic importance in the region in terms of being able to scale-up HIV-therapeutic and preventive health services.	43 Sub-Saharan African countries	Most countries had developed national ART guidelines as part of a comprehensive national HIV programme. Concordance with WHO recommend-ations were strong on starting the first-line ART regimens and routine monitoring but weaker for second-line recommendations.	This analysis was limited to 43 WHO '3 by 5' focus countries and did not involve all middle- and lower-income countries currently scaling up HIV treatment and care. This evaluation was focused on the development of national guidelines based on WHO recommendations and did not consider their effective implementation and use of the guidelines at health facility level, and substantive differences may well exist between the development of national guidelines and programme implementation resulting in actual clinical practice.
Duber et al.[17] 2015 Paper 7	2013	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO policy implementation	The study examined if WHO guidelines were adopted into practice in Kenya, Uganda and Zambia and the pace at which they were adopted at the health-facility level.	Observational analysis.	The level at which countries in regions of high HIV and AIDS burden, including Kenya, Uganda and Zambia, adopted WHO guidelines into their national guidelines	Kenya, Uganda and Zambia.	Patient-level data from a wide range of ART facilities in Kenya, Uganda and Zambia supports the assertion that national HIV programmes have moved quickly to adopt WHO-ART first-line treatment recommendations into clinical practice.	This study benefits from a large and diverse sample in terms of time, geography and facility type, but it is not without limitations. Despite efforts to sample from all patient charts, facilities use different practices in storing charts of dead or defaulted patients, and this may have differentially affected the sample of charts across facilities. Electronic data records were from a small number of facilities, whilst for the majority of facilities, chart extractions were performed by hand; therefore, it is possible that the quality of the data included differs for these facilities. However, a separate analysis of these facilities finds that they are within the expected range of prescribing patterns. Furthermore, as charts were weighted based on the size of the ART programme in the year of ART initiation, we do not expect that the facilities with electronic records had undue influence on our overall descriptive findings.

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TABLE 1 (Continues...): Summary of studies.

Author and year	Guidelines year	Theme identified	Study objectives	Type of study	Study focus	Study location	Major outcomes of study	Strength/weakness of design
Hontelez et al.[18] 2011 Paper 8	2010	Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	Quantifying the potential net costs and life-years saved because of the 2010 WHO guidelines compared with treating patients at ≤ 200 cells/μL.	Quantification and costing model	The study aimed at estimating the impact of fully adopting the new WHO guidelines on HIV-epidemic dynamics and associated costs.	Hlabisa sub- district of UMkhanyakude in KZN, South Africa	The findings show that starting ART at CD4 ≤ 350 recommended by WHO will lead to an increase in programme costs, but significantly more patients on ART. Compared with ART initiation at CD4 ≤ 200 initiating ART according to the new WHO guidelines will result in a cumulative net cost-saving starting around 2026.	The baseline predictions methodology concerning the Hlablisa sub-district could have been too optimistic for South Africa as a whole, where dropout rates are higher, health-seeking behaviour is less. However, the sensitivity analysis shows that these differences have a limited impact on the timing of the break-even point and the number of life-years saved. This can be explained by the fact that we compare two scenarios (ART at ≤ 200 cells/μL versus ≤ 350 cells/μL), which are both largely affected in the same way, so that the comparison between the two remains relatively unchanged.
Kuznik et al.[7] 2016 Paper 9	2015	Timely implementation of WHO and ART initiation policy guidelines at country level. Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The study evaluated the cost-effectiveness of immediate versus deferred ART- initiation amongst patients with CD4 cell counts exceeding 500 cells/mm^3 in four resource-limited countries according to the 2015 WHO-ART recommendations.	Cost-effectiveness analysis	The study focused on evaluating if treatment for all patients with HIV would pose an additional strain for national ART programmes, particularly amongst those that were already struggling to meet treatment targets based on the previous CD4+ cell count threshold of 500 cells/mm^3 proposed by the WHO.	South Africa, Nigeria and Uganda	In the studied countries, immediate versus deferred initiation of ART in HIV-positive patients with CD4+ cell counts above 500 cells/mm^3 is cost-effective and likely cost saving. The findings support the recommendation for resource-limited countries to provide ART for all HIV-infected patients even though there were delays in policy implementation.	The 5-year Markov model used in the study allowed annual cycles to be compared including patients at different CD4 count threshold, which resulted in robust findings to changes in model parameters as observed in our one-way sensitivity analyses, and simultaneous variation in multiple parameters as observed in probabilistic sensitivity analyses. The START trial that serves as the clinical basis for our cost-effectiveness model was largely conducted outside of SSA and more than half of enrolled patients were MSM, a mode of transmission that is less commonly reported in SSA.
Ross et al.[19] 2014 Paper 10	2013	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The aim of the study was to quantify the impact of revised ART initiation thresholds on the outcome of cluster-randomised treatment-as-prevention trials, and assess how changes in trial characteristics could be used to augment the observed incidence reduction in the context of policy change.	Cost-Effectiveness and HIV-transmission analysis models	The study focused on assessing the incidence reduction using the revised (CD4 < 500 c/mm^3) and prior (CD4 < 350 c/mm^3) control ART initiation thresholds. In addition, it also evaluated changes to trial characteristics that could bolster the incidence reduction.	KwaZulu Natal, South Africa	Implementing the 2013 WHO HIV-treatment threshold could substantially improve the incidence reduction in HIV-population as seen in prevention trials. The feasibility of HIV-population prevention trials should be reassessed as implementation of treatment guidelines evolves.	The cross-cluster contamination method that was used proved to be highly influential on trial outcomes. The model of HIV transmission used was neither age- nor sex-stratified and did not explicitly account for behavioural factors such as concurrent sexual partnerships or sexual networks. Likewise, sex differences in HIV testing frequency and ART uptake were not modelled.

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TABLE 1 (Continues...): Summary of studies.

Author and year	Guidelines year	Theme identified	Study objectives	Type of study	Study focus	Study location	Major outcomes of study	Strength/weakness of design
Walensky et al.[5] 2010 Paper 11	2010	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The study aimed to answer the question whether countries should begin by replacing stavudine with tenofovir or by making CD4 count monitoring universally available as recommended by the 2010 WHO guidelines. Use of a model-based analysis with data from South Africa to project the clinical and economic outcomes of alternative stepwise implementation scenarios towards the 2010 WHO and ART guidelines	Cost-effectiveness and survival analysis model	The article considers what to do first in resource-limited settings where immediate implementation of all the 2010 WHO recommendations is not feasible considering that many countries in SSA were still struggling to implement 2006 guidelines.	South Africa	In settings where immediate implementation of all the new WHO treatment guidelines is not feasible, ART initiation at CD4 < 350 cells/μL provides the greatest short- and long-term survival advantage and is highly cost-effective, however considering the high HIV-incidence and prevalence in South Africa meeting the targets timely would be a challenge. Limited infra-structure in implementing the 2010 guidelines was a challenge.	The article only focused on one aspect of mathematical models and ignored other aspects, which might influence cost implications. The study also used a simulation model combining clinical and cost data for HIV treatment into this model and then used it to project survival and costs in a hypothetical group of South African HIV-positive patients. This strengthened the findings of the study because simulation provides a unique opportunity to highly control the environment, scenario and other features that are often unpredictable and inconsistent in real-life clinical care.
Stanecki et al.[29] 2010 Paper 12	2006 and 2010	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at country level Barriers and facilitators to WHO-policy implementation	The study estimated the number of adults (age ≥ 15 years) in need of ART from 1990 through 2009 based on the 2006 WHO guidelines and, secondly, estimated the number of adults (age ≥ 15 years) eligible for ART based on the revised 2010 WHO guidelines for the same time period in low- and middle-income countries, with a primary focus on SSA discussing the implication of these revisions	Retrospective study. Time series estimates of ART-initiation models	The ART need estimates based on ART-eligibility criteria promoted by the 2010 WHO guidelines were compared with the need estimates based on the 2006 WHO guidelines.	Botswana Cameroon Central African Republic Kenya Lesotho Malawi Mozambique South Africa Swaziland Uganda United Republic of Tanzania Zambia Zimbabwe	When adopting the new recommendations, countries failed to adapt their planning process to accelerate access to life-saving drugs to those in need. These recommendations have a significant impact on resource needs as countries in SSA struggle to implement WHO policies on time. The number of people in low- and middle-income countries eligible for ART under the revised 2006 WHO guidelines was 10.1 million compared with the estimated 14.6 million people in need under the 2010 guidelines	The study used multicountries to ensure high quality evidence from experts and multiple comparison of various national guidelines. Whilst Spectrum work well for countries where survey-derived data constitute the bulk of the surveillance data, they are not well adapted for countries that rely mostly on HIV and AIDS case reporting for HIV surveillance.
Labhardt et al.[21] 2012 Paper 13	2006 and 2010	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO policy implementation	The study compared the rate of adoption of the new guidelines and substitution of first-line drugs by health centres (HC) and hospitals in two catchment areas in rural Lesotho.	Retrospective cohort analysis	The study aimed at comparing nurse-based ART initiation at health centres in terms of adherence to treatment guidelines after the introduction of the 2006 guidelines and number of drug substitutions because of side effects.	Lesotho	Health centres took longer to adopt the new guidelines and substituted drugs less frequently because of limited knowledge on policy-change implementation Decentralised ART programmes need close support, supervision and mentoring to absorb new guidelines and to adhere to them.	It is a retrospective analysis, patients have not been randomly assigned to health centres or hospitals. This results in two cohorts with quite different baseline characteristics that may interfere with the assessed outcome variables. However, in the methodology patients were stratified according to the type of the facility where they received ART: health centres and hospitals. Analyses run, are adjusted for all baseline characteristics and the results remained significant. However, there might be other confounders that have not been assessed.

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TABLE 1 (Continues...): Summary of studies.

Author and year	Guidelines year	Theme identified	Study objectives	Type of study	Study focus	Study location	Major outcomes of study	Strength/weakness of design
Teasdale et al.[22] 2015 Paper 14	2006 and 2010	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO policy implementation	Determine time to ART initiation amongst patients eligible at enrollment compared with those ineligible or of indeterminate eligibility who become eligible during follow-up	Retrospective study	The study examined time to ART eligibility amongst adult patients (≥ 15 years of age) and time to ART initiation amongst eligible patients receiving care at health facilities in Rwanda from 2005 to 2010 according to WHO guidelines.	Rwanda	There were higher rates of ART initiation within 3 months amongst patients who were ART eligible at enrollment. From 2006 to 2011, earlier initiation of ART after eligibility was observed likely reflecting improved programme quality. The Rwanda National HIV Care and Treatment Programme have achieved significant success in scaling up ART with 94% of eligible patients receiving treatment in 2012. Rwanda was also one of the first countries in SSA to adopt a higher CD4+ threshold for ART eligibility, instituting ART initiation at CD4+ ≤ 350 by July of 2007 proving benefits of timeous ART initiation.	The strengths of this study include the large and representative cohort; the 31 033 HIV-infected ART-naive adults included in this analysis represent 24% of all adult patients enrolled in care in Rwanda between 2005 and 2010. Patients in the analysis came from 41 different health facilities ranging in size from primary health clinics to large district hospitals and were located in both rural and urban areas. The use of routinely collected data from HIV care and treatment programmes is both an asset and limitation of this analysis. Although highly representative of actual care in Rwanda, the data do not include variables of interest, such as viral load and patient demographic characteristics that might be important predictors of ART initiation, such as distance of residence from health facility.
Konings et al.[23] 2012 Paper 15	2010	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at country level Barriers and facilitators to WHO-policy implementation	The study assessed the implications of implementing the WHO's 2010 guidelines for ART initiation in adults and adolescents with HIV-infection compared with the earlier threshold.	Retrospective and prospective medical chart reviews	Study estimated the total number of patients who would need ART if Ethiopia adopted the 2010 guidelines, the number of patients needing ART based on current guidelines were added to the number of asymptomatic patients enrolled in pre-ART with a CD4+ count > 200 but ≤ 350 cells/mm³.	Addis Ababa (Ethiopia)	Without concurrent increases in funding and governmental support, it will not be possible to scale up ART to accommodate the increased patient demand in Ethiopia. These increased costs are not currently affordable for Ethiopia, which decided to continue observing the 2006 ART guidelines. Whilst the 2010 revision is sound in principle and value, resources in Ethiopia are not enough to absorb the ensuing increased demand for existing services. Findings proved that there were shortages in staff to initiate ART because of increased numbers of eligible individuals.	Nineteen health centres were used as research sites offering a large representative sample of patients on ART in health centres in Ethiopia. Some of the medical charts had missing information affecting the quality of collecting data in some files.
Walsh et al.[24] 2017 Paper 16	2015	Timely implementation of WHO and ART initiation policy guidelines at country level Adoption of WHO and ART initiation policy guidelines at national level Barriers and facilitators to WHO-policy implementation	The study was designed to determine the feasibility, acceptability, affordability and scalability of offering early antiretroviral treatment to all HIV-positive individuals in Swaziland's public health system based on the WHO 2015 ART initiation guidelines	Prospective 3-year stepped-wedge randomised control study	The study measured how eligible individuals accepted immediate ART initiation, levels of drug stock out, staff preparedness on implementing UTT, retention and viral suppression patient. They also measured cost per patient per year.	Swaziland	The economic evaluation proved to be a burden on Swaziland's public sector health system with scaling up numbers on early ART initiation. There were continuous drug shortages in most facilities, which resulted in delayed initiations.	The study was a randomised control study, which used both quantitative and qualitative methods resulting in high-impact evidence.

ART, antiretroviral therapy; CDC, Centre for Disease Control and Prevention; FGDs, focus group discussions; HCW, healthcare workers; KZN, KwaZulu Natal; SSA, Sub-Saharan Africa; UTT, universal test and treat; WHO, World Health Organization.

countries, the barriers and facilitators to WHO and ART initiation policy adoption in SSA and the similarities in country characteristics in policy implementation in different SSA countries.

Ethical consideration

Ethical approval was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Committee (UKZN BREC, reference number: BREC/00000819/2019).

Results

Overview of selected studies

We reviewed 16 studies from an initial collection of 293 articles in Google Scholar, PubMed, Cochrane, Embase and EBSCOhost (Figure 1). We only reviewed studies that examined how different SSA countries adopted changes in WHO and ART initiation guidelines based on CD4 threshold and how the guidelines have impacted ART programmes in SSA. The following four themes were identified from the 16 papers: (1) Adoption of WHO and ART initiation policy guidelines at country level in SSA, (2) timely implementation of WHO and ART initiation policy guidelines at country level, (3) barriers and facilitators to WHO policy implementation in SSA and (4) characteristics at country level.

Of the 16 reviewed articles 4 (articles 4, 13, 14 and 16) addressed all 4 themes, 8 articles addressed 3 themes (articles 1, 2, 7, 9, 10, 11, 12 and 15) and 4 articles (articles 2, 5, 6 and 8) addressed only 2 themes. The theme of the adoption of the WHO-ART initiation guidelines at country level was dominant in all articles.

Theme 1: Adoption of World Health Organization antiretroviral therapy initiation policy guidelines at country level in sub-Saharan Africa

The results confirm that all the countries in SSA that are part of this review have adopted the WHO and ART initiation guidelines since 2002. Hsieh et al. reported that between July 2013 and July 2015, seven national policy documents incorporating the 2013 WHO guidelines were developed in Kenya, Malawi, Tanzania, Uganda, Zimbabwe and two in South Africa.[6] This was further supported by Ross et al. who found that SSA countries had some national explicit policies that targeted increasing ART access in line with the WHO 2013 guidelines on ART.[19] In his study, Hsieh et al. indicated that community consultations are crucial if policies are to be effectively implemented.[6] Labhardt et al. found that health centres in Lesotho took longer to adopt the new guidelines because of limited knowledge of WHO policy changes.[21]

Rwanda implemented the 2006, 2010, 2013 and 2015 WHO and ART initiation guidelines in a timely manner, that is, on an average within 6 months of international release.[25] Part of Rwanda's success is attributed to the cooperation of government and non-governmental service providers.

Theme 2: The timely implementation of World Health Organization antiretroviral therapy initiation policy guidelines at country level

Teasdale et al. describe high rates of early – within 3 months – ART initiation amongst ART-eligible Rwandan patients. Indeed, by 2012, the Rwanda National HIV Care and Treatment Programme had managed to initiate 94% of eligible PLWH on ART in line with the 2006 and 2010 WHO guidelines. Rwanda was also one of the first countries in SSA to implement the higher CD4+ initiation threshold for ART eligibility.[22] In an observational study in Kenya, Uganda and Zambia, Duber et al. indicate that national HIV programmes have implemented WHO 2013 guidelines at health facility level.[17] These findings suggest that several countries have moved quickly to align with the WHO.

However, in a study conducted in 15 SSA countries, facilities were slow to align with the WHO's 2006 and 2010 guidelines. They experienced delays in the actual implementation and expanding access to ART.[20] Burrage et al. noted that few Tanzanians were initiated on ART at CD4 counts of $\leq 500/\mu L$ in 2015 despite the country's earlier adoption of the 2013 WHO guidelines. As a result, only 64% of eligible PLWH were initiated on treatment.[14] Stanecki et al. recorded that the number of PLWH eligible for ART in low- and middle-income countries (LMICs) under the revised 2010 WHO guidelines was 14.6 million at a time when only an estimated 10.1 million people actually received ART.[20] As of 2015, all 20 SSA-supported U.S. President's Emergency Plan for AIDS Relief (PEPFAR) countries had adopted the 2013 WHO guidelines for ART eligibility. Nevertheless, alignment and implementation with national guidelines took at least 2 years in all 20 countries.[14] This demonstrates the failure of SSA countries to align and implement country guidelines timeously with the WHO.

Theme 3: Barriers to and facilitators of antiretroviral therapy initiation policy implementation

Fourteen studies examined the barriers to and facilitators of ART-initiation policy implementation in SSA. Ambia et al. reported a significant increase in ART initiations, from 42% to 87%, in some facilities in the urban centres of Kenya, Malawi, South Africa (SA), Tanzania, Uganda and Zimbabwe.[13] Healthcare workers' (HCWs) attitudes were found to be both a barrier and a facilitator of implementation at the facility level. Teasdale et al. reported that positive learning attitudes from HCWs were found to be an enabler for WHO policy adoption in Rwanda. Furthermore, the Rwandan government's health department assembled a task team to ensure that the entire country was supported in the implementation of the revised guidelines.[22] Hsieh et al. found, however, that HCWs in Malawi and Uganda were slow to implement the 2013 WHO guidelines because their communities 'had not been consulted and hence lacked understanding' of the guidelines.[6] Similarly, Labhardt et al., in Lesotho found that HCWs especially in rural facilities, took longer to adopt and implement the 2006 and 2010 guidelines because of limited training.[21] There was little support, mentoring and supervision and overall, less

knowledge of health policy. The trainings were conducted in the cities. Travel from remote areas proved a challenge as facilities would have been left without clinical staff. The authors make the point that the government did not make sufficient effort to deploy trainers in the remote areas where more people needed the services.

The cost-effectiveness articles namely 8, 9, 10 and 11, in Table 1, indicate that economic constraints hindered various countries from implementing guidelines timeously. An Ethiopian study by Konings et al., revealed major financial constraints for the state even before ART services could be expanded as per the 2013 WHO guidelines. The government continued implementing the 2006 ART guidelines for more than a year after the 2010 guidelines were released because their financial capacity could not absorb the increased demand.[23] Hontelez et al., in rural SA, reported that changes to the 2010 WHO guidelines led to an increase in programme costs requiring the SA government to add at least ZAR 3 billion to the healthcare budget to allow for an increase in personnel and medication.[18]

Most facilities in SSA failed to fully implement the policy guidelines on time because of limited ARV-stock.[13] In a study from Swaziland, ARV-shortages delayed the implementation of the 2015 WHO guidelines on UTT. The available stock was not sufficient for those already on treatment.[24] Walensky et al. reported that delays in obtaining baseline blood-test results delayed the SA-implementation of ART-guidelines in 2010. The 2-week turnaround time resulted in people not returning for results. Laboratory services were not readily accessible in rural areas and specimen-transport-delays resulted in the samples clotting and being discarded.[5] Staff shortages in Ethiopia were identified as a barrier to implementation of the 2010 ART guidelines. In some facilities, there was neither a doctor nor a qualified nurse trained to initiate ART and PLWH had to be referred to distant hospitals.[23]

Theme 4: Characteristics at country level

World Health Organization guidelines are based on the best available scientific evidence and are directed to the ART-needs of LMICs. International guidelines unfortunately cannot speak to the individual economic and social realities of individual SSA countries. Of the 20 countries addressed in this review, there are nonetheless considerable similarities such as strained healthcare systems, structural and operational barriers and the need of cost-cutting measures to support healthcare systems. With the largest ART-programme on the continent, SA also carries the largest ART-related financial burden.[8] Nigeria and Uganda have similar challenges.[7] Funding-cuts from international donors exacerbate these challenges.[12] Burrage et al. had noted that despite the expanded ART eligibility criteria, 20 PEPFAR-supported SSA countries with a high HIV-burden, had funding cuts before the release of the 2013 guidelines. This created continuing regional gaps in ART coverage.[14] Drug-stock outs have been reported from Kenya, Malawi, SA, Tanzania, Uganda and Zimbabwe.[13] Walsh et al. reported a similar challenge in Swaziland.[24] This review has highlighted delays in aligning and implementing the WHO-ART-initiation guidelines in 20 SSA countries.[14] This suggests a need for greater guidance with regard to strategy and implementation in the communities of SSA.

Discussion

This review provides detailed information regarding WHO and ART initiation guidelines on CD4 count threshold changes and adoption of the guidelines in SSA. There were some variations in study designs, however, all the articles focused on CD4 ART-initiation changes in the WHO guidelines. The findings indicate that delays in adoption and implementation were frequent and widespread throughout SSA. We employed a thematic analysis and identified four crucial themes that were in all the articles. Several barriers to implementing the guidelines were identified. These include costs related to providing ART to eligible individuals, the shortage of staff and drugs in healthcare facilities and limited training of staff when guidelines were changed.

Our findings are consistent with those of Pell et al., who reported that the implementation of the 2015 guidelines took > 12 months to be adopted in all SSA countries after their official release.[1]

Mikkelsen et al. noted that in an effort to contain the demand for ART, most African countries were forced to defer treatment-initiation to those eligible PLWH who were well.[26] Whilst policy is well intentioned, it is informed only by epidemiological data. The state of the healthcare system and sociocultural factors are critical for controlling and ending the epidemic. Our analysis of the financial, infrastructural, human resources for health and governance landscape in SSA, the feasibility associated with costs of implementing a UTT programme indicates health systems and societal perceptions related shortcomings. Although with clinical benefits, increasing the CD4 threshold has implications that reverberate across sectors: it affects budgets, infrastructure and human resources.

The WHO-ART guidelines are crafted by an international committee of experts drawn from rich and poor nations whose mandate is to provide the world's low- and middle-income countries (LMICs) with affordable high-quality ART guidelines. Historically, ART-guideline development in high-income countries is independent of the WHO and takes a more local character, for example, the International AIDS Society (IAS)-USA division, the Southern African HIV Clinicians Society, the European AIDS Clinical Society (EACS), the British HIV Association and the ASIA-Pacific HIV Society, etc. Liaison between the WHO and these regional societies and associations is constant. WHO guidelines committee members are also members of their national HIV-agencies. International ART guidelines are almost never produced in isolation.

Local guidelines frequently predate the release of the WHO's guidelines as local bodies require less administration/bureaucracy and can respond to new data in real time, for example, UTT and the Insight-Start and the Temprano Studies, dolutegravir in first-line ART and the ADVANCE Trial, etc.[27] Mehraj et al. noted that Canada implemented the 2002 WHO and ART guidelines 2 months before its general release.[28] Canada had all the required capacity with regard to resources and regular staff trainings as well as mentoring in implementing the guidelines. Within a space of 1 month after the release of the 2015 WHO and ART initiation guidelines, 60% of the facilities in Spain were already implementing rapid ART initiation.[29] This suggests that Spain had already started preparing for the changes based on EACS guidelines. Larsen et al. revealed that despite significant funding from PEPFAR, the South African National Department of Health is still failing to implement rapid ART initiation. Indeed most SSA countries have experienced fundings cuts in the past few years.[30]

There is a worrisome trend in SSA countries concerning the national adoption of the WHO-ART initiation guidelines. This may explain why countries in SSA are still struggling to achieve the 90-90-90 target. Despite the increase in HIV testing, rapid ART initiation based on the 2015 WHO guidelines are yet to be achieved in SSA. Furthermore, there is need for African governments to seriously consider local situations and experiences when embracing global guidelines.

Limitations

One of the limitations of our study is that we reviewed data from SSA and possibly excluded some important articles published in languages other than English. The study included only articles focusing on CD4 threshold changes on ART initiation. More articles might have been captured if language and the CD4 threshold had not been a filter.

Conclusion

We conclude that although countries in SSA have generally adopted the WHO-ART guidelines, implementation has frequently been delayed. We noted that the changes in guidelines were fraught with many challenges like switching from treating at a CD4 count of 200 cells/mm^3 in 2002 to rapid ART initiation in 2015 regardless of the CD4 level. Implementation has been variable across the countries of SSA because of differences in the health systems and the availability of resources. Because of the financial burden on governments, the reduction in donor funding, the rising incidence and prevalence of HIV and sometimes and the attitudes of healthcare workers, the majority of SSA countries have experienced a delay in the implementation of the guidelines. A comprehensive approach to reduce barriers whilst enhancing facilitators may improve the situation of adopting and implementing timely ART initiation guidelines.

Acknowledgements

Competing interests

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

Authors' contributions

S.M.G. and M.J.C. conceptualised the study. S.M.G. did literature searches, analysis, writing and compilation of manuscript. M.J.C. supervised the processes, reading all versions. Both authors have read and approved the final article.

Funding information

This research was funded by the University of KwaZulu-Natal through a PhD studentship bursary awarded to SMG by the College of Health Sciences.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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1.3 Problem statement and significance of study

Antiretroviral therapy (ART) is the key strategy in prevention of HIV transmission (32). Currently 15 million people are living with HIV, mostly in low-and middle-income countries (33). The World Health organization now recommends ART for all HIV infected people on the same day of HIV diagnosis regardless of CD4 count and WHO clinical staging unless the patient is not ready to commit to starting therapy (3). This has resulted in nearly 20 million additional people eligible to start ART globally (34). South Africa has approximately 6.5 million HIV-infected people with 2.5 million receiving ART making it the largest program in the world (35). Despite these efforts, only 42% of ART- eligible South African adults over 15 years of age are receiving ART (35). Nevertheless, there are still many people, not on ART, presenting with advanced HIV at health facilities (13). This shows that increased access to HIV testing alone might not be enough to reach the 95-95-95 targets and effectiveness of UTT policy if initiation is erratic.

South Africa's continuing high HIV incidence has increased the burden on expansion of the ART programme (21). In order to meet the UNAIDS targets to end the AIDS epidemic by 2030 there is need to ensure all individuals diagnosed with HIV are initiated on ART under the treatment and prevention strategy (36). Without (ART), most people living with HIV will eventually develop progressive immunodeficiency leading to AIDS-defining illnesses and premature death. Accelerating the steps required for ART initiation has been proposed to reduce attrition and achieve rapid treatment initiation. Therefore, there is need to seek ways of overcoming the barriers that can arise when trying to implement programs associated with rapid initiation of HIV treatment both from the patients and healthcare worker's perspectives.

As the HIV programs continue to focus on identifying HIV-infected people and starting ART at higher CD4 thresholds (37), there is need to assess public health sector capacity to implement policy guidelines (37). Patient delays on ART initiation may be attributed to lack of an individual's acceptance of their status, stigma, concerns about ARVs side effects and adherence to daily pill regimens, personal socio-economic challenges as well as non-disclosure. Rapid ART initiation on the same day of HIV diagnosis is resource-intensive, requiring the availability of clinicians, counsellors, and laboratory staff to facilitate clinical evaluation, counselling, required intake laboratory testing, and systems in place to assure linkage to ongoing care (33). The limited

availability of these personnel in resource constrained health facilities remains a challenge which might affect the effectiveness of the program.

There must be clarifications for people tested and diagnosed with HIV but not initiated on ART. Linkage and retention to treatment cascade remains a challenge in HIV care (9). However, there is limited evidence to evaluate factors that lead to people who test HIV positive exhibiting willingness or unwillingness to be rapidly initiated on ART. Retention in care relative to rapid ART initiation (Universal Test and Treat policy); have not been studied in detail. The implementation levels of the policy with healthcare workers has to be assessed to evaluate the effectiveness of the policy. Clinical outcomes at patient level both for early and delayed ART initiators need to be assessed to determine the effectiveness of the policy on treatment management to reach the second and last 90 on the 90-90-90 strategy. In order to reach the 95-95-95 targets by 2030, it is not only important to test people for HIV but to rapidly initiate them onto ART and have their viral load suppressed as well as retaining them in care (38). Viral load suppression of PLWHIV in a large population will lead to reduction of new infections (39). The findings will possibly help in generating evidence evaluating the barriers and facilitators of UTT policy implementation in low and middle-income countries and identify the gaps.

This study determined factors that influence acceptability, implementation and patient outcomes in a rapid ART initiation program. The study findings will inform policy makers and government on strengthening the UTT policy and identify enablers for reaching the 95-95-95 target; it will assist in benchmarking rapid ART initiation processes in other facilities. More broadly the knowledge gained from the participants and service providers will inform medical practices and public health policies in other similar contexts.

Figure 1 shows the HIV testing and treatment cascade framework that outlines the processes of care that people living with HIV receive from initial diagnosis to achieving viral suppression and impacts at different levels. The concept of an HIV testing and treatment cascade helps to identify gaps in the continuum of HIV care. The framework was modified from WHO's HIV testing and treatment cascade. Under continuum of care, the study focused on the beneficiary-level which shows the clinical outcomes of rapid and delayed ART initiators, program-level which assessed facility compliance with policy implementation and population-level which measured cohort's

outcomes. The HIV cascade deals with patient-level factors that contribute to rapid or delayed ART acceptance, clinic level assessing facility HIV testing activities as well as linkage to treatment, healthcare worker's perspectives and community level determining levels of disclosure as well as family support. The study evaluated how continuum of care and the HIV testing cascade framework contributes to rapid ART initiation policy.

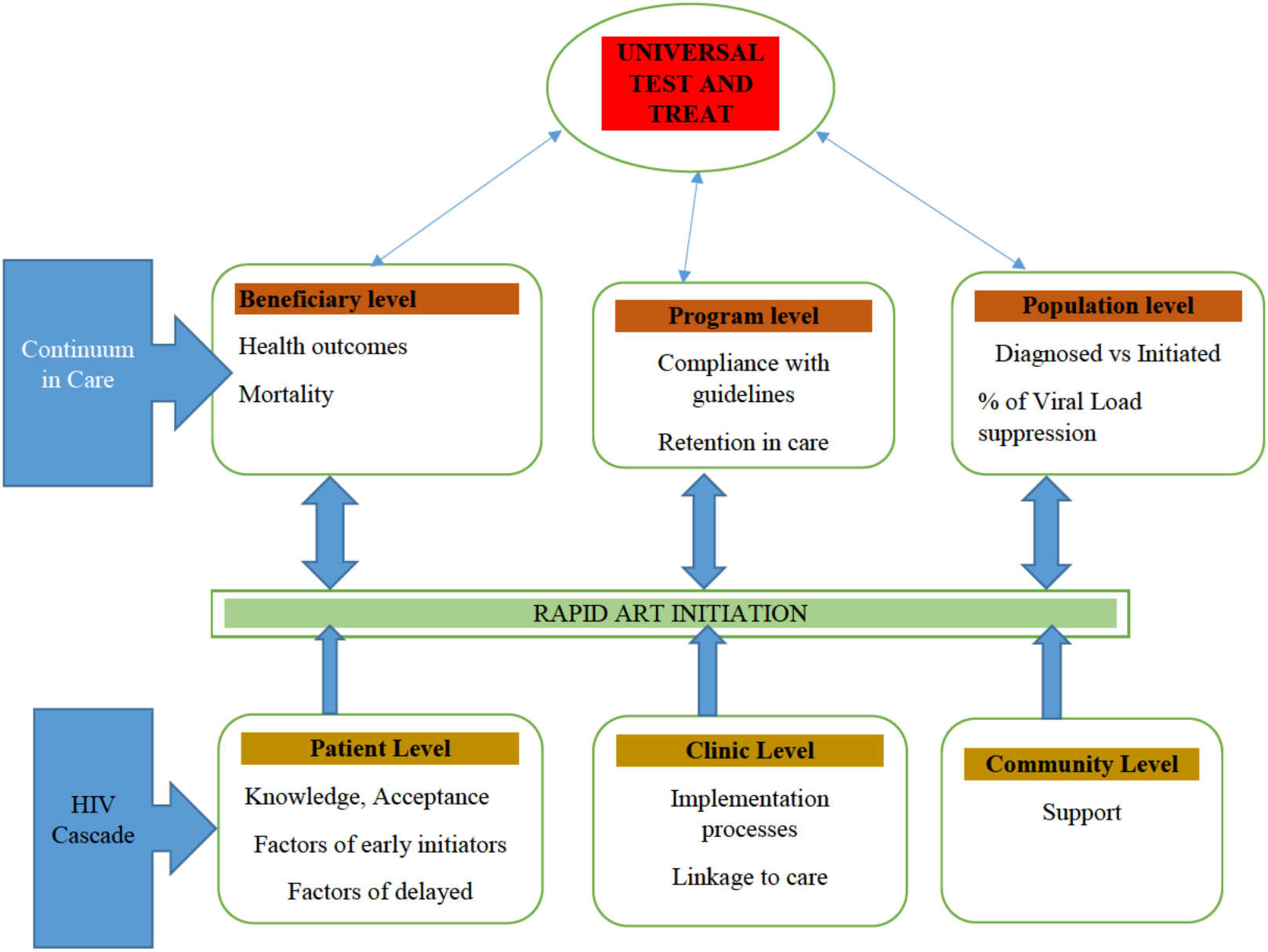

Fig 1: The HIV Testing and treatment Cascade: Adapted from the Centers for Disease Control and Prevention, HIV Care cascade December 2nd, 2017.

1.5 Research Questions and Objectives

1.5.1 General Research Question

The main research question for this work was "What factors influence acceptability, implementation and patient outcomes of the Universal Test and Treat policy (rapid ART initiation) in eThekwini clinics?" To address this, question several sub-questions were posed and recast to state specific objectives.

Specific Questions and Objectives

Research questions	Objectives
1. What are the factors associated with patients' acceptance of same day ART initiation?	To determine factors associated with individuals' acceptance of same day ART initiation.
2. How is the rapid ART initiation program implemented in the different facilities?	To describe and evaluate the implementation of rapid ART initiation in different clinics
3. What are the experiences, observations and experiences of healthcare workers in implementing same say ART initiation?	To explore the experiences, knowledge and observations influencing implementation of same day ART initiation in four eThekwini clinics
4. What is the impact of rapid or delayed ART initiation on patient retention in care, and clinical outcomes?	To compare patient retention in care and clinical outcomes (virology suppression, hospitalizations, co-infections and mortality) at 6 months after ART initiation for same day ART initiation and delayed ART initiation.

1.6 Research Methodology

A prospective mixed methods study design using cross-sectional survey and key informant qualitative interviews was used to evaluate the impact of same day ART initiation on patients and healthcare workers. The study population comprised of adults (i.e. 18 years and above) with an

HIV positive result who were either initiated on ART on the same day of HIV diagnosis or deferred same day ART initiation. In this study anyone not initiated on the first day of HIV diagnosis was considered as deferred SDI. Healthcare workers involved in the Testing and initiation of ART were interviewed as key informants. Three objectives of the study were assigned under the quantitative methods, while one objective was assigned to both quantitative and qualitative method. The study was conducted in four clinics (D, Pinetown, Qadi and Ithembalabantu) of eThekwini district, Kwazulu Natal (KZN). The selection of the sites was informed by the location of the facility, high volume of people receiving treatment in the facility and the diversity of patients who receive services in the facility. Fig 2 shows the maps of KwaZulu-Natal province indicating demarcations of the districts and Fig 3 shows the map of eThekwini municipality with the different suburbs where the study was conducted. The study focused on factors that served as barriers to or facilitators to same day ART initiation Including the clinical outcomes 6 months after HIV diagnosis. Details on study designs, measurement of variables and the analysis of the data obtained for each component of the study are in individual papers under different chapters.

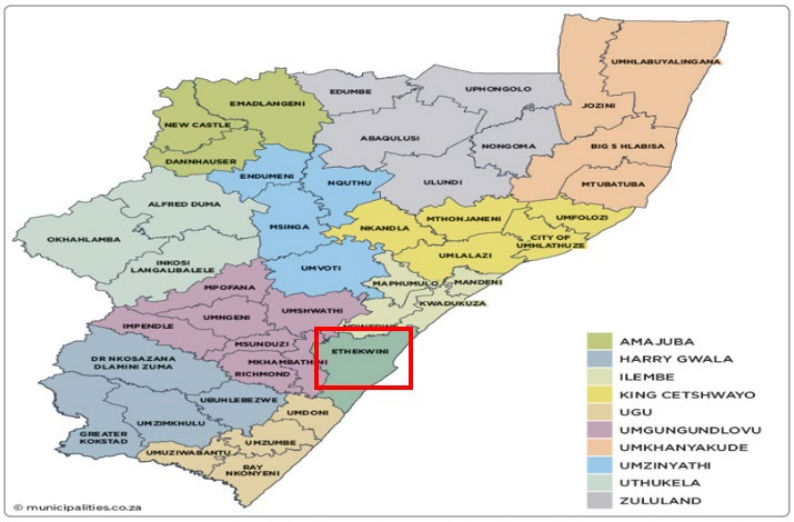

Figure 2. Map of KwaZulu-Natal province showing all the districts and eThekwini municipality. Adapted from municipality of KZN.

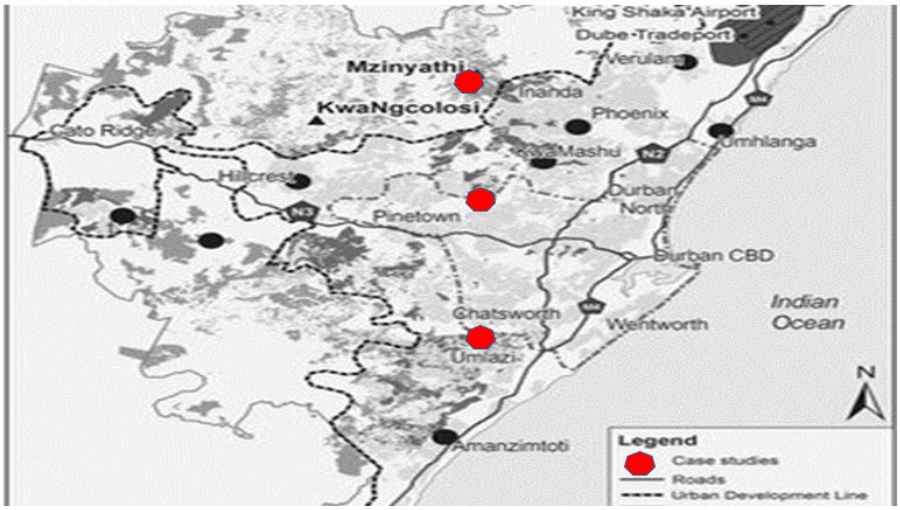

Figure 3. Map of eThekwini Municipality showing the suburbs where the clinics are located. Adapted from municipality of eThekwini.

1.8 Ethical Considerations

Ethical approval to conduct this study was obtained from the Biomedical Research Ethical Committee in the University of KwaZulu-Natal and Department of Health Provincial Research Office. Study participants were required to complete and sign a written informed consent prior to recruitment after the study purpose was explained. During recruitment participants were assigned unique participant identities (PIDs). The researcher assured the participants that the findings of the study would not reveal their actual names. Hence information provided by participants was kept anonymous. There were no harmful procedures inflicted on participants since data collection was solely through interviews and chart reviews.

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Reviewed literature in Chapter 1 identified the need to understand the current ART initiation guidelines, facilitators and barriers of ART initiation implementation under the same day ART initiation guidelines in order to improve clinical outcomes. Factors determining the implementation of ART initiation guidelines in SSA countries were explored. Some of the factors indicated were related to patients, healthcare providers and of a structural nature. It is in this respect that Chapter 2 was designed to gather data through interviews to determine individual patient factors affecting the uptake of same day ART initiation. Thus Chapter 2 addresses objective 1 of the overall study constituting this thesis.

CHAPTER 2: FACTORS INFLUENCING RAPID ANTIRETROVIRAL THERAPY INITIATION AT FOUR ETHEKWINI CLINICS, KWAZULU-NATAL, SOUTH AFRICA.

Published: AIDS and Behavior

AIDS and Behavior
https://doi.org/10.1007/s10461-021-03530-3

ORIGINAL PAPER

Factors Influencing Rapid Antiretroviral Therapy Initiation at Four eThekwini Clinics, KwaZulu-Natal, South Africa

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Accepted: 6 November 2021

Abstract
Timely uptake of Antiretroviral therapy considerably improves the health of people living with the Human Immunodeficiency virus. We conducted a cross-sectional study of newly HIV diagnosed individuals in four clinics in eThekwini municipality, KwaZulu-Natal. Data was collected between June 2020 and December 2020. Participants completed an interviewer-administered questionnaire after HIV testing, on the day of HIV diagnosis. We evaluated factors influencing uptake of same-day ART initiation in eThekwini clinics, KwaZulu Natal, South Africa. Demographic information, health status, sexual behaviour, knowledge of universal test and treat (UTT), ART initiation uptake, and disclosure data was collected. Among the 403 participants, same-day initiation (SDI) was 69.2% (n = 279). We observed the number of sexual partners (aOR 0.35; 95% CI 0.15–0.81), HIV status of the partner (aOR 5.03; 95% CI 2.74–9.26) and knowledge of UTT (aOR 1.97; 95% CI 1.34–2.90) were identified as major factors influencing uptake of same-day ART initiation. More strategies are needed to achieve the SDI uptake within the framework of UTT.

Keywords Universal test and treat · Rapid ART initiation · Same-day ART initiation · Antiretroviral therapy

Background

The World Health Organization (WHO) defines rapid initiation of antiretroviral therapy (ART) as the commencement of highly active antiretroviral therapy (HAART) on the same day of HIV diagnosis [1]. Substantial progress has been observed in recent years in the roll-out of antiretroviral therapy (ART) to populations in sub-Saharan Africa [2]. WHO also recommends ART initiation on the same day as HIV diagnosis, after ensuring the person's willingness and readiness to start ART unless there are clinical reasons to delay treatment [1]. Global effort on decreasing continuous HIV transmission emphasizes the need for routine HIV testing and timely uptake of ART [3]. Advanced, cost-effective, and scaling up strategies are needed to meet the Joint United Nations Program on AIDS/HIV (UNAIDS) ambitious 95-95-95 goals: 95% of people living with HIV (PLHIV) know their serostatus, 95% of those are on sustained (ART) and 95% of those are virally suppressed [4]. Whilst focussing on multi-faceted prevention measures in areas with hyper endemic HIV infection, intensified provision of ART is seen as an important component with a direct impact on population HIV transmission [5, 6].

South Africa carries about 17% of the world's HIV-positive population [2, 7] making it the heaviest carrier of the global HIV burden. Within South Africa, KwaZulu-Natal province is the worst affected having about 1.6 million HIV-positive individuals and over 50% prevalence between the ages 15 to 25 years [4]. Despite the well-known need for protection from HIV infections and other reproductive health risks, their age and their social and economic status limit access to information and services in many settings. Adolescence and young adulthood is typically a period of experimentation, new sexual experiences, and vulnerability. Some adolescents and young adults may experiment with injecting drugs, sexuality, and sexual orientation (men may begin to have unprotected sex with other men), and some are exploited sexually [8]. To shrink continuous HIV transmission, South Africa adopted the universal test and treat (UTT) policy for eligible individuals in September 2016 [8]. The

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Published online: 15 November 2021

UTT policy aims to reduce HIV infection through expanding prevention and treatment preferences. UTT was evaluated in four randomized population-based trials (BCPP/Ya Tsie, HPTN 071/PopART, SEARCH, ANRS 12249/TasP) conducted in sub-Saharan Africa (SSA) resulting in formulation of World Health Organization guidelines and the UNAIDS 90-90-90 campaign." [5]. By June 2019, an estimated 91% of people living with HIV (PLHIV) knew their HIV infection status [4] and of these, 68% were on ART and 83% had viral suppression To improve ART initiation and retention especially among men who have been observed to have poorer treatment uptake, retention and viral suppression compared to women living with HIV [3, 10] there is need to have targeted interventions. HIV prevalence in eThekwini District accounts for 17% of KwaZulu-Natal's prevalence. The district reported 82% of people testing positive for HIV, 72% of those diagnosed with HIV were initiated on ART and 68% of those initiated on treatment were found to be virally suppressed [18]. These results suggest a gap in reaching the 90-90-90 targets.

It is crucial to understand the complexity of factors influencing a person's decision to get on treatment following diagnosis. One of the most persistent challenges facing ART programs in Africa is the late presentation for testing as well as high rates of attrition between HIV testing and ART initiation [11]. Loss to care before starting ART has constantly been high among diagnosed individuals that are eligible for treatment [12]. The recommendation by WHO to offer ART to all who test positive regardless of CD4 count and clinical staging has little benefit if people who test positive fail to initiate treatment immediately [13]. Loss of ART-eligible clients before treatment initiation experienced in many sub-Saharan African countries including South Africa [14] can be addressed through SDI.

The reasons for an individual's rapid or deferred ART uptake may be complex and unintentional. Previously in the HIV cascade of care, there was a gap between having an HIV test and initiating ART. Individuals had to provide CD4 count blood samples and returning for results [24]. Under the new guidelines, CD4 counts will no longer be required to establish ART eligibility to reduce the loss HIV diagnosed individuals at this stage. Losses at this stage were likely related to both health system barriers, such as requirements for multiple clinic visits and delays in receiving laboratory test results, and to patient factors; such as time constraints or reluctance to commit to lifelong treatment [24]. Although several observational studies on SDI in Sub-Saharan African settings have been conducted, the focus was mainly on pregnant and breastfeeding women hence the results may therefore not be generalizable to the broader adult population [15]. Other studies have been restricted to hospitals settings [16] or have described SDI in the context of specialized interventions such as peer-delivered linkage case management or have been implemented at a single facility [17]. There is therefore paucity of data on the uptake of SDI by the adult population in high HIV prevalence settings. It is against this background that we conducted this study which aimed to identify factors affecting uptake of same-day ART initiation in eThekwini clinics.

Methodology

Study Design and Setting

This prospective cross-sectional study was conducted at 4 clinics in eThekwini municipality KwaZulu-Natal (KZN), South Africa between June 2020 to December 2020. The study sites were *Ithembalabantu*, Pinetown, D, and *Qadi* clinic. KZN has 1.9 million people living with HIV of which only 1.1 million are on ART [18]. Of the estimated 650,000 people living with HIV in eThekwini, there are approximately 383,869 people in the ARV program [4]. The eThekwini district is densely populated (3,702,231) comprising of urban, semi-urban, and rural areas [11]. We selected study clinics from the three settings; (i) 2 facilities (*Ithembalabantu* and D clinic) in a densely populated Umlazi township also known to have high HV prevalence, (ii) Pinetown clinic in Pinetown, a semi suburb town (these are places that offer a balance between township and suburb tranquillity) surrounded by townships and informal settlements who all seek services at the facility and (iii) *Qadi* clinic in rural *Umzinyathi* district municipality north of eThekwini municipality. UMzinyathi district has high levels of poverty, unemployment, and HIV/AIDS [18].

Study Population and Data Collection

Four hundred and sixty-one individuals seeking voluntary HIV testing and counseling were recruited for the study. We included newly HIV-diagnosed adults (18 years or older) who presented for voluntary HIV counselling and testing between June to December 2020. Eligible participants were enrolled in the study after self-reporting that they have never tested positive for HIV before. Selection bias was possible if participants decide to report not having an HIV-positive diagnosis before yet they are aware they are HIV positive and have actually taken ART before. After explaining the study to the participants, obtaining written consent, and excluding individuals previously on antiretroviral therapy (ART), 403 adults were included in the study.

Data Collection

The participants were first tested for HIV by clinic HIV Counselling and Testing Counsellors who were

non-research staff members. Individuals who tested HIV positive were referred to a research assistant for enrolment irrespective of accepting same-day ART initiation or different ART. Participants completed an interviewer-administered baseline questionnaire after HIV testing and either received ART initiation or not, on the day of HIV diagnosis. Initiation of ART was also confirmed using prescription cards in the medical charts. A qquestionnaire was prepared in the local language *IsiZulu* and was administered to participants at the clinic through face-to-face interviews by a team of two community research assistants (CRAs) supervised by the investigator. The CRAs were native *IsiZulu* speakers and had post-high school qualifications and were trained on the study including the data collection process. The questionnaire captured participant's demographic information (age gender, marital status, employment status, education level), health status, and sexual behaviour history (number of current sexual partners, status of sexual partner, perceived risk of HIV infection) knowledge of UTT, ART initiation uptake as well as disclosure data. The questionnaire was pre-tested on a sample of 6 participants from the exact target group at Ithembalabantu clinic.

Data were collected electronically using the Kobo Collect application (Cambridge, MA, USA) on Android mobile devices. Non-research trained HIV testing counselors conducted HIV tests according to the South African guidelines [19]. We enrolled approximately 100 participants in each of the four clinics including individuals who rapidly initiated ART and those that delayed. The same-day initiation (SDI) of ART was defined as acceptance of ART on the day of HIV diagnosis and given prescribed medication (ART) on the same day. We used prescription cards in the medical charts to confirm and check ART initiation. At the time of enrolment, there were changes on ART regimen guidelines in South Africa. Dolutegravir (DTG), an integrase inhibitor drug was introduced as part of fixed-dose combinations of Tenofovir, Lamivudine, and Dolutegravir (TLD) from Tenofovir, Emtricitabine, and Efavirenz (TEE). With a high genetic barrier to resistance, DTG has the potential to curb the spread of antiretroviral resistance, as it is highly effective, well-tolerated, and affordable in resource-limited settings. All healthcare facilities offering ART in South Africa are recommended to initiate individuals on DTG unless pregnant or women of child-bearing age are not willing to take DTG due to fear of tubal defects.

Ethical Considerations

This study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC/00000819/2019).

Patient and Public Involvement

The participants and general public were not involved in the development of the research question, outcome measures, design, recruitment, and conduct of this study.

Data Analysis

Data cleaning and analysis were done using Stata SE version 17 [20]. Summary statistics including frequencies were used to describe the characteristics of the study subjects. The variable of interest was ART initiation time. South Africa has adopted a UTT and SDI of antiretroviral therapy [7]. Thus, for our study, we have SDI and not same-day initiation (NSDI). This was converted into a dichotomous variable. In our analysis, we determined the relationship between socio-demographic characteristics and the response variable using the Pearson chi-square test and a Fisher's Exact test when frequencies were small. Variables that were significant in the Pearson chi-square test as well as those that had the p-value of <0.20 were included in the univariate analysis. We fit a multivariate logistic regression model to examine the relationship between several explanatory variables and ART initiation time. The estimated odds ratio with their 95% confidence interval was used to determine the strength of association and significant variables were identified.

To test the goodness of fit for the final model, the Hosmer Lemeshow test was applied. The analysis also explored clustering of the health facilities. However, the ICC (intra-class correlation coefficient) estimated from this data was 0.046 indicating that there would be no need for a multilevel model that would take into consideration variations among the health facilities [21].

Results

Of 461 individuals invited to participate in the study, 403 agreed to take part (response rate = 87.3%). Only participants who provided complete information relating to variables of interest were included in the final analytical sample. Participant characteristics of the sample and unadjusted associations between the response variable and the socio-demographic characteristics of participants are presented in Table 1. The mean (SD) age of respondents was 32.7 ($\pm$9.1). The majority (42.7%, n = 172) of the respondents were aged between 29 and 39 years and 63.1% (n = 254) were females. The overall prevalence of SDI was 69.2% (n = 279) (Table 1). The study also showed that 47.3% (n = 140) of participants on SDI were single. The median number of children that the participants had was 2 (IQR = 1). Our results suggest that age, marital status, education, education level, employment status, number of

Table 1 Descriptive statistics for study variable

Variables	Same-day initiation (SDI)		Not same-day initiation (NSDI)		p-value
	Freq (n)	%	Freq (n)	%	
Age					
18–28	73	49.3	75	50.7	**0.001***
29–39	145	84.3	27	15.7	
40–50	43	70.5	18	29.5	
51–62	18	81.8	4	18.2	
Gender					
Female	177	69.7	77	30.3	0.796
Male	102	68.5	47	31.5	
Marital status					
Cohabiting	56	76.7	17	23.3	**0.001***
Divorced	5	45.5	6	54.5	
Married	66	83.5	13	16.5	
Single	132	60.6	86	39.4	
Widowed	20	90.9	2	9.1	
Education					
Primary	67	68.4	31	31.6	**0.002**
High school	119	62.3	72	37.7	
Tertiary	93	81.4	21	18.4	
Employment status					
Employed	104	83.2	21	16.8	**0.001**
Self employed	19	61.3	12	38.7	
student	24	51.1	23	48.9	
Unemployed	132	66	68	34.0	
Biological children					
No	54	61.4	34	38.6	**0.071**
Yes	225	72.4	90	28.6	
Knowledge of UTT					
No	137	56.6	105	43.4	**0.001***
Slightly	46	79.3	12	20.7	
Yes	96	93.2	7	6.8	
Number of current sexual partners					
One	75	90.4	8	9.6	**0.001**
More than 2	204	63.8	116	36.2	
HIV status of sexual partner					
Negative	4	28.6	10	71.4	**0.001***
Unknown	130	55.6	104	44.4	
Positive	145	93.6	10	6.4	
Infection risk prior to testing					
Definitely not going to acquire HIV	15	50.0	15	50.0	**0.001**
Probably not going to acquire HIV	73	49.7	74	50.3	
Probably will become Infected	40	61.5	25	38.5	
Definitely will become positive	150	93.2	11	6.83	

*Fisher's test conducted die to small frequencies in some cells

biological children, knowledge of UTT, number of current sexual partners, the HIV status of the sexual partners and risk of infection prior to testing were significantly associated ($p < 0.05$) with SDI of antiretroviral therapy. Gender was the only variable which was not significantly associated with SDI (Table 1).

Initiation on First-Line Antiretroviral Regimen

Participants who accepted same day initiation (SDI), 33.0% (n = 94) opted not to be initiated on the new first-line drug Tenofovir 300 mg, Lamivudine 300 mg and Dolutegravir 50 mg (TLD) preferring to be initiated on Tenofovir 300 mg Emtricitabine 200mh and Efavirenz 600 mg (TEE). In addition, the study showed that among those who were not initiated on TLD, 95.7% (n = 90) were females while 4.3% (n = 4) were males.

Univariate and Multivariate Analysis of Same-Day Initiation

In a univariate analysis, age of respondent (OR: 0.49, 95% CI 0.36–0.67), marital status (OR: 1.27, 95% CI 1.04–1.56), employment status (OR: 1.21, 95% CI 1.06–1.39), education (OR: 1.39, 95% CI 1.03–1.87), number of current sexual partners (OR: 0.18, 95% CI 0.08–0.40), HIV status of the sexual partner (OR: 8.75, 95% CI 4.91–15.59), infection risk before testing (OR: 0.514, 95% CI 0.41–0.64), knowledge of UTT (OR: 3.17, 95% CI 2.21–4.55), gender (OR: 0.94, 95% CI 0.61–1.46), and having biological children (OR: 1.57; 95% CI 0.96–2.57) were significantly associated with SDI (Table 2).

In a multivariate analysis, the number of sexual partners (aOR 0.35; 95% CI 0.15–0.81), the HIV status of the partner (aOR 5.03; 95% CI 2.74–9.26) and knowledge of UTT (aOR 1.97; 95% CI 1.34–2.90) were the factors that influenced SDI. We observed that the likelihood of SDI among participants with more than one sexual partner were 0.35 (95% CI 0.15–0.81) fold lower than those who had one sexual partner. On the other hand, the likelihood of SDI for those who didn't know the HIV status of their partners and those whose partners were HIV positives were 2.18 (95% CI 1.02–6.92) and 4.83 (95% CI 5.43–8.77) fold higher, respectively compared to those whose partners were HIV-negative. We also observed that those who had knowledge on UTT were 4.39 (95% CI 1.82–10.65) times more likely to initiate SDI compared to those who had no knowledge. No differences in initiation of SDI were observed between those who were slightly knowledgeable and those who had no knowledge about UTT (Table 2).

Discussion

This study found that the magnitude of same-day ART initiation demonstrated some progress in the uptake of test and treat programs in eThekwini clinics. The findings are comparable with those obtained from a study conducted by Koenig et al. where an SDI prevalence of 57% [22] was reported. The results obtained from the current study suggest the need for increased community sensitization on the benefits of SDI for clients who are HIV positive.

In sub-Saharan Africa, only about 26–37% of persons diagnosed with HIV have been observed to enrol in care and immediately initiate ART when provided with standard referral services [17]. Elsewhere, studies have shown that Italy reported a 78% progress in reaching the "second 95" in SDI [23] while Uganda which has a high HIV prevalence reported 71% SDI [24]. In contrast, our results from eThekwini, as well as those reported from a study conducted in Johannesburg show that 65.9% of individuals initiated ART under UTT [7]. Altogether, our results from South Africa suggest the need for enhanced efforts to reach the "second 95" of the UNAIDS 95-95-95 targets [4, 25] by 2030 on timely initiation of ART to realize a meaningful change in ART initiation coverage.

Our results suggest that gender does not influence the uptake of SDI. This outcome is similar to the findings from a study conducted in Zimbabwe [16]. However, our results on the influence of gender on SDI contrast the observations made by Lilian et al. These authors suggested that men tend to take longer to accept a positive diagnosis. The prevailing hegemonic masculinity in the study area which suggests that males must be dominant over females and must exhibit physical and emotional toughness, strength and endurance [17, 35] may explain the men's poorer outcomes to HIV care and treatment when compared to women. Their results suggest that denial was high in males compared to females. Other studies observed that men were less likely to initiate treatment when diagnosed with HIV [19, 26]. In eThekwini where the current study was conducted, an earlier study concluded that men presented late for HIV testing [27]. The late presentation of men is likely due to work demands that keep them from seeking treatment earlier in the course of the disease.

We observed that behavioural factors such as self-reported sexual behaviour relating to the number of current sexual partners and HIV status of the sexual partners influenced SDI. For instance, we observed that participants with more than one sexual partner were less likely to start ART immediately. Fear of disclosing and losing the partners might be contributing factors to delay in SDI. Furthermore, individuals with multiple sexual partners were less likely to rapidly initiate ART increasing the risk of infecting others as well as re-infecting their partners [31, 32]. It is crucial for HIV-positive individuals engaging in multiple sexual partner relationships to immediately initiate ART to prevent a chain of transmission and reinfection. We further observed that participants who didn't know the HIV status of their partners and those whose partners were positive were more likely to initiate SDI. Immediate initiations of ART for these groups especially those with HIV positive partners is essential among people with HIV-positive partners may be a way

Table 2 Univariate and multivariate analysis for factor influencing same-day initiation

Determinant	OR (unadjusted)	95% CI	aOR (adjusted)	95% CI
Age				
18–28	Reference			
29–39	**5.52**	**3.27–9.30**		
40–50	**2.45**	**1.29–4.64**		
51–62	**4.62**	**1.49–14.31**		
Marital status				
Cohabiting	Reference			
Divorced	**0.25**	**0.068–0.93**		
Married	1.54	0.69–3.45		
Single	**0.46**	**0.25–0.85**		
Widowed	3.03	0.64–14.32		
Education				
Primary	Reference			
High school	0.76	0.45–1.28		
Tertiary	2.05	1.08–3.87		
Employment status				
Employed	Reference			
Self Employed	**0.319**	**0.14–0.76**		
Student	**0.21**	**0.10–0.44**		
Unemployed	**0.39**	**0.22–0.68**		
Knowledge of UTT				
No	Reference			
Slightly	**2.94**	**1.48–5.82**	**1.21**	**0.55–2.81**
Yes	**10**	**4.68–23.58**	**4.39**	**1.82–10.65**
Number current of sexual partners				
One	Reference			
More than 2	**0.19**	**0.09–0.40**	**0.35**	**0.15–0.81**
HIV status of sexual partner				
Negative	Reference			
Unknown	3.12	0.95–10.25	**2.18**	**1.02–6.92**
Positive	**6**	**4.63–13.35**	**4.83**	**5.43–8.77**
HIV Infection risk prior to testing				
Definitely not going to become HIV positive	Reference			
Probably not going to become HIV positive	1.01	0.46–2.22		
Probably will become HIV positive	1.6	0.67–3.83		
Definitely will become HIV positive	**13.6**	**5.31–34**		

of early reduction of the viral load [30]. It is crucial for HIV positive individuals engaging in multiple sexual partner relationships to immediately initiate ART to prevent a chain of transmission and reinfection.

Our results from the multivariate analysis indicates that self-acknowledged risk perception of HIV infection did not influence SDI uptake. The way PLHIV process a positive result can influence their engagement with HIV treatment and care. Available evidence suggests that acceptance of HIV status is exacerbated by associating oneself with HIV through judgments about sexual behaviours, which shape a sense of personal risk of infection [30]. One possible explanation from our findings is that the SDI individuals were more willing to acknowledge living with HIV and hence initiated SDI more readily. In a study conducted in Swaziland, people who reported few sexual partners felt they were not at risk of HIV infection and struggled to accept a positive result thus delaying ART initiation [34]. Perception of HIV risk continues to have associations with the concepts of morality or social standards despite the generalized HIV prevalence [35]. This is supported by a study conducted in Malawi on adolescent girls and young women who reported low levels of vulnerability but suffered denial and delayed ART initiation after testing positive for HIV [33].

The establishment of the level of knowledge and perception of UTT is essential in facilitating designing and delivery

of the context-specific educational program for the attainment of UNAIDS 95-95-95 targets. several participants from our study were not aware of UTT. This may further imply that such individuals were expecting continuous counselling after their HIV tests and not being initiated on ART on the same day of diagnosis. This outcome indicates the need for enhanced community awareness and health education on UTT and rapid ART initiation. This can be achieved through various modes of communication such as television advertisements, radio shows, and campaigns. Lessons drawn from a study conducted in the United States of America suggest that awareness of HIV testing can be successfully done using social media platforms and billboards [35].

The risk of attrition remains a challenge among men under "Treat All"; additional research is required on how ART delivery can be made efficient to link them in care. Most studies, including ours, have focused on patient-level factors on ART initiation. Grouping patients from different facilities together may cause loss of evidence on specific facility-level factors that influence ART initiation. This, therefore, calls for studies looking into the impact of health facility-level characteristics on ART initiation since performance might differ across facilities.

Strengths and Limitations of this Study

- Our study was conducted in urban and peri-urban communities, and this provides a reasonable basis for generalizability for the majority of people living with HIV in South Africa and sub-Saharan Africa. Participants were enrolled immediately after HIV diagnosis, allowing for observation of willingness to immediate ART initiation. However, our study was limited to adults and hence the results on characteristics of SDI and delayed ART initiators may not apply to infants and children. Our data collection was based on self-reported measures, which may have been subjective to social desirability and recall bias.

Conclusion

The findings highlight several factors that influencing same-day ART uptake in eThekwini Municipality in line with national guidelines. The HIV status of the partner, knowledge of UTT and number of current sexual partners were identified as factors influencing uptake of SDI. Interventions to support client readiness for treatment uptake are therefore essential and emphasize a need to increase SDI ART initiation to avoid further transmission of the virus. The results also emphasize a vital need to not only streamline processes to increase immediate ART implementation/uptake further but also ensure individuals who test HIV positive receive adequate counselling in addressing the inhibiting factors.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10461-021-03530-3.

Acknowledgements We thank the people who participated in this study and UKZN College of Health Sciences for funding the work.

Author Contributions SMG and MJC conceptualised the study. MJC supervised the study processes. SMG wrote the main manuscript text. CK and SMG conducted the analysis. MJC and CK reviewed the paper and approved the final manuscript.

Funding This research was funded by the University of KwaZulu Natal through a PhD studentship bursary awarded to SMG by the College of Health Sciences.

Data Availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

Ethical Approval The study was approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (# 00000819/2019).

Consent to Participate Written informed consent was obtained from all participants in the study.

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Individual factors affecting uptake of same day ART initiation in eThekwini municipality in KwaZulu-Natal province were identified and discussed in Chapter 2. Gradual progress in the uptake of same day ART initiation in eThekwini clinics was noted. The rate of SDI uptake was lower (69%) than the UNAIDS 2030 target of 95%. This low uptake was attributed to various demographic factors including sexual behaviour characteristics found in high HIV prevalence settings especially in low-middle income countries. Patient attributes were identified as contributing factors to delayed implementation of ART initiation guidelines in Chapter 1 indicating the importance of considering demographic and individual attributes during policy formulation especially in low-middle income countries. The rollout of effective SDI of ART policy implementation in underprivileged communities warrants clear understanding and consideration of socioeconomic gaps that should be addressed to ensure successful and acceptable SDI uptake. Chapter 3, therefore, investigated the healthcare workers' knowledge, experiences and observations in relation to same day ART initiation in eThekwini municipality thereby addressing objective 2 of this thesis.

CHAPTER 3: EXPERIENCES, KNOWLEDGE AND OBSERVATIONS INFLUENCING IMPLEMENTATION OF SAME DAY ART INITIATION IN FOUR ETHEKWINI CLINICS: HEALTHCARE WORKER'S PERSPECTIVE.

Experiences, knowledge and observations influencing implementation of same day ART initiation in four eThekwini clinics: healthcare worker's perspective.

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Status: Under review in The Qualitative Report Journal

Abstract

Background: World Health Organisation (WHO) recommends that individuals should be offered same day Antiretroviral therapy ART after a positive HIV diagnosis. South Africa commenced implementation of the Universal-Test-and-Treat (UTT) and same day antiretroviral therapy initiation (SDI) policies in September 2016, striving to achieve the UNAIDS 95-95-95 targets by 2030. We assessed experiences, knowledge and observations made by a diverse group of healthcare workers on the implementation of Universal-Test-and-Treat (UTT) to strengthen and improve the policy implementation.

Methods: A cross-sectional qualitative study was conducted in four health facilities of eThekwini municipality KwaZulu-Natal Province in South Africa. Key informant semi-structured interviews were conducted with 20 diverse healthcare workers. Interviews were conducted in English or IsiZulu depending on preference of interviewee and responses were recorded on Kobo collect. Major themes were identified and categorised using the Health Belief Model stages.

Results:

Healthcare workers demonstrated detailed knowledge of the Universal Test and Treat and same day ART initiation policy and its importance as an HIV prevention measure for reducing morbidity and mortality. Healthcare workers experienced episodes of medication stock shortages, frequent changes in reporting tools and increase in workload during the inception stages of policy implementation. Healthcare workers observed that newly HIV diagnosed individuals who accepted ART on the same day made the decision because they were feeling sick, not rushing to go back home or work, had better knowledge of HIV as well as ART, were willing to leave longer and with some feeling it was mandatory. Denial, Fear of disclosure, fear of side effects, limited knowledge on ART, structural and system factors and limitations of healthcare worker's expertise were cited as some of the factors affecting SDI.

Conclusion

Our findings identified extensive knowledge presented by HCW about same day ART initiation as an HIV prevention measure and crucial gaps impeding the attainment of the UNAIDS second 95% intended to ensure that HIV diagnosed individuals are initiated on ART on the same day. The study results illustrate the strain experienced by HCW in implementing the SDI policy, particularly

work overload, skills development and facility readiness. Community awareness on the importance of SDI of ART is needed to increase patient understanding for early ART.

Keywords: Same day ART initiation, Universal Test and Treat, Policy implementation.

Introduction

Early initiation of antiretroviral therapy (ART) is critical for decreasing morbidity and mortality among individuals living with HIV, and to prevent further HIV transmission (1). In 2015, the World Health Organization (WHO) announced the new Universal Test and Treat (UTT) policy guidelines for antiretroviral treatment (ART), which recommends initiation of ART for all individuals living and diagnosed with HIV, independent of their immunologic or clinical status (1, 2). Sub-Saharan Africa (SSA) region remains the most affected by the HIV pandemic, with more than two thirds of the global HIV burden (3, 4). Countries throughout sub-Saharan Africa adopted the UTT strategy to contribute in improving client outcomes and attaining UNAIDS 95-95-95 treatment targets, specifically the ART uptake coverage target (5).

Globally, clinical guidelines for HIV treatment are being improved to reflect novel research findings that have shown that successful treatment with (ART) can prevent the onward transmission of HIV(1, 6). This has resulted in healthcare providers being challenged to find ways to increase "treatment as prevention" as a public health measure (7, 8). However, several healthcare facilities across SSA remain resource constrained and overburdened by the ART program expansion (7, 9). Furthermore, many countries in the region faced challenges in meeting the second 95 of the UNAIDS HIV targets and fully realising the benefits of UTT policy due to persistent health system insufficiencies (5, 10). The effectiveness of treatment programmes in reducing HIV-related mortality, however, is predicated on effective implementation of policies around HIV testing, care and treatment to ensure timely treatment initiation (4, 11).

South Africa has the largest HIV burden in SSA, with an estimated eight million people living with HIV, and over five million of these receiving ART in 2019 (12, 13). However, despite considerable efforts to scale-up access to treatment, an additional three million individuals need to

start ART to reach 95% of HIV diagnosed patient on ART by 2030 (14). The SDI policy makes ART uptake quicker and easier for patients and can further necessitate increase in linkage to care by reducing patient losses in the pre-ART phase of care (10). However, in South Africa and most low-and-middle-income countries (LMIC), the implementation of the UTT and SDI policies increased the strain on human resources and infrastructural capacity (15). This study aimed to understand health care professionals' experiences, knowledge and observations influencing UTT and SDI policy implementation in four health care facilities to strengthen and improve the policy implementation.

Methodology

Study Design and setting

A cross-sectional qualitative study was conducted at four primary health facilities of eThekwini municipality KwaZulu-Natal Province in South Africa between June 2020 to March 2021. Purposive sampling was used to select 20 participants involved in different aspects of UTT and SDI. Study participants were recruited from four health facilities located in urban and rural areas. Study sites were eligible if they had a medium to large ART cohort size (defined as >2000 patients currently on ART). All included sites began the UTT policy and SDI rollout in October 2016.

Key informant interview procedures

We conducted key informant semi-structured interviews with 20 diverse healthcare workers. Seven of them were NIMART trained professional nurses, four data capturers, five lay HIV counselling and testing counsellors, two pharmacy assistants, one pharmacist and one phlebotomist. Interviews were conducted in a private space within the facility by trained interviewers and lasted on average for 1 hour. Interviews were conducted in English, or IsiZulu depending on the preference of the interviewee and were audio-recorded. IsiZulu audio recordings were transcribed verbatim and translated to English for analysis.

The interview guide was intended to gather information on attitudes of healthcare workers towards UTT and SDI implementation, healthcare workers' observations on factors influencing patients'

SDI uptake and assess the knowledge of healthcare workers on the policy changes and implementation processes for UTT and SDI.

Data analysis

Data was analysed using content analysis approach and thematically using NVIVO software which enabled data management and coding. Two research team members individually read and drafted a summary of preliminary themes within and across sites. Themes were drawn from topics covered in the interview guide. Major themes were identified and categorised using the Health Belief Model stages. The HBM suggests that a person's belief in a personal threat of an illness or disease together with a person's belief in the effectiveness of the recommended health behaviour or action will predict the likelihood of the person to adopt the behaviour (16). Patients move along a continuum of care from HIV diagnosis to commencement of ART. Barriers, facilitators and benefits of UTT and SDI were fitted into the five theoretical Health Belief Model stages. The HBM derives from psychological and behavioural theory with the foundation that the two components of health-related behaviour are 1) the desire to avoid illness, or conversely get well if already ill; and, 2) the belief that a specific health action will prevent, or cure, illness (17). Ultimately, an individual's course of action often depends on the person's perceptions of the benefits and barriers related to health behaviour. Any code and theme variations identified were resolved through discussion and consensus from all research team members.

Ethical considerations

All study participants provided voluntary written informed consent before data collection processes. We de-identified details including healthcare workers' names as well as clinic names to protect confidentiality. This study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC/00000819/2019). All the participants provided written informed consent before all data collection processes.

RESULTS

Socio-Demographic Characteristics of Study Participants

Twenty healthcare workers from four primary healthcare facilities were invited to participate in the study. Seven were NIMART trained Professional Nurse responsible for counselling and

initiating HIV diagnosed patients on ART, 4 were Data Capturers who does daily capturing of information recorded in patient files on TIER.NET, one was a Phlebotomist who withdraws baseline bloods as well as routine bloods. We also interviewed two pharmacists and one pharmacy assistant responsible for providing ART education and dispensing medication to patients and five HIV Testing Counsellors who provide Pre and Post HIV counselling as well as testing for HIV. Numerous factors influencing same day ART initiation policy implementation were highlighted by primary health care workers at clinic level based on their experiences and observations.

Health care workers' understanding of UTT and SDI policy in the context of South Africa

Sixteen of the primary care providers exhibited good operational knowledge and understanding of the policy and importance of rapid ART initiation as an HIV prevention measure and for reducing morbidity and mortality. Healthcare workers with frequent direct contact with patients like nurses and pharmacists displayed pertinent knowledge about UTT and SDI. One professional nurse had this to say:

> *This is a policy from WHO that the SA government started implementing in September 2016. It recommends that people who test positive for HIV must be initiated on ARVs on the same day of diagnosis. This is being done as treatment as a prevention to meet the 90-90-90 target by 2020 and 95-95-95 strategy by 2030. People should know their status and those who test positive initiate on ART to promote viral suppression. (Professional Nurse B)*

A Pharmacist at one of the facilities also shared comprehensive comments demonstrating related knowledge on the UTT and SDI policies.

> *It is HIV prevention policy which SA started to implement in 2016. 90 % of SA citizens must test and know their status, 90% of those diagnosed for HIV must initiate on ART immediately and 90% of those on ART must be virally suppressed. people must be initiated on treatment on the same day of diagnosis. (Pharmacist A)*

One of the data capturers precisely summarised the policy.

> *It is testing most people in South Africa and making sure there are initiated on treatment quickly. (Data capturer A)*

However, four healthcare workers showed limited knowledge of UTT and SDI. This shows that some healthcare workers require more trainings in understanding guidelines and policies to ensure effective implementation. The below quote from Counsellor A was hanging and showed poor knowledge about the policy.

> *It is when we try to encourage people to test for HIV and then try to make them start on ARVs. (HIV Testing Counsellor A)*

Another HIV testing Counsellor from another facility also showed limited knowledge about the policy particularly the 95-95-95 target. They heard the number not its significance.

> *It is a process of testing people for HIV and making 90% of those tested have viral load suppressed. People can then look for help at the clinic (HIV Testing Counsellor B)*

Results Integrated with the Health Belief Model

Stage 1 and 2: Perceived susceptibility and Perceived severity

Healthcare workers reported that newly HIV diagnosed individuals who accepted ART on the same day made the decision because they were feeling sick, not rushing to go back home or work, had better knowledge of HIV as well as ART, were willing to leave longer and some felt it was mandatory. One of the HCW shared the following:

> *Most of the patients I have initiated on ART on the same day of diagnosis agreed to start ART because they were sickly, having partners who are already on ART, proved to have good understanding of HIV shown by the questions they asked including their answers, willing to wait for all processes and afraid of death. (Professional Nurse C)*

Furthermore, HIV Testing Counsellors reported that:

> *… people who have partners already taking ART are easy to accept their status and willing to start treatment, those who come for HIV testing already sick start treatment on the same day unless if they have TB symptoms…. (HIV Testing Counsellor C)*

Stage 3: Perceived benefits

HCWs reported benefits (7/20) of SDI both on participants and healthcare workers. Early antiretroviral treatment lowered the risk of serious AIDS-related events by 230 000 (72%) from 320 000 (18). Early treatment also lessened the risk of serious non-AIDS events by 72 000 (39%) from 185 000 (19). This was supported by a HCW who said:

> *…. most people start ART before there are sick which assists us to manage them better than when there are sick. (Professional Nurse A)*

Numerous clinical trials as well as observational data (i.e. studies from clinical practice) have demonstrated beyond reasonable doubt that the benefits of antiretroviral treatment for people with HIV/AIDS far outweigh their risks (20). One of the nurses had the following to say:

> *… the number of sickly people who start ART has been reduced because we start them whilst there are still healthy and only has to manage side effects for a few weeks after starting treatment. Which now makes ART management easier... (Professional Nurse B)*

The introduction of UTT brought a reduction in multiple clinic visits between HIV diagnosis and ART initiation. This has improved linkage to care where a number of HIV diagnosed individuals are lost in care. Two HCWs highlighted the below as a benefit to SDI:

> *The SDI policy has reduced the patient number of visits to the facility after HIV diagnosis giving us joy that we have given them medication to start taking early. (Pharmacist B)*

> *I think its beneficial because it saves time by not seeing the same patient twice within the same week. I think its beneficial because it gives an opportunity to quickly suppress viral load. (Professional Nurse D)*

Stage 4: Perceived barriers

Inception of SDI policy

Healthcare workers reported facing challenges during the inception stages of the UTT and SDI policy implementation. The HCW highlighted various issues which were directly related to their roles.

Administrative/operational challenges

Increase in healthcare workers' workload without corresponding increase in manpower was observed and reported by the HCW as contributing factors to the challenges for linkage to care and early/immediate initiation of antiretroviral therapy. Human health resource shortages were cited as a critical barrier to policy implementation. HCW perceived current staffing capacity as already overwrought, and that the SDI policy would worsen the already overburdened clinics. Drug stock outs and staff burnout were reported by HCW. The policy rollout was implemented and program expanded with no additional personnel. Most facilities in South Africa failed to fully implement the policy guidelines on time because of limited ARV drugs stock outs, increased paperwork, ever-changing reporting tools coupled with patient naivety.

One of the participants mentioned that:

> *The beginning of the program was very challenging because forms would regularly change as well as reporting tools……. (Professional Nurse B)*

Similarly, another nurse from a different facility noted the following:

> *There has been a lot of teething problems when we started because of medication stock outs…. (Professional Nurse E)*

A pharmacist assistant from one of the facilities reiterated the following:

> *…. We have had episodes of medication stock shortages because the demand was very high….*

A non-clinical healthcare worker also shared operational challenges saying:

> *The program has increased the number of files we capture daily. Before 2016, we were capturing less than 5 files on new initiations but now the number has almost tripled. (Data Capturer B)*

Patient naivety

Healthcare workers mentioned some concerns about the perception of patient psychosocial needs and circumstances. Despite patients' diverse level of knowledge of the need for ART, they may persist in the contemplation phase (without action) due to the perceived fear of HIV-related

discrimination and stigma. The fear of ART drug side effects was also reported to be a barrier to initiate ART. Some patients need more time to understand the implications of their HIV test result and thereafter make decisions. It was apparent that patient naivety was a contributing factor as observed and experienced by HCWs. The following sentiments were shared by the HCWs:

> *…. However, it's not everyone who agrees to be initiated on the same day which I understand because you need to be ready to take the lifelong medication. (Professional nurse F)*

In Addition to what the nurse reported, an HIV Testing Counsellor shared related ideas:

> *…. patients complain of being rushed to initiate before processing all the information. It is still difficult in our community because patients still refuse to initiate quickly after testing. Convincing them is a big problem which affects our linkage to care. (*HIV Testing Counsellor D)

Furthermore, another HIV Testing Counsellor from a different facility supported the comment:

> *….. It is easy on patients who already know about the policy and have partners with known HIV positive status however difficult encouraging patients who are in denial and no / limited knowledge of UTT. (HIV Testing Counsellor E)*

Health care workers also stated that fear of side effects particularly among healthy individuals continue to be a significant barrier to ART acceptance. Healthy individuals believe the risks of side effects outweigh the benefits of ART initiation. Fear of possible harmful reactions hinders healthy individuals to willingly accept same day ART initiation.

> *Fear of side-effects led some individuals not to accept ART on the day of HIV diagnosis. The common side-effects they are afraid of includes vomiting, diarrhoea, body pain, skin rashes and weight loss. (Professional Nurse D)*

A HIV testing Counsellor also spoke about the fear of side effects as a barrier to ART initiation He said.

> *I have noticed that some individuals refuse to start ART because they don't feel sick hence they believe taking ARVs will trigger health problems. The fear of side effects when starting ART becomes a deciding factor for healthy individuals. (HIV testing Counsellor E)*

Misinformation and inadequate information about ART was alluded by health workers as a barrier to starting ART immediately. Some individuals demonstrated that there were not aware of the new Test and Treat policy and felt confused and unprepared to start treatment immediately after a positive test. Health care workers highlighted that individuals from urban areas seemed better knowledgeable about HIV and ART compared to those from rural communities, posing differences between ART readiness challenges. The SDI policy does not allow sufficient time between an HIV positive diagnosis and time to ART initiation. There are still existing myths around HIV and ART information which requires healthcare workers to correct before a person commits to ART. One of the HIV Testing Counsellor had the following to say

> *.... It is easy on patients who already know about the policy and have partners with known HIV positive status however difficult encouraging patients with no / limited knowledge of UTT. (HIV Testing Counsellor C)*

Denial

Healthcare workers reported that denial and shock of an HIV positive diagnosis was a reason some individuals mentioned for not accepting SDI. Some "healthy" clients needed time to accept their HIV positive status before accepting ART initiation. Some healthcare provider felt that the time given to clients to accept their status in the pre- versus post-Test and Treat is little which might be the reason for high defaulter rates.

> *……Maybe give patients some days to process the results and not push them to start ARVs. We need to give patients at least a week to process the results then come back to initiate treatment. It's better for them to disappear before starting than after starting causing drug resistance problems. (Pharmacy Assistant)*

Similar sentiments were shared by another HCW from a different facility:

> *It has been a challenge because we face people who refuse to start ARVs saying there are not ready. We struggle to convince them on the benefits of starting affecting our linkage to care numbers. Some will agree but defaults after a few months on treatment then come back when there are sickly. (Phlebotomist)*

Fear of disclosure

Health providers described the fear of disclosure to significant others as one of the reasons why some individuals who recently tested HIV positive refused to start ART immediately.

Fear of being discriminated, stigmatized, and lack of trust towards significant others was mentioned by the majority of HCW as the main reason for not disclosing the sero-status to family members, friends, neighbours and the larger community. Several individuals feared that disclosing their sero-status openly and discussing ART initiation with their partners would negatively impact their relationship and could result in rejection. This statement is supported by the quotations below.

> *…. some individuals are worried that some people may be aware of their HIV status if there are seen taking ARVs so they prefer not to start especially if their partners are not taking treatment with nowhere to hide… (HIV Testing Counsellor C)*

Additionally, a nurse responsible for ART initiation at another clinic mentioned that:

> *Disclosure to family and friends is usually mentioned by some people as a reason why they are not willing to start ART. Some fear they will be rejected by their partners and family. (Professional nurse G)*

Limited Community awareness

The results show limited community awareness of SDI. There seem to be lack of publicising the policy in our communities and explaining why it is done. Most of the people tested for HIV are clueless of the policy and its benefits on clinical outcomes hence the refusal to uptake SDI. One of the HCWs shared that:

> *……there is also need of advertising the program more even in radios and TVs so that our communities can know about this. There get angry when we tell them they have to start ART immediately yet they have never heard about that. (Professional Nurse A)*

The use of media to inform people of the policy changes was a popular opinion. Media platforms were preferred because they are an accessible medium for communicating different important issues.

The government should consider intensifying marketing of the policy on different media platforms to make sure communities are aware of the information…. (Data Capturer D)

Health Care Providers Expertise

Lay Counsellors serve as the entry points in the HIV cascade. Healthcare workers reported that individuals who are hesitant, in denial and with limited information about starting ART require professional counselling, possibly beyond the scope and knowledge of lay counsellors found in most if not all healthcare facilities. Hence the need for trained counsellors to handle increasingly complex pre and mostly post HIV counselling to prepare patients for SDI and lifelong adherence to treatment. One of the HCW noted that:

The government needs to intensify skills for counsellors to encourage patients to accept initiation on the same day…. (Data Capturer C)

The notion was seconded by another HCW who said that:

…. there is need to increase adherence counsellors in clinics and train them more so that there can offer quality counselling to newly diagnosed patients. (Professional Nurse D)

Stage 5: Cue to action

Some healthcare workers made several suggestions which might make the systems to be more efficient both for the benefit of individuals seeking the services and healthcare workers.

Personnel recommendations in Improving SDI policy implementation

Shortage of staffing was mentioned as one of the barriers in effectively implementing SDI. Increased caseloads for staff in the ART programmes due to the removal of CD4 count as eligibility criteria for ART initiation meant the sudden expansion of ART uptake. The scale up of ART programmes undeniably puts pressure on staff at health facilities particularly ART professionals. A Pharmacist Assistant made the following suggestion on that regard:

..... there is need to increase the number of NIMART trained nurses in the clinics to reduce long waiting times and Skills development of Testing Counsellors in offering quality pre and post HIV counselling. (Pharmacist Assistant)

Similarly, another HCW stated the following:

The government and supporting organisations need to increase the number of nurses, skilled counsellors and data capturers in all clinics in order to strengthen the ART program…. (Data Capturer D)

Recommendations on SDI processes

There are some important concerns with respect to rapid ART initiation, notably with respect to the risk of loss to follow up. It might be meaningful that ART is initiated within 7 days following a confirmed HIV diagnosis and clinical assessment, and that ART initiation on the same day as HIV is diagnosed should be offered to patients who voluntarily decide to start. One of the nurses had the following suggestion:

The policy should at least give patients a week to process the results get enough counselling to ensure their readiness reduce defaulting and missed appointments. (Professional Nurse G)

Recommendations on personnel training

The revision and clarification around the timing and content of the counselling session for fast-track initiation counselling entailed more accurately the role counsellors played in facilitating patient status acceptance, ART initiation uptake. retention in care and adherence to treatment in the months after initiation. Suggestions to upskills the counsellors was brought up as a recommendation in improving the policy.

The governments and facilities have to intensify counselling skills for our testing counsellors to capacitate them in knowing how to empower status acceptance and importance of starting ART early. (Pharmacist A)

Discussion

The findings of this study are similar to those reported in the literature, in terms of identifying important potential benefits of SDI and key concerns calling for further improvements. Our results contribute to the growing body of literature on barriers, facilitators and benefits to rapid ART initiation. Healthcare workers identified facilitators and barriers of SDI including denial and feeling healthy, fear of disclosure, limited knowledge about ART, fear of ART side effects, fear of stigma and discrimination, healthcare worker's expertise, structural and system factors. Similar to our findings, other studies have reported that feeling healthy, fear of side effects and denial were linked to refusing to initiate ART (21, 22).

Our findings show that there were disparities in UTT and SDI policy knowledge among the different healthcare workers. Clinical healthcare workers like nurses and pharmacy personnel reported more detailed knowledge and understanding highlighting the clinical and public health benefits of UTT and SDI policy compared to non-clinical healthcare workers like data capturers. Similar sentiments were reported by healthcare workers in high-income and other LMIC settings after UTT policy adoption, and initiation of lifelong ART among all HIV-positive pregnant and breastfeeding women (23, 24). This shows the knowledge gaps among diverse HCWs calling for trainings with similar content to be offered to all HCW. It is evident that diverse healthcare workers at various operational levels understand and interpret information differently. The expectation is that healthcare workers working in the HIV clinics at different levels fully understand the policy and be in a position to explain it to patients. The HCW knowledge will enable determination and awareness of the policy to the community at large.

Our study found the facilitators and benefits mentioned by healthcare workers influenced individual willingness to start ART on the same day of HIV diagnosis. These included better knowledge about the benefits of ART and the willingness to live longer and stay healthy. The desire to live a healthy long life has been linked to individuals seeking to test and starting ART early in other settings (25). At the population level, some HCW stated that fear disclosure to avoid stigma and dis-crimination hindered uptake of SDI in some HIV diagnosed individuals. A study conducted in Tanzania described how anticipated stigma and discrimination was associated with non-disclosure and poor uptake in treatment initiation (26).

Our findings pointed to the increase in HCWs' workload as a significant concern especially in developing countries facing staffing challenges. The expansion of the ART program resulted in increased volume of patients seeking ART services in healthcare facilities. Expanding staffing may also be needed to accommodate the influx of new clients. Studies have shown the negative impact of an increase in HCWs' workload without corresponding increase in manpower, especially in contexts with limited health system infrastructures (15, 22). Investing in additional in staffing is necessary to sustain the increasing number of individuals initiating ART.

Individual HIV pre and post counselling is crucial to help patients to accept their HIV positive diagnosis and prepare for life-long treatment. Post HIV counselling is fundamental mostly among individuals diagnosed whilst in a healthy state and may not realise the benefits to early ART initiation. The previous ART initiation processes which consisted several clinic visits from HIV testing, followed by determination of treatment eligibility, adherence counselling, HIV/ ART education, as well as baseline blood tests and a physical examination before receiving ARVs allowed for counselling sessions (27). The period between HIV diagnosis and ART initiation gave individuals adequate time to process the HIV positive result before deciding to start ART. Some HCWs stated concerns regarding counsellors' skills capability to manage rapid ART initiation hesitancy individuals. The need for upskilling counsellors' techniques in the era of SDI of ART was highlighted with HCWs, a factor which has been previously highlighted in other studies (27, 28). Furthermore, UTT and SDI policy awareness at population level through community and media campaigns are necessary to improve understanding of the benefits of SDI of ART at individual and population level.

Strengths and limitation of the study

This study included the perspectives of diverse healthcare workers directly involved in implementing the national Test and Treat program. The Healthcare workers were from four different high volume clinics providing ART services. However, there are several limitations of the study including a small sample size of health facilities. Data presented is from KwaZulu- Natal province, which may be different from other facilities in the province and the country. Lastly, findings were based on opinions and perspectives of key informants limited to primary health care facilities excluded provincial and private hospitals, as well as rural health facilities, where perspectives of HCWs may be different

Conclusion

Our findings identified crucial gaps impeding the attainment of the UNAIDS second 95% intended to ensuring HIV diagnosed individuals are initiated on ART on the same day. The study results illustrate the strain experienced by HCW in implementing the SDI policy, particularly work overload, skills development and facility readiness. Community awareness on the importance of SDI of ART is needed to increase patient understanding for early ART. Policymakers will need to address the identified implementation challenges in collaboration with HCWS implementing the policy to maximise the demonstrated benefits of the UTT and SDI policies.

Declarations

Ethics approval and consent to participate

The study was approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (# 00000819/2019). Written informed consent was obtained from all participants in the study**.**

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

Funding

This research was funded by the University of KwaZulu Natal through a PhD studentship bursary awarded to SMG by the College of Health Sciences.

IREX funding through the UASP alumni small grants program is acknowledged for providing a platform for the development of this publication.

Authors Contributions

S.M.G. and M.J.C. conceptualised the study. M.J.C. supervised the study processes. S.M.G wrote the main manuscript text. C.K, T.M and S.M. G conducted the analysis. M.J.C, T.M and C.K. reviewed the paper and approved the final manuscript.

Conflict of Interest*:*

All authors report no potential conflicts of interest

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Chapter 3

Chapter 3 findings revealed variations in UTT knowledge, experiences and observations among diverse healthcare workers from the four clinics in different geographical settings. While training on UTT and SDI of ART initiation was conducted at the inception of the implementation phase, the understanding and interpretation varied especially between clinicians and non-clinical healthcare providers. Denial, feeling healthy, fear of disclosure, limited knowledge about ART, fear of ART side effects, fear of stigma and discrimination were some of the factors HCW observed as hindering uptake of SDI. These findings relate to some of the reasons given by patients with fear of disclosure frequently mentioned by those who deferred SDI of ART. Chapter 1 drug stock outs and shortage of personnel were noted as some of the challenges experienced by HCW in implementing ART initiation guidelines in most SSA countries. Similarly, in chapter 3 medication stock shortages, frequent changes in reporting tools and increase in workload were noted as challenges experienced by HCW's in implementing SDI of ART. In order to understand the structural and systematic factors either promoting or hindering SDI implementation, chapter 4 investigated individual clinic level processes. The Chapter addresses objectives 3 of the thesis.

CHAPTER 4: An assessment on the implementation of same day Antiretroviral Therapy initiation in EThekwini clinics, KwaZulu Natal, South Africa

Journal of Public Health in Africa

An assessment on the implementation of Same Day Antiretroviral Therapy initiation in eThekwini clinics, KwaZulu-Natal, South Africa

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Accepted for publication in Journal of Public Health in Africa

Keywords: Universal Test and Treat implementation, Same day Antiretroviral treatment initiation.

Abstract Word count: 396/250

Main text: 2736/3500

Abstract

Introduction

The World Health Organization (WHO) recommends same-day initiation (SDI) of antiretroviral therapy (ART) for all individuals diagnosed with HIV irrespective of CD4+ count or clinical stage. The implementation of program is still far from reaching its goals. This study assessed the level of implementation of same day ART initiation.

Methods

A longitudinal study was conducted at four primary healthcare clinics in eThekwini municipality KwaZulu-Natal. Data was collected between June 2020 to October 2020 using a data extraction form. Data on individuals tested HIV positive, number of SDI of ART; and clinicians working on UTT program were compiled from clinic registers, and Three Interlinked Electronic Registers.Net (TIER.Net). Data on Non-governmental organisations (NGO) supporting the facility and services they provided was collected.

Results

Among the 403 individuals who tested HIV positive, 279 (69.2%) were initiated on ART on the same day of HIV diagnosis from the four facilities. There was a significant association between health facility and number of HIV positive individuals initiated on SDI of ART (chi-square = 10.59; p-value = 0.008). There was a significant association between facilities with support from all NGOs and SDI of ART (chi-square = 10.18; p-value= 0.015. There was a significant association between staff provision in a facility and SDI of ART (chi-square = 7.51; p value = 0.006). Urban areas clinics were more likely to have high uptake of SDI compared to rural clinics (chi-square =11,29; p-value = 0.003)

Conclusion

Implementation of the Universal Test and Treat program varies by facility indicating the need for the government to monitor and standardize implementation of the policy if the program is to yield success.

Introduction

Human Immunodeficiency Virus (HIV) treatment access is key to the global effort to end AIDS as a public health threat. An estimated 1.5 million individuals worldwide acquired HIV in 2020 (1). As of the end of 2020, 27.4 million people with HIV (73%) were accessing antiretroviral therapy (ART) globally while the rest were still waiting to start ART (2). South Africa in particular bears the greatest brunt of this epidemic with an estimated 500 000 new HIV infections and a prevalence of 18.8% among the 15-49-year age group in 2019 (1). Timely provision of antiretroviral treatment (ART) to individuals diagnosed with HIV is critical in reducing the transmission of HIV and its associated morbidity and mortality (1, 3). In September 2015, the World Health Organization (WHO) released revised global guidelines for HIV treatment and care, recommending lifelong ART for anyone testing positive for HIV - an approach that has been dubbed "test-and-treat" (4). The WHO recommended same-day ART initiation for all eligible individuals testing positive for HIV (5). Studies in South Africa have proved that immediate ART initiation soon after diagnosis is effective in improving clinical outcomes for individuals' viral suppression and thus reducing transmission of infection (6).

Despite the indisputable achievements in early ART initiation, the problem is far from being resolved even in regions with full access to ART (7). Estimates from healthcare facilities in United States of America (USA) suggest that of the 85% diagnosed with HIV, only 62% are initiated on ART on the same day of diagnosis (7). On the other hand, studies conducted in Sub-Saharan Africa suggest that there is delayed initiation among those diagnosed with HIV (5, 8) partly due to healthcare facility challenges (9) and people living with HIV (PLWH) may wait for over a month before being initiated on ART after establishment of eligibility (5, 10). For instance, in Uganda and Lesotho, clinics typically initiate ART to diagnosed individuals after an average of 8 and 10 days respectively (11, 12). The reasons for these delays are complex and involve a combination of structural, social, psychological factors and poor healthcare infrastructure in some settings (13-15).

The South Africa Department of Health has implemented the Universal Test and Treat (UTT) program since September 2016 (16, 17). However, there is a need to optimise facility- level implementation to ensure the program is effective. The demand for ART expansion in South Africa

has increased the pressure on an already burdened primary health care system. In South Africa the implementation of the UTT and SDI policies in facilities were not supported with expanded facility infrastructural development and strengthening of processes. The COVID-19 pandemic has made it worse with HIV testing and ART initiations heavily reduced due to more clinicians being allocated to COVID-19 clinics (18). South Africa encourage same-day ART initiation but evidence on how best to implement it, particularly in resource constrained communities remains scarce (19). As part of quality assurance, the National Department of Health developed the National Core Standards against which service delivery by health establishments can be assessed. It is crucial to understand how public primary healthcare facilities are standardising implementing the UTT policy against the set policy expectations of SDI. We assessed facility implementing of same day ART initiation at 4 facilities in eThekwini, KZN, South Africa to identify gaps and formulate solutions to strengthen the policy benefits to meet the second 95% of the 2030 HIV targets within the Sustainable Development Goals which requires initiation of 95% of the HIV positive individuals.

Methods

Study Design and Setting

A longitudinal study was conducted at four primary healthcare clinics in eThekwini municipality in KwaZulu-Natal (KZN), South Africa between June 2020 and October 2020. The study sites were Ithembalabantu, Pinetown, D and Qadi clinics. KZN has 1.9 million people living with HIV 32.5% of province population (1) of which only 1.1 million have been initiated on ART (20). Of the estimated 650 000 people living with HIV in eThekwini 383 869 people are on the ARV programme (4). The eThekwini district is densely populated with 1 446.8 people per square kilometre and comprises of urban, semi urban and rural areas. We selected study clinics from three settings; i) 2 facilities (Ithembalabantu and D clinic) in a densely populated township of Umlazi with a high HV prevalence, ii) Pinetown clinic in Pinetown, a semi suburban town surrounded by townships and informal settlements and iii) Qadi clinic in rural Umzinyathi district municipality north of eThekwini municipality. Ithembalabantu clinic focuses on HIV testing and treatment management with has approximately 14 100 patients on ART with about 100 people testing for HIV, nearly 70 testing HIV positive and an average of 45 individuals initiated on treatment each

month. Ithembalabantu clinic offers HIV and Tuberculosis (TB) services for the people of Umlazi and surrounding areas. D clinic tests an average of 150 people for HIV monthly with approximately 80 HIV positive with 60 initiating on ART. D clinic is a government comprehensive primary health care facility which provides medical facility that focuses on the initial treatment of medical ailments including HIV and TB-related treatment. The clinic covers a large catchment area of D, W, R, V, B sections of Umlazi. Pinetown Clinic is a municipal primary healthcare facility which provides HIV and TB-related treatment as well other minor health conditions. It is a multi-racial town servicing people from Pinetown, Westville, Cowies Hills, Marianhill and surrounding townships such as Kwandangezi and Nazareth. The clinic tests an average of 200 people for HIV, with 110 testing HIV positive and about 80 initiating on ART monthly. Qadi clinic is government rural facility offers health services to the rural community of Umzinyathi district. The clinic tests an average of 70 people for HIV, with 50 testing HIV positive and about 35 initiating on ART monthly.

The selection of the clinics was intended to ensure comparison of the level of policy implementation across study clinics. The clinics were located in socio-economically different settings; peri-urban, urban and rural. As such their infrastructure and the level of support from NGOs, availability of sufficient consultation rooms, water, sanitation and electricity availability varied across the facilities. These factors may have effect on the level of implementation of SDI in different facilities.

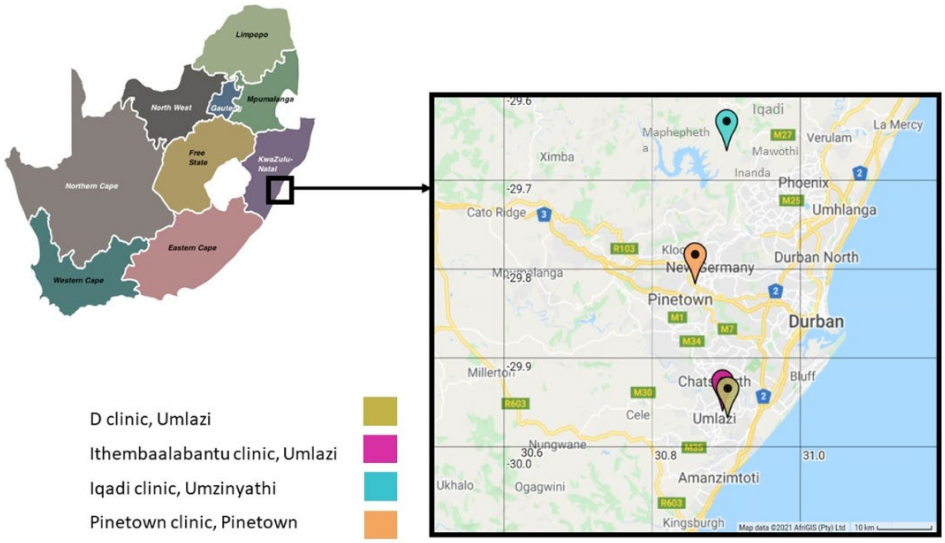

Fig 1: Geographical locations of the four healthcare facilities in eThekwini municipality Source: Adapted from Moodley et al. (21)

Data collection

This study was a longitudinal as it involved continuous collection of daily data on HIV testing, ART initiations and support from Non-Governmental Organisations on SDI. The same data elements were collected at different time points. Data was collected from the same sources over monthly intervals and used to track changes in numbers each month. The data was compiled from paper patient registers, staff registers and Three Interlinked Electronic Registers Net (TIER.Net), which is an electronic ART database developed by the University of Cape Town's Centre for Infectious Disease Epidemiology and Research. TIER.Net is used in public health facilities in South Africa to monitor baseline clinical care and client outcomes over time, and is also the platform into which HIV tests are electronically captured. Patient characteristics and demographic information are routinely captured into TIER.Net by staff working at the healthcare facilities. The data extraction form was used to collect information on the number of Non-governmental organisations (NGO) supporting the facility, and the services provided to compare the level of support the facilities received from partner organisations. Furthermore, data on the number of nurses in the facility, daily HIV diagnosis, number of ART initiations, number of clinic staff members involved in ART initiation and number of days taken by the facility to

initiate a newly HIV diagnosed individual on ART were also captured. The data extraction form used to collect the data was loaded on the Kobo Collect application (Cambridge, MA, USA) on Android mobile devices.

Data Analysis

We used descriptive statistics (median, interquartile range [IQR]) to report the number of professional nurse's in the clinic on a typical day, number of adults tested for HIV each day, new adults diagnosed with HIV per day, number of NGOs supporting the facilities and the actual support provided by the NGO's. We assessed facility related factors that determine SDI such as number of NGO's supporting the facility, number of staff provision from NGO's, number of nurses in the facility and number of nurses trained on SDI in the clinic. We determined association between the number or proportion of HIV positive individuals on SDI for ART and the facility as well as the characteristics of the facilities including clinic setting (i.e. rural, peri-urban and urban, number of NGOs supporting the facilities, number of clinic staff and staff provision from NGO's using the chi-square test.

Ethical considerations

This study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC/00000819/2019).

Results

Clinic profile characteristics

On a typical day the median number of professional nurses in the clinic was 9 (IQR, 6-13). The median (IQR) number of adults tested for HIV each day was 38 (IQR, 19-75) with 8 (IQR, 7-10) new adults diagnosed with HIV per day and 70 (1QR, 60-90) new adults getting a positive HIV diagnosis each month. From those diagnosed with HIV each month, a median of 55 (IQR, 50 -70) were initiated on ART on the same day of HIV diagnosis. The study also showed a median (IQR) of 7806 (4006-13800) patients on HIV treatment management in the four facilities with a median

of 700 (IQR, 325-2150) lost to follow up. The median number of clinic staff members involved in the ART initiation program was 6 (IQR, 5-7). An individual spent at least 2 hours to complete all the processes in the clinic after getting an HIV diagnosis (Table 1). Individuals spent more time at clinic D (3-4 hours) compared to clinic B (1-2 hours). Urban areas clinics were more likely to have high uptake of SDI compared to rural clinics (chi-square =11,29; p-value = 0.003)

Same day ART Initiation Individual Clinic Performance

A total of 403 individuals were diagnosed with HIV and 279 (69.2%) of them were initiated on ART on the same day in 4 facilities during the study period June 2020 to October 2020. Out of the 279 individuals on SDI in the four facilities clinic A recorded the highest number (82 individuals (29.4 %)) and clinic D reported the least number (61 (21.9%)). There was a total of 124 individuals who were not part of SDI, clinic D recorded the highest number of 40 (32.3%) while clinic A had the lowest (18 individuals i.e14.5%).At a facility level, at clinic D 101 individuals had a positive HIV result with 61 (60.4%) of them initiated on ART on the same day, clinic B had 102 individuals tested HIV positive with 67 (65.7%), clinic A recorded 100 HIV diagnosed individuals and 82 (82.0%) went on SDI and clinic C had 100 individuals tested HIV positive with 69 (69.0%) initiated on the same day. There was a significant association between health facility and number of HIV positive individuals initiated on SDI (chi-square = 10.59; p-value = 0.008) Table 2.

Enablers of SDI implementation

Non-Governmental Organisations Support on SDI of ART

There were 7 seven Non-Governmental Organisations (NGOs) supporting SDI of ART in the study area. Only 3 of these NGOs i.e. Health Systems Trust (HST), TB HIV, THINK were found to be supporting the four facilities considered in this study. There was a significant association between facilities with all 7 organisations supporting them and ART SDI (chi-square = 10.18; p-value= 0.015 (Table 3). Clinic A was the facility supported by all 7 NGOs operating in eThekwini and reported the highest number of SDI (Health Systems Trust, TB HIV, THINK, Aids Healthcare Foundation, Right-to-Care, MATCH, CAPRISA) 7 vs clinic B with 3 NGO's (Health Systems

Trust, TB HIV, THINK). Extensive support on staff trainings, HIV Counselling and Testing services, TB program support, site performance assessments, provision of personnel, conducting HIV research studies, CCMDD program, provision of equipment and resources and data validation and verification was provided by the NGOs (Table 2)

Staff provision from NGOs and number of nurses in a clinic

Staff provision from NGO's varied in the four facilities to cover up for staff shortages. There was a significant association between staff provision in a facility and SDI (chi-square = 7.51; p value = 0.006) (Table 2). Clinic A had the highest number of staff provision with 6 nurses, 6 HIV Counselling and Testing Counsellors, and 5 Data Capturers vs clinic C with 2 nurses, 3 HIV Counselling and Testing Counsellors and 2 Data Capturers. Twenty-six nurses were trained by HST, HIV TB, MATCH and THINK on ART initiation program focusing on UTT and SDI. Out of the 26 nurses, clinic D had the most number of nurses (11) who were trained, 9 from clinic A and the least trained nurses (3) from clinics B and C. Clinic A had the most number of nurses available for consultations 14 vs clinic B and C with the least nurses 6. Clinic B was the only facility with a Doctor/s available daily for complicated patients' cases as well as for referrals compared to other 3 facilities (A, C and D clinic) which had a Doctor coming to the facility once a week for complicated booked patients' cases (Table 2). The facilities reported different amount of time spent to complete all the ART initiation processes when SDI was implemented. Clinic D reported the longest time (3 hours) compared to clinic B (2 hours).

Discussion

Our assessment of same day ART initiation implementation in eThekwini clinics indicated that all the four facilities were implementing the UTT policy but at varying levels. Contrary to the observed SDI exceeding 90% (Pascoe et al.,) observed in high-income countries, uptake of SDI in our study facilities was low varying between 60% and 82% reflecting differences in how the policy was being implemented at the different facilities. Moreover, none of the four facilities achieved the second 95% of the 2030 HIV targets within the Sustainable Development Goals which requires initiation of 95% of the HIV positive individuals. This indicates the need for more effort on the second 95, particularly among resource constrained communities so as to reach the 95–95–95 targets.

We observed an association between staff provision in a facility and SDI which may explain the long waiting times in facilities with less staff provision. Shortage of staff has been reported as a barrier to SDI implementation at a health-facility (2). The expansion of the ART program caused staff shortages and several countries in SSA coped by hiring additional staff and training of health care staff to prepare them for task shifting (22). There has of high demands in the health care system under UTT due to increased number of individuals on ART. Under such circumstances staff shortage leads to long queues, often frustrating both patients and health care providers as some patients are not initiated to ART on the same day.

Patients spent most of their time waiting between service points for the ART initiation processes after diagnosis. They spend an average of 2 hours to complete ART initiation processes because of several queues that they should join to complete the process. Patients are expected to start with the COVID-19 screening, get counselled and tested for HIV, have a record file, consult with the clinician for all baseline history, phlebotomist for baseline blood withdrawals and finally collect medication at the pharmacy point. Uganda has overcome this challenge by having centralised ART start processes (McRobie et al.,). Generally, the waiting time we observed is similar in other infectious disease clinics in Sub-Saharan Africa. (23). Until these delays are fixed, some patients may prefer to delay their initiation period than wait leading to poor linkage to HIV care.

A heavy dependence on NGO's to assist with the implementation of UTT was observed at all the facilities. Such support was on personnel provision, resources, technical and training assistance. Similar situations prevail in Gauteng clinics where NGOs were the backbone for the SDI program (22). While the support of NGOs is important in improving services it does not guarantee sustainable achievement of the SDI goals if resource and systems shortfalls are not addressed by the government. This is because some NGOs lose funding or change scope of work thus disrupting services they will be supporting.

The study was conducted in large urban, peri-urban and rural communities and this provides a reasonable basis for generalizability for the majority of people living with HIV in South Africa. We collected data on multiple providers at multiple times of the day without interfering with patient flow. Our study was limited to adults and hence no generalisations can be made regarding the characteristics of facility performance on SDI among infants and children.

Conclusion

There are variations in how facilities even in in the same municipality are implemented SDI program. There is need for the government to monitor and standardize implementation of processes at facility level. Nongovernmental organizations are a valuable source of technical and financial input, but perhaps their greatest contribution is their political freedom to promote innovation. However, the government has to step up the mobilization of expertise and fostering of partnerships to develop innovative approaches to delivering HIV services, to strengthen the system, and to enhance effective program implementation.

Declarations

Ethics approval and consent to participate

The study was approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (#00000819/2019). Written informed consent was obtained from all participants in the study**.**

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

Funding

This research was funded by the University of KwaZulu Natal through a PhD studentship bursary awarded to SMG by the College of Health Sciences.

IREX funding through the UASP alumni small grants program is acknowledged for providing a platform for the development of this publication.

Authors Contributions

S.M.G. and M.J.C. conceptualised the study. M.J.C. supervised the study processes. S.M.G wrote the main manuscript text. C.K, T.M and S.M. G conducted the analysis. M.J.C, T.M and C.K. reviewed the paper and approved the final manuscript.

Acknowledgements:

We thank the people who participated in this study and UKZN College of Health Sciences for funding the work.

Conflict of Interest*:*

All authors report no potential conflicts of interest.

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Table 1. Clinics profile characteristics

	Median, [IQR]
Number of headcount patients serviced by the clinic monthly	8 250 (7 250-10750)
Number of professional nurse's in the clinic on a typical day	9 (6-13)
Number of adults tested for HIV each day	38 (19-75)
New adults diagnosed with HIV per day	8 (7-10)
New adults getting a positive HIV diagnosis each month	70 (60-90)
Adults initiated on ART on the same day of HIV diagnosis	55 (50 -70)
Number of patients on HIV treatment management in the four facilities	7 806 (4006-13800)
Number of lost to follow up patients	700 (325-2150)
Number of clinic staff members involved in ART initiation program	6 (5-7)

Variables	Same-day initiation (SDI) Freq (n)	%	Not same-day initiation (NSDI) Freq (n)	%	*p-value*
Staff Provision from NGO's					
More Staff provision	82	89.28	61	53.72	0.006
Less staff provision	31	10.72	7	46.28	
Non-Governmental Support in clinic					
All NGO's	82	70.23	18	6.77	0.014
Less than 7 organisations	197	29.77	106	93.23	
Health facility SDI initiations					
Differences in SDI per facility	279	69.24	124	30.76	0.008
Clinic Setting					
Urban	82	29.40	18	14.51	
Peri- Urban	128	45.90	75	60.48	0.035
Rural	69	24.70	31	25.01	

Table 2: Association of SDI implementation in individual facilities

Facility(s)	**NGOs supporting the facility(s)**	**Services supported by the NGO's**
	Health Systems Trust	Staff trainings
A, B, C, D	TB HIV	TB program support
	THINK	HIV Counselling and Testing services
A, C, D	Aids Healthcare Foundation	Site performance assessments
A, D	Right-to-Care	Provision of personnel
	CAPRISA	Provision of equipment resources
		Data validation and verification
A	MATCH	Conducting HIV research studies
		CCMDD program

Table 3: Non-Governmental Organizations clinics support

Chapter 4 on facility assessment results highlighted clinic level inconsistencies in implementing UTT policy thus indicating non-standardisation of policy guidelines compliance. Variations in staff provision among the clinics were observed and that compromised the effectiveness in implementation of the policy. Support from Non-Governmental Organisations tended to increase the effectiveness of implementation of SDI policy as noted in Chapter 1 which showed that countries with NGO support were quick to implement changes in policy guidelines. Chapter 5 therefore evaluated the impact of SDI vs delayed ART initiators on clinical outcomes and retention to care. The Chapter addresses objective 4 of thesis.

CHAPTER 5: The impact of Same Day Antiretroviral Therapy initiation on retention in care and clinical outcomes at four EThekwini clinics, KwaZulu Natal, South Africa.

The impact of same-day antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa.

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Under Review in BMC Global Health Research and Policy.

Contributorship

S.M.G. and M.J.C. conceptualized the study. M.J.C. supervised the study processes. S.M.G wrote the main manuscript text. C.K and S.M. G conducted the analysis. M.J.C and C.K. reviewed the paper and approved the final manuscript.

Abstract

Although same-day initiation (SDI) of antiretroviral therapy (ART) consistently increases ART uptake, retention in care after ART initiation is still a challenge. Public health behaviours, such as retention in HIV care and adherence to antiretroviral therapy (ART) pose major challenges to reducing new HIV transmission and improving health outcomes among HIV patients. We evaluated 6-month retention in care, and clinical outcomes of an ART cohort comprising of SDI and delayed ART initiators. We conducted a 6 months (December 2020 to May 2021) observational prospective cohort study of 403 patients who had been initiated on ART between June 2020 and November 2020. A structured questionnaire was used to abstract data from patient record review which comprised the medical charts, laboratory databases, and Three Interlinked Electronic Registers.Net (TIER.Net). We collected patients' socio-demographic characteristics, the number of scheduled hospital visits and the number of actual visits after diagnosis, patient adherence, retention in care and clinical outcomes after 6 months. Treatment adherence was ascertained by patient visit constancy for the clinic scheduled visit dates. Retention in care was determined by status at 6 months after ART initiation. Bivariate and multivariate logistic regression was used to determine factors that influenced clinical outcomes at 6 months. Among the 403 participants enrolled in the study and followed up, 286 (70.97%) and 267 (66.25%) complied with scheduled clinics visits at 3 months and 6 months, respectively. Seventeen (4.22%) participants of those that had not remained in care after six months had died, 6 (1.49%) had been transferred to other health facilities and 113 (28.04%) had been lost to follow-up. Among those that had been lost to follow-up, 30 (33.63%) deferred SDI of ART while 75 (66.37%) initiated ART under SDI. One hundred and eighty-nine (70.79%) participants who had remained in care were SDI patients while 78 (29.21%) were SDI deferred patients. In the multivariate analysis

results showed that among those remaining in care (aOR: 2.44; 95% CI: 1.61–3.87) and contraction of other diseases during the period of the study (aOR: 1.21; 95% CI: 1.03–1.43) were the predictors of viral load detection. Furthermore, SDI patients who had not remained in care were 2.4 (95% CI: 1.17–4.93) times more likely to have increased viral load than those who had been returned in care. Viral suppression under UTT proved higher but with poor retention in care. Individuals initiating ART under SDI policy may often start treatment in better health, subsequently remaining in care showed clinically meaningful outcomes. However, the results also emphasise a vital need, to not only streamline processes to increase immediate ART uptake further, but also to ensure retention in care.

Key words

Same day ART initiation, retention in care, ART adherence, clinical outcomes.

Introduction

Availability of antiretroviral therapy (ART) to individuals diagnosed with Human Immunodeficiency Virus (HIV) has led to improved disease prognosis, healthier quality of life and reduction of HIV transmission (1). However, treatment adherence and retention in care among such individuals remains fundamental in attaining these outcomes (2, 3). In 2015, the World Health Organization (WHO) recommended 'same-day ART initiation' (SDI) of antiretroviral therapy (ART) under the Universal Test and Treat (UTT) policy for people living with HIV (PLHIV) (4, 5). Many countries in sub-Saharan Africa (SSA) including South Africa, have introduced the SDI into their national HIV guidelines (6, 7). However, WHO noted that the anticipated achievements of such an approach could only be accomplished if improvements were made in retaining patients in care (8).

The Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO) introduced the 95-95-95 initiative to further decrease new infections globally (9). The initiative maximizes the effect of ART coverage by emphasizing that 95% of HIV-positive people should know their status, 95% of those eligible for ART should be initiated on ART, and 95% of those on ART should achieve and maintain viral suppression (9, 10). However, sub-Saharan Africa (SSA) region may miss the UNAIDS) 95-95-95 target of reducing HIV epidemic by 2030 (11). By the end of 2019, SSA had reported that 77% of PLHIV knew their HIV status, 72% of those diagnosed were initiated on ART and only 65% of those on ART achieved sustaining viral load suppression (12). Retention in HIV care intensely affects HIV disease outcomes at individual and population levels (13, 14). Currently, retention in HIV care programmes has varied widely worldwide (15). In a 2015 review, the global retention in HIV treatment management was 74% at 6 months and 60% at 12 months (16).

South Africa has registered moderate success with HIV testing, ART initiation and viral suppression, achieving 85% and 86% success rates, respectively; however, only 71% of the people eligible for ART are on treatment (17). It is well documented that young people aged less than 30 years and men, are being lost to follow-up along the entire HIV care cascade (18). Furthermore, most individuals are lost in the HIV care cascade between HIV diagnosis to the start of treatment (19). Effective care of people living with HIV/AIDS (PLWH) requires that patients are provided with satisfactory care, adhere to their treatment regimen, and are retained in care (6, 20).

In the field of HIV medicine, patients who receive regular medical care and attend scheduled clinic visits are considered retained in care (16). Retention in care is not only important for the individual health of people living with HIV, but also for public health (21). HIV-positive individuals who adhere to treatment and are retained in care can suppress the HIV viral level in their serum to undetectable levels, thus eliminating the risk of transmitting HIV to others (22, 23). Accordingly, retention in care is a critical pillar of public health strategy to eliminate HIV transmission. Our study assessed the association between retention in care, clinical outcomes, and predictors of attrition by comparing individuals who accepted same day ART initiation and those who deferred same day ART initiation.

Materials and Methods

Study design and population

We conducted an observational prospective cohort study among patients who had taken antiretroviral treatment from 4 primary healthcare facilities in eThekwini municipality, KwaZulu-Natal province, South Africa. KZN has 1.9 (27%) million people living with HIV of which only 1.1 million are on ART (18). Of the estimated 650 000 (11.4%) people living with HIV in

eThekwini, there are approximately 383 869 people in the ARV program (9). The eThekwini district is densely populated (3, 702,231) comprising of urban, semi-urban, and rural areas (24). We selected study clinics from the three settings; i) 2 facilities (*Ithembalabantu* and D clinic) from a densely populated Umlazi township which is also known to have high HV prevalence (24) ii) Pinetown clinic in Pinetown, a semi suburb town (these are places that offer a balance between township and suburb tranquillity) surrounded by townships and informal settlements which all seek services at the facility and iii) *Qadi* clinic in rural *uMzinyathi* district municipality north of eThekwini municipality. uMzinyathi district has high levels of poverty, unemployment, and HIV/AIDS (25).

The study recruited participants meeting the eligibility criteria for the national guidelines on ART initiation. The guidelines state that all HIV-positive diagnosed individuals should rapidly initiate on ART regardless of CD4 count, receive treatment adherence counselling, those not ready to start ART and Tuberculosis asymptomatic awaiting for TB results initiate later as per program guidelines. We purposively enrolled 403 participants who tested positive for HIV and either accepted or deferred ART initiation from June to November 2020. The study participants were followed up for a period of six months after ART initiation from December 2020 to May 2021.

Data Collection

A structured questionnaire was used to extract information on patient adherence to treatment, and retention in care and clinical outcomes using patient chart reviews. Data were collected electronically using the Kobo Collect application on Android mobile devices(26). Data was collected from HIV patient medical charts, National Health Laboratory Services (NHLS) database for specimen results and Three Interlinked Electronic Registers.Net (TIER.Net). Routinely collected HIV patient level data that was entered into the electronic medical record system, called

Three Interlinked Electronic Registers.Net (TIER.Net), an electronic ART database developed by the University of Cape Town's Centre for Infectious Disease Epidemiology and Research. TIER.Net. We extracted individual demographic characteristics, clinic visit dates, recorded comorbidities, specimen results and clinical outcomes at 6 months visit after ART initiation.

Ethical considerations

Participants consented to be followed up using their medical records after 6 months of ART initiation. This study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC/00000819/2019)

Data Analysis

Adherence to treatment was ascertained by consistently attending scheduled patient visit dates. Retention in care was determined by clinic visits status at 6 months after ART initiation. Data collected was analysed using Stata version 17.0 (College Station, TX, USA). Descriptive and bivariate analysis were used to summarize socio-demographic characteristics of the participants as well as evaluating their association with the study outcome which was viral load detection and retention in care. Bivariate associations between each independent variable and viral load detection were determined using unadjusted logistic regression model, and variables associated with viral load detection at the level of $p \leq 0.2$ were included in the multivariable logistic model. Viral load detection was associated to a number of factors which were also correlated with CD4 count. Therefore, our analysis considered all these factors in the model to minimize confounding effects. To achieve this, we estimated a step-wise model building for our outcome on the initial model by adding more controls at each stage (First level model: unadjusted (socio-demographic

characteristics of participants); Second level model: added health outcomes and haematology laboratory results weight; Final-model: adjusted for date of start of ART. We also tested for interaction and for clustering by hospital site in order to fit it as a random effect. However, when site was included as our random effect to allow for robust estimate of viral load detection within and between the study clinics there, was no evidence of interaction. Goodness of fit and model adequacy were tested using the fit is the Hosmer–Lemeshow test (27). The primary outcomes were retention in care and viral suppression at 6 months after ART initiation. Retention in care was defined as consistently attending all (1, 3 and 6 months) scheduled clinic visits for treatment collection and clinical management. Viral suppression was defined as ≤50 copies/ml considered as viral suppressed within 6 (months of ART initiation, a time period selected to capture the 6 months routine monitoring visit according to ART national guidelines. Secondary outcomes evaluated in the study included the prevalence of comorbidities, hospitalisations, demographic predictors and level of CD4 results.

Results

Participants characteristics at the time of ART initiation

All 403 study participants were followed up using routine health data collected in tier.net and medical charts for 6 months from the date of HIV diagnosis. Two hundred and eighty-six (70.97%) and 267 (66.25%) visited scheduled clinics at 3 months and 6 months, respectively. Among those that had not remained in care after six months, 17 (4.22%) had died, 6 (1.49%) had been transferred to other health facilities and 113 (28.04%) had been loss to follow-up. Among those that had been lost to follow-up, 30 (33.63%) deferred SDI of ART while 75 (66.37%) initiated ART under SDI. Participants who had remained in care, 189 (70.79%) were SDI patients while 78 (29.21%) were SDI deferred patients (Table 1). Among the 189 SDI patients, 178 (94.18%) had their viral load

undetected while 11 (5.82%) had a detectable viral load. In addition, the SDI deferred patients, 29 (37.18%) had their viral load suppressed while 49 (62.82%) had a detectable viral load. However, there was no evidence (p=0.34) of association between viral load suppression and time of initiation when controlled for remaining in care or not.

Although there was no association between viral load and age (p=0.82), most respondents aged between 29- 39 years 71.8% (n=92) years had an undetectable viral load. We also observed that 75.8% (n=138) of the females had suppressed viral load. The majority 69.1% (n=98) of the respondents were single and of these, 69.0% (n=98) had an undetectable viral load. Among the (n=142) unemployed patients, we observed that 71.1% (n=101) had an undetectable viral load. We observed that there was a correlation between viral load and the number of sexual partners (p=0.027). Two hundred and twenty-five participants had more than one sexual partner and of these, 68.4% (n=154) had an undetectable viral load. Knowledge of UTT, HIV status of partner, scheduled clinic visits at 3month after initiation, remaining in care (6 months after initiations), number of hospitalisations after testing and time between testing and initiation were all associated with viral load ($p<0.05$) (Table 1).

Table 1: Socio-demographic characteristics of patients based on their viral load detection

	Viral load				
	Undetectable		**Detectable**		***p-value***
Variables	(n)	%	Freq (n)	%	
Age					
18-28	65	69.15	29	30.85	0.820
29-39	92	71.88	36	28.12	
40-50	42	76.36	13	23.64	
51-62	14	70	6	30	
Gender					
Female	138	75.82	44	24.18	**0.048**
Male	75	65.22	40	34.78	
Marital status					
Cohabiting	39	72.22	15	27.78	0.307
Divorced	5	55.56	4	44.44	
Married	54	73.97	19	26.03	
Single	98	69.01	44	30.99	
Widowed	17	89.47	2	10.53	
Education Level					
Primary	54	70.13	23	29.87	0.912
Matric	98	69.01	35	27.13	
Diploma	65	71.43	26	28.57	
Employment status					
Employed	75	74.26	26	25.74	0.826
Self Employed	18	72	7	28	
student	19	65.52	10	34.48	
Unemployed	101	71.13	41	28.87	
Biological children					
No	40	64.52	22	35.48	0.157
Yes	173	73.62	62	26.38	
Knowledge of Universal Test and Treat (UTT)					
No	151	51.01	90	84.11	**0.001**
Slightly	47	15.88	11	10.28	
Yes	98	33.11	6	5.61	
Number of sexual partners					
One	59	81.94	13	18.06	**0.027**
2 or more	154	68.44	71	31.56	
HIV status of sexual partner					
Negative	6	75	2	25	0.069
Unknown	108	66.26	55	33.74	
Positive	99	78.57	27	21.43	
Tested positive for HIV before					
No	176	70.12	75	29.88	0.153

Yes	37	80.43	9	19.57	
Time between HIV test and initiation					
Later	30	34.48	57	65.52	**0.000**
Same Day	183	87.14	27	12.86	
Clinic scheduled visit at 1 month					
Yes	211	71.53	84	28.47	0.373
No	0	100	0	0	
Clinic scheduled visit at 3 month					
Yes	208	76.19	65	23.81	**0.000**
No	5	20.83	19	79.17	
Clinic scheduled visit at 6 month					
Yes	207	77.53	60	22.47	**0.000**
No	20	20	24	80	
Patient still in care					
Yes	207	77.53	60	22.47	**0.001**
No	5	38.46	8	61.54	
Infections during the study period (6 months)					
Yes	53	39.26	82	60.74	**0.000**
No	160	98.77	2	1.23	
Number of hospitalisations					
None	4	23.53	13	76.47	**0.000**
One	3	15	17	85	
Two	206	79.23	54	20.77	

SDI initiation and its association with CD4 count and co-infections

Forty-five point seven percent (45.7%; n=184) of the respondent had contracted another disease during the six months' follow-up period. Of the 403 56.5% (n=104) were SDI deferred patients while 43.5 (n=80) (p=0.001) were SDI. The most common coinfection contracted by both the SDI (n=44) and SDI deferred patients (n=49) was STI shingles. On the other hand, 42.3% (n=44) of the SDI deferred patients had TB while only 1.25% (n=1) of the SDI patients had TB. We also observed that 9.78% (n=18) of the SDI patients had contracted hypertension while none of the SDI deferred patients had contracted the same. Furthermore, 12.5% (n=10) and 7.5% (n=5) of the SDI patients had contracted Covid-19 and Cryptococcus Meningitis respectively while 5.8% (n=6) and 2.9% (n=3) of the SDI deferred patients had contracted the same diseases.

In addition, we observed that among the SDI patients, 65.2 (n=182) had high CD4 count and 34.8% (97%) had low CD4 count below 200ml copies. On the other hand, among the SDI deferred patients, 37.9% (n=47) and 62.1% (n=77) had high and low CD4 count. We also observed that of the 78 SDI deferred patients who had remained in care, 33.3% (n=26) had high CD4 count while 66.7% (n=52) had low CD4 count. On the other hand, of the 189 SDI patient, 82% (n=155) had high CD4 count while 18% (n=34) had low CD4 count.

Factors associated with viral load suppression 6 months after initiation

Among the variables observed to be associated with the viral load detection in the bivariate analysis; gender (OR: 1.672; 95% CI: 1.002–2.791), number of sexual partners (OR: 2.092; 95% CI: 1.07–4.061), age (OR: 0.941; 95% CI: 0.734–2.791), ART start date (OR: 0.078; 95% CI: 0.042–0.141) and partner HIV status (OR: 0.621; 95% CI: 0.387–0.995) were significantly associated with viral load detection. Missing clinic scheduled visits at 3 months (OR: 2.16; 95% CI: 1.368-4.384), remaining in care (OR: 3.52; 95% CI: 1.743–5.498) and the number of hospitalizations after HIV diagnosis (OR: 0.173; 95% CI: 0.092–0.326) were also significantly associated with the viral load detection (Table 2).)

Table 2: Bivariate analysis on factors associated with viral load detection.

Determinant	OR (Unadjusted)	95% CI	P-value
Age			
18-28	Reference		
29-39	0.877	0.489–1.571	
40-50	0.693	0.324–1.484	
51-62	0.96	0.335–0.691	**0.629**
Gender			
Female	Reference		
Male	1.67	0.546–1.37	**0.049**
Marital status			
Married	Reference		
Single	0.96	0.78–1.18	0.683
Employment status			
Employed	Reference		
Unemployed	1.06	0.88–1.27	0.566
Biological children			
No	Reference		
Yes	0.65	0.36– 1.18	0.159
Number of sexual partners			
One	Reference		
2 or more	2.09	1.08–4.06	**0.029**
HIV status of sexual partner			
Negative	Reference		
Positive	0.62	0.39–0.99	**0.048**
Time between HIV test and initiation			
Later	Reference		
Same Day	0.08	0.04–0.14	**0.000**
Clinic scheduled visit at 3 months			
Yes	Reference		
No	1.16	1.03–4.85	**0.000**
Patient still in care			
Yes	Reference		
No	3.52	1.743–5.498	**0.023**
Infections during the study period (6 months)			
Yes	Reference		
No	1.277	29.42–520.68	**0.000**
Hospitalizations			
Yes	Reference		
No	0.17	0.09–0.33	**0.000**

Our results showed that among those remaining in care (aOR: 2.44; 95% CI: 1.614–3.872) and contraction of other diseases during the period of the study (aOR: 1.212; 95% CI: 1.031–1.425) were the predictors of viral load detection. We also observed that the odds of viral load surge were 2.313 (95% CI: 1.591–4.987) higher among those not remaining in care than those who remained in care. In addition, patients with chronic conditions such as hypertension were 0.082 (95% CI: 0.008–0.257) times more likely to have reduced viral load than those with Covid-19.

Table 3: Multivariate logistic regression on factors influencing viral load suppression.

Determinant	OR (Unadjusted)	95% CI	p-value	OR (adjusted)	95% CI	p-value
Remain in care						
Yes	Reference					
No	**3.52**	**1.743–5.498**	**0.023**	**2.313**	**1.591-4.987**	**0.001**
Infections during the study period (6 months)						
Covid-19	Reference					
Hypertension	**0.031**	**0.004-0.257**	**0.001**	**0.071**	**0.006-0.732**	**0.026**
STI shingles	0.905	0.724-1.074	0.831			
Tuberculosis	0.374	0.100-1.403	0.145			

Viral load suppression among same day initiators at 6 months after ART initiation were influenced by retaining in care and having co-morbidities like hypertension. We observed that among SDI patients, retaining in care was a significant (aOR: 3.869; 95% CI: 1.091–4.037) predictor of viral load suppression. Same day ART initiation patients who had not been retained in care were 2.4 (95% CI: 1.165–4.928) times more likely to have increased viral load than those who had been retained in care. Also, SDI patients with hypertension were 0.071(95% CI: 0.006–0.732) more likely to have reduced viral load than those who had contracted Covid-19.

Discussion

In a cohort of HIV diagnosed individuals who chose to start or defer ART initiation under the UTT policy, we observed a gradual reduction in the number of patients who went for treatment collection at three months and six months after ART initiation. Earlier studies conducted such as the the Rapid Initiation of Treatment (RapIT) trial and the Simplified Algorithm for Treatment Eligibility (SLATE) study in South Africa and Kenya, demonstrated that SDI improved viral suppression rates but showed limited evidence for improved retention in care (28).

The increase in loss of patients to follow up among participants who initiated ART on the same day of HIV diagnosis we observed corroborates with results from the SLATE trial conducted in South Africa and Kenya that in that same-day treatment initiation increased rapid ART uptake but not necessarily retention in care especially in the early months after initiation (29). Trends in South Africa indicate that individuals increased risk of being lost to follow-up at six months' months as a result of accelerated ART initiation. Treatment readiness , pill burden and in some cases disclosure may contribute to increased loss to follow up (30).

Intensified patient education focussing on the benefits of ART initiation and consistent treatment is crucial to increase patient retention (31, 32). Furthermore, additional treatment support such as weekly treatment literacy classes and continuous adherence counselling sessions are most relevant in the first six months of care to reduces cases of patient attrition which our data and other studies indicated that it is substantial in the first six months of care (33, 34). In a study conducted by Pascoe, Fox (31), Fast-Track Initiation Counselling (FTIC) had some short-term but no long-term benefits suggesting that for FTIC initiation had treatment adherence benefits, particularly in the test-and-treat era with higher chances of initiating individuals who are not psychologically ready for treatment. To achieve this, FTIC support post-initiation may need to be strengthened and paired

with other effective interventions designed to support patients with adherence and retention (31). Consistent with previous studies (34, 35), the time restrictions to initiate ART in line with SDI policy probably resulted in the overall decline in the quality of extensive post HIV counselling before ART initiation

Our findings indicate that substantial effort is required to encourage treatment adherence and further sustain retention of PLHIV in care, especially during the first six months of ART initiation. Several socio-demographic characteristics such as sex, gender, marital status, and employment status must be considered when developing policy and HIV care interventions since these pose technical hitches in effective policy implementation and sustainability on public health benefits.

We found that individuals who remained in care were more likely to have a suppressed viral load at 6 months. Unsuppressed viral load at 6 months was associated with sub-optimal ART adherence, and this is corroborated by findings in studies conducted in Nigeria and Malawi amongst individuals attending a public ART programme (2, 36). According to these authors, patients who were tracked back into care after missing their scheduled visits had detectable viral loads and presented with comorbidities with some patients requiring hospitalisations (2, 36). Their findings corroborated with our results which showed high reported cases of comorbidities, hospitalisations among patients with unsuppressed viral load with hypertension and tuberculosis being the common infections due to declining immune functioning.

We identified that SDI individuals were more likely to be virally suppressed compared to those that deferred ART at 6 months after ART initiation. We also found that individuals who deferred same day ART initiation had greater odds of getting opportunistic infections with the common infection being TB. This might have been caused by low CD4 count results in the deferred SDI group. These findings were consistent with a study conducted in Johannesburg South Africa which

showed that individuals who delayed to initiate on ART later on presented with advanced HIV disease, co-infections and low CD4 counts which were complicated to manage (8) .

Strengths and limitations of this study

Some of the strengths of our study include; i) being done in an urban and peri-urban communities of KwaZulu-Natal, a province with large numbers of patients on treatment thus providing a reasonable basis for generalizability for many people living with HIV in South Africa and sub-Saharan Africa, ii) being able to analyse at 6 months after ART initiation which is crucial in clinical assessments to observe if patients are responding well to treatment. However, some of the weaknesses of our study include that the population comprised of adults only hence the results on retention in care, viral suppression and clinical outcomes may not apply to infants and children and the Tier.Net is individualised per facility implying that some patients might have self-transferred themselves to other clinics or migrated and not actually lost to follow up. This is because patients exiting care from the ART initiating clinic may re-enter care elsewhere (i.e., silent transfers) and appear as lost to follow-up when they are still in care.

Conclusion

We found evidence of a significant relationship between SDI and viral suppression but poor retention in care during the first 6 months of ART initiation. Individuals who initiated ART on the same day of HIV diagnosis and remained in care showed clinically meaningful outcomes. The CD4 count results, suppressed viral load, and reduced incidence of co-infections supported "proof of principle" for same day ART initiation algorithm. This study also provides much needed evidence on the relationship between adherence and viral suppression in this setting and supports

the 3rd 95% of the UNAIDS 95-95-95 target. However, the results also emphasise a vital need, to not only streamline processes to increase immediate ART uptake, but also ensure retention in care.

Declarations

Ethics approval and consent to participate

The study was approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (# 00000819/2019). Written informed consent was obtained from all participants.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

Funding

This research was funded by the University of KwaZulu Natal through a Ph.D. studentship bursary awarded to SMG by the College of Health Sciences.

Acknowledgments:

We thank the people who participated in this study and the UKZN College of Health Sciences for funding the work.

Conflict of Interest*:*

All authors report no potential conflicts of interest.

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Previous Chapters highlighted various factors determining same day ART initiation from a patient, healthcare provider and facility level perspective including clinical outcomes. Chapter 6 gives the general a synthesis of the whole study and shows how the individual studies link to address the overall objective of the thesis. The chapter also describes the implications of these findings on same day ART initiation, retention in care and clinical outcomes, thereof. Future research on the subject matter is indicated.

CHAPTER 6:
Synthesis, Conclusion and Implications for future research

6.1 Synthesis

This thesis sought "to determine factors that influence acceptability, implementation and patient outcomes in a same day ART initiation program". The thesis comprises of background chapters providing literature review which informed the studies carried out and the general methodology adopted for the studies. The data chapters were informed by the specific objectives of the thesis which are organized in a cascading manner such that latter chapters are informed by former chapters linked by connecting text which thread the chapters together. This synthesis chapter highlights the key findings from each chapter demonstrating how the chapters tell a solid story about acceptance of the same day ART initiation program, how it has been implemented in South Africa and what outcomes were observed. In doing so the findings of the studies in this thesis are interpreted in local and global contexts. The following sections interpret key findings of each chapter followed by a general conclusion of the thesis and implications of the work on policy as well as identification of further research gaps.

6.2.1 The evolution and adoption of World Health Organization policy guidelines on antiretroviral therapy initiation in sub-Saharan Africa

Despite past and present global interventions, the human immunodeficiency virus (HIV) pandemic remains a public health problem in low- and middle-income countries (LMICs (1, 2). Several structural, systemic, and individual factors were identified as hindering various countries from implementing ART initiation guidelines timeously (3, 4). Most countries in SSA have been experiencing cuts in international donor funding and that has caused regional gaps in ART coverage (5). The attitude of healthcare workers is an important determinant in the implementation of same day ART initiation program. Healthcare workers limited support from government, lack of mentoring and inadequate knowledge of changing ART initiation guidelines negatively affected effective implementation of policy changes at facility level (6). The differences in the health systems and the availability of resources partly explain the observed variations in the implementation of ART initiation guidelines across countries. Other factors that have delayed implementation of the guidelines include the rising incidence and prevalence of HIV and attitudes of healthcare workers (7). A comprehensive approach to reduce barriers whilst enhancing

facilitators may improve the situation of adopting and implementing timely ART initiation policies effectively and hence contribute to the achievement of the 95-95-95 UNAIDS 2030 target.

6.2.2 Factors Influencing Rapid Antiretroviral Therapy Initiation at Four eThekwini Clinics, KwaZulu-Natal, South Africa.

Chapter 2 addressed the underlying individual factors promoting or hindering the uptake of same day ART initiation in diverse health facilities in eThekwini municipality in KwaZulu-Natal, South Africa. A gradual progress in the uptake of test and treat programs in eThekwini clinics was observed. Similar observations have been reported by Koenig et al. who reported an SDI prevalence of 57% (8). Certain demographic factors, excluding gender, were significantly associated with SDI of ART and recommendations to consider them during policy development and in strengthening policy changes were made. This aligns with a previous study conducted in Zimbabwe (9). Other studies have reported high denial among males than females and gender stereotyping expects men to display physical fitness resulting in poor clinical outcomes among men (10, 11). The reason why gender was reported not significantly associated with SDI contrary to the general notion reported elsewhere might be because healthcare providers are encouraged to emphasise the importance of SDI regardless of gender. These individual contributing factors which includes age, marital status, level of employment and level of education ought to be considered and addressed if SDI of ART is to be effective to reach the second 95% of the 95-95-95 UNAIDS targets by 2030 which focusses on linkage to care and rapid ART initiation of all HIV diagnosed individuals.

6.2.3 Experiences, knowledge and observations influencing implementation of same day ART initiation in four eThekwini clinics: healthcare worker's perspective.

Individuals should be offered SDI of ART after a positive HIV diagnosis as recommended by WHO guidelines (12). In Chapter 3 healthcare workers identified several patient, systematic and HCW'S contributing factors to SDI of ART uptake. These findings corroborate those in other studies that reported that feeling healthy, fear of side effects and denial were linked to refusing to initiate ART (13-15). This illustrates the constraints experienced by HCW in implementing the

SDI policy, particularly work overload, limited skills and delayed facility readiness. Investing in additional staffing is necessary to sustain the increasing number of individuals initiating ART and continuous treatment management. Community awareness on the importance of SDI of ART is needed to increase patient understanding for early ART uptake. Policymakers will need to address the identified implementation challenges in collaboration with HCWs implementing the policy to get full beneficiation from the UTT and SDI policies. Healthcare workers are the drivers for reaching the 95-95-95 UNAIDS targets by 2030. Hence ensuring adequate buy-in and detailed policy understanding by the HCW will facilitate implementation of the policy. The main patient factors identified during interviews with patients as affecting SDI of ART were age, marital status, education level, employment status, partners' status and knowledge of UTT policy. However healthcare providers indicated that patients who accepted SDI of ART were motivated by being feeling sick, not rushing to go back home or work, had better knowledge of HIV as well as ART, were willing to live longer and with some feeling it was mandatory. Furthermore, HCWs reported denial, fear of disclosure, fear of side effects, limited knowledge on ART, and limitations of healthcare worker's expertise as some of the factors affecting SDI uptake.

Chapter 4 addressed contributing structural and systematic clinic factors affecting implementation of SDI. There was a significant association between facilities with support from many NGOs, adequate staff provision, urban area clinics and high uptake of SDI. There is need for the health department to monitor and standardize implementation of the policy in clinics if the program is to yield success. Variations in how facilities in the same municipality are implementing SDI program were noted. Nongovernmental organizations are a valuable source of technical and financial input. In addition NGOs have the advantage of having political freedom to promote innovation (5). The government has to step up the mobilization of expertise and fostering of partnerships to develop innovative approaches to delivering HIV services, to strengthen the system, and to enhance effective program implementation. Community clinics are the centre for healthcare service provision to the larger population. Therefore, these facilities require structured systems that allow effective SDI of ART in order for the HIV cascade to be implemented to attain the 95-95-95 targets.

6.2.4 The impact of same-day antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa.

Beyond SDI of ART treatment adherence and retention in care remains fundamental in attaining the desired clinical outcomes. The goal is to ensure that 95% of all people on ART are virally suppressed and remain in care. Chapter 5 results compared clinical outcomes and retention in care of SDI vs deferred ART initiators. Individuals who deferred same day ART initiation had greater odds of getting opportunistic infections with the common infection being TB. These findings are similar to those from a study conducted in Johannesburg South Africa which showed that individuals who delayed to initiate on ART later on presented with advanced HIV disease, co-infections and low CD4 counts which were complicated to manage (16). In this thesis an increase in loss to follow up among participants who initiated ART on the same day of HIV diagnosis was observed and this corroborates results from the 12 SLATE trial conducted in South Africa and Kenya which reported that same-day treatment initiation increased rapid ART uptake but not necessarily retention in care especially in the early months after initiation (17). In this thesis there was evidence of a significant relationship between SDI and viral suppression but poor retention in care during the first 6 months of ART initiation. This indicates the need for streamlined processes to increase SDI of ART uptake further ensuring that retention in care is emphasised through intensified counselling.

6.3 General conclusion

The work constituting this thesis presents a positive move towards same day ART initiation after the implementation of the UTT and SDI policy. Patient factors like age, marital status, education level, employment status, partners' status and knowledge of UTT policy were identified as key in uptake of SDI of ART. Healthcare workers cited that individuals who accepted SDI of ART made the decision because they were feeling sick, not rushing to go back home or work, had better knowledge of HIV as well as ART, were willing to live longer and with some feeling it was mandatory. However, HCWs reported denial, fear of disclosure, fear of side effects, limited knowledge on ART, and limitations of healthcare worker's expertise as some of the factors

affecting SDI uptake. Facility structural and systematic factors like provision of adequate personnel need to be reviewed. Furthermore, the results also emphasise a vital need to not only streamline processes to increase immediate ART uptake further but also ensure retention in care in order to meet the 95-95-95 targets. Going forward, there is need to improve intensified adherence counselling and retention in care. While rapid ART initiation remains pertinent to achieve HIV prevention as a public health measure, there is need for the policy makers and government health departments to review the policy and strengthen treatment adherence strategies on HIV diagnosed individuals emphasising commitment to lifelong treatment.

6.4 Recommendations

Significant patient level factors, healthcare provider and structural factors were identified as contributing to slow uptake of SDI of ART. There is need to review the SDI of ART policy considering the amount of time some individual require to process and accept a positive HIV diagnosis before committing to lifelong treatment. Counsellors are the entry point in the HIV cascade hence upskilling them regularly especially with detailed policy guidelines will assist in addressing acceptance and adherence. Given the high HIV prevalence in eThekwini municipality and other areas in South Africa, adequate staff provision especially NIMART trained professional nurses needs to be addressed to reduce time taken initiating ART and effective continuous treatment management considering that NGO support is not sustainable and consistent.

6.5 Study limitations

Several challenges compromised some aspects of the initial conceptualization at different levels. However, the study was carried out satisfactorily and the set objectives were achieved. Some of the specific obstacles that should be considered in interpreting the findings of the thesis include:

- **During the enrolment stage:** participants were recruited on the same day after receiving an HIV diagnosis which could have been a sensitive and emotional time for some participants to fully give thoughtful responses.

- **During the enrolment stage:** the study participants was limited to adults and hence the results on characteristics of SDI and delayed ART initiation may not apply to infants and children.
- **During follow up:** The results on retention in care, viral suppression and clinical outcomes may not apply to infants and children who were not eligible for the study.
- **During follow up:** Tier.Net is individualised per facility. This may indicate that some patients might have self-transferred themselves to other clinics or migrated and not actually lost to follow up. This is because patients exiting care from the ART initiating clinic may re-enter care elsewhere (i.e. silent transfers) and appear as lost to follow-up when they are still in care.

6.6 Future research

Further research is needed to compare same day ART initiation among paediatrics and adolescents including their clinical outcomes and retention in care. It is also important to compare same day ART initiation in different districts and provinces in South Africa. It is also crucial to evaluate the different times of deferred ART for instance same week or within 2 weeks and comparing if the outcomes would be as effective as same-day. Such a study will assist to decide on optimal time to initiate ART. Additionally, future studies need to follow up beyond 6 months for measuring clinical outcomes over a longer duration.

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APPENDICES

Appendix A: CONSENT FORM

Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

Consent Form

Good morning/ afternoon my name is Sabina Govere.
You are being invited to consider participating in a study titled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat by evaluating the impact on patient and healthcare workers." In this study we want to find out the factors that influence rapid and delayed ART uptake and how different PHC facilities in EThekwini Municipality are implementing the policy. We also want to assess the clinical outcomes of both early and delayed ART initiators. I will conduct the interview, record and take notes. I will ask you several questions. Your personal opinions and views are very important for us.

There are no right or wrong answers. Please feel welcome to express yourself freely during the interview. This conversation will be recorded on tape. This is only for purpose of the research, only the lead researcher indicated on the consent form (and I) will listen to the tape. No names or personal information will be used in the report. There are no risks in participating in this study. We also seek your consent to check your clinic visits and results at six months from the day you initiated treatment.

Participation is entirely voluntary: refusal to participate will not result in penalty and you can discontinue the study at any time, without penalty. You will not be denied any healthcare services that you are generally entitled to as a result of refusal or withdrawal from the study. Confidentiality: interviews will take place in a private place. All information given during the interview will be kept confidential. The interview will last for about twenty minutes.

If you have any questions about the research, please contact the principal investigator, Sabina Govere, on 084 464 8815. If you have any questions or concerns regarding your rights as a research participant you may contact the Biomedical Ethics Research Office, UKZN, Private Bag X54001, Durban 4000. Telephone: 0027 (0) 31 260 4769/ 260 1074 Fax: 0027 (0) 31 260 4609 Administrator: Email: BREC@ukzn.ac.za

I …….

Have been informed about the study entitled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers." I understand the purpose and procedures of the study. I have been given an opportunity to ask questions about the study and answered to my satisfaction.

Participant: Name and Surname Participant Signature:

Interviewer: Name and Surname Interviewer Signature:

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

APPENDIX B: PARTICIPANT QUESTIONNAIRE

Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

Consent Form

Good morning/ afternoon my name is Sabina Govere.
You are being invited to consider participating in a study titled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat by evaluating the impact on patient and healthcare workers." In this study we want to find out the factors that influence rapid and delayed ART uptake and how different PHC facilities in EThekwini Municipality are implementing the policy. We also want to assess the clinical outcomes of both early and delayed ART initiators. I will conduct the interview, record and take notes. I will ask you several questions. Your personal opinions and views are very important for us.

There are no right or wrong answers. Please feel welcome to express yourself freely during the interview. This conversation will be recorded on tape. This is only for purpose of the research, only the lead researcher indicated on the consent form (and I) will listen to the tape. No names or personal information will be used in the report. There are no risks in participating in this study. We also seek your consent to check your clinic visits and results at six months from the day you initiated treatment.

Participation is entirely voluntary: refusal to participate will not result in penalty and you can discontinue the study at any time, without penalty. You will not be denied any healthcare services that you are generally entitled to as a result of refusal or withdrawal from the study. Confidentiality: interviews will take place in a private place. All information given during the interview will be kept confidential. The interview will last for about twenty minutes.

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I …….

Have been informed about the study entitled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers." I understand the purpose and procedures of the study. I have been given an opportunity to ask questions about the study and answered to my satisfaction.

Participant: Name and Surname Participant Signature:

Interviewer: Name and Surname Interviewer Signature:

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

Thank you for agreeing to participate in this study. The first sets of questions are about yourself

PART I: DEMOGRAPHIC INFORMATION

Number	Question	Response	Coding Categories
1.	Name and Surname		
2.	Date of Birth		
3.	Age	----------years	
4.	Gender	Male Female Transgender	0 1 2
5.	South African ID		
6.	Marital Status	Married Cohabitation Widowed Divorced Separated Single	0 1 2 3 4 5
7.	Highest level of education	None Primary School Some High School (but not Matric) Matric (completed High School) Higher Degree (University)	0 1 2 3 4
8.	Employment Status	Unemployed	0

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

		Self-employed Student Intern Professional employment	1 2 3 4
9.	Do you have children of your own?	Yes No	1 2
10.	If yes, how many children?		

HEALTH STATUS AND SEXUAL BEHAVIOUR

Number	Question	Response	Coding Categories
11.	Have you ever been tested for HIV before today?	Yes No	1 2
12.	Have you ever tested POSITIVE for HIV before today?	Yes No	1 2
13.	If yes, when was the FIRST time you tested POSITIVE for HIV	Day / Month / Year	
14.	How many sexual partners did you have in the past 12 months?		
15.	Have you ever received treatment (ART) for HIV before today?	Yes No	1 2
16.	Has your sexual partner tested for HIV?	No Unknown Status Yes, HIV negative Yes, HIV positive	0 1 2 3
17.	What was your perceived risk for getting HIV today?	Definitely NOT going to acquire HIV	1

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

		Probably NOT going to acquire HIV	2
		Probably WILL become HIV-infected	3
		Definitely WILL become HIV-infected	4

KNOWLEDGE OF UTT (RAPID ART INITIATION) AND ATTITUDES of ACCEPTABILITY

Number	Question	Response	**Coding Categories**
18.	Did you know about UTT (Rapid ART initiation)?	Yes No Slightly	1 2 3
19.	If yes, where did you hear about its	Clinic Family and friends Media Other	1 2 2 4
20.	Have you accepted initiating on ART today?	Yes No	1 2
21.	Date of HIV Test	Day / Month / Year	
22.	Date of ART initiation	Day / Month / Year	
23.	If yes, What do you think are the benefits?	Starting before I get sick Live a longer life Suppressing my viral load To prevent transmitting to other uninfected people	1 2 3 4
24.	If no, What are the reasons?	Afraid of pills I'm still in shock and denial	1 2

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

		I feel Healthy Not ready today It wasn't explained clearly I will use traditional medicine I will go for prayers	3 4 5 6 7
25.	Will you disclose your status to someone?	Yes No Not Sure yet	1 2
26.	If yes, who will you disclose to?		
27.	Will you recommend rapid ART initiation to your family or friends?	Yes No	1 2

Thank you for taking the time to participate in this study. Your responses will be very helpful to the study and to the Department of Health to better understand how to improve health programs in the country.

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

Appendix C: Patient Follow up form

Title: Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

6-Month Patient Follow-up form

A. ART FOLLOW-UP			
A1	Did the participant come for their scheduled clinic visit at month 2 after ART initiation?	No……...……...0 Yes ……1 Not Sure……...……...……...2	
A2	Date patient came for their clinic scheduled visit month 2	Day / Month / Year	
A3	Information source used:	Chart Review……..……0 ART Register……....1 Tier.net ……...….2	
A4	Did the participant come for their scheduled clinic visit at month 4 after ART initiation?	No……...……...0 Yes ……1 Not Sure……...……...……...2	
A5	Date patient came for their clinic scheduled visit month 2	Day / Month / Year	
A6	Information source used:	Chart Review……..……0 ART Register……....1 Tier.net ……...….2	
A7	Did the participant return to clinic for follow up scheduled visit at month 6?	No……...……0 Yes……1 Not sure…….....2	
A8	Date of follow-up clinic scheduled visit at month 6.	Day / Month / Year	
A9	Information source used: *Check all that apply*	Chart Review……..……0 ART Register……1 Tier.net ……..….2	

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

A10	Did the patient remain in care during the 6-month study follow-up?	No……0 Yes……1 Unknown……...-1	
A11	Did the participant have viral load bloods done at 6-month follow up visit	Undetectable……..……0 Detectable……...…...1 Value if detectable: _____	
A12	Participant's CD4 cell count at 6-month follow up visit	_____ Unknown……....1	
A13	Last date seen in clinic:	Day / Month / Year Unknown…… 1	
A14	Did the patient contact any other infections during the 6 months of the study?	No……..…0 Yes……....1	
A15		TB……0 Kidney Failure……1 Liver failure……2 Meningitis……3 Cryptococcus Meningitis…….4 STI……5 Other ……6	
B. DEATH			
B1	Did the participant die during the study period?	No……..…0 Yes……....1	
B2	Date of death	Day / Month / Year Unknown……....1	
B3	Cause of death	_____ Unknown……1	

Today's Date: day / month / year Study ID: _____

Interviewer: _____ Facility: _____

B4	Source information about the cause of death	Clinic records…….....….....0 Death Certificate…….....…….1 Family/Friends…….....…..….2 Tier.net.....…3 Other..... 4	

Appendix D: Clinic Staff Consent form

Title: Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

Clinic Staff Consent Form

Good morning/ afternoon my name is Sabina Govere. You are being invited to consider participating in a study titled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat by evaluating the impact on patient and healthcare workers." In this study we want to find out the factors that influence rapid and delayed ART uptake and how different PHC facilities in EThekwini Municipality are implementing the policy. We also want to assess the clinical outcomes of both early and delayed ART initiators. I will conduct the interview, record and take notes. I will ask you several questions. Your personal opinions and views are very important for us.

There are no right or wrong answers. Please feel welcome to express yourself freely during the interview. This conversation will be recorded on tape. This is only for purpose of the research, only the lead researcher indicated on the consent form (and I) will listen to the tape. No names or personal information will be used in the report. There are no risks in participating in this study. We also seek your consent to check your clinic visits and results at six months from the day you initiated treatment. Participation is entirely voluntary: refusal to participate will not result in penalty and you can discontinue the study at any time, without penalty. You will not be denied any healthcare services that you are generally entitled to as a result of refusal or withdrawal from the study. Confidentiality: interviews will take place in a private place. All information given during the interview will be kept confidential. The interview will last for about twenty minutes.

If you have any questions about the research, please contact the principal investigator, Sabina Govere, on 084 464 8815. If you have any questions or concerns regarding your rights as a research participant you may contact the Biomedical Ethics Research Office, UKZN, Private Bag X54001, Durban 4000. Telephone: 0027 (0) 31 260 4769/ 260 1074 Fax: 0027 (0) 31 260 4609 Administrator: Email: BREC@ukzn.ac.za

I …….

Have been informed about the study entitled "Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers." I understand the purpose and procedures of the study. I have been given an opportunity to ask questions about the study and answered to my satisfaction.

Participant: Name and Surname Participant Signature:

Interviewer: Name and Surname Interviewer Signature:

Clinic staff Appendix E: Clinic Staff Interview Guide

Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

Interview Guide

INTRODUCTION:

Thank you for agreeing to talk to me today and to help us with our study. I will be talking to clinic staff, such as you, with interests and expertise in the area of HIV care. The purpose is to get feedback from healthcare experts about their ideas and experiences implementing the Universal Test and Treat program paying particular attention on rapid ART initiation. The information we collect from these interviews will be used to help us understand how the Universal Test and Treat program works, and what changes could be made to better provide long-term HIV care to patients and emphasize treatment as a prevention measure.

All information that you share with me today is completely confidential and will only be used to help us with the research. Once we complete our study, we will destroy the link between your name and your answers to our interview questions. With your permission, I will audio tape this interview to supplement my notes, but the tape will be erased after we complete the study. To protect your confidentiality, no one outside of the research team will see the notes or listen to the tapes. We will not provide any information that will allow linking of your name to your specific comments or to your specific clinic.

The interview is completely voluntary, you can stop participating at any time, and you can skip any questions you'd rather not answer.

Finally, this interview will take approximately 30 minutes.

Do you have any questions at this time?

INTERVIEW

First, I'd like to know your understanding of Universal Test and Treat program.

1. From your understanding, what is the Universal Test and Treat/ rapid ART initiation policy?
2. What has been your experiences in implementing the UTT policy?

	SERVICE PROVIDER FACTORS	**RESPONSES**	**Coding Categories**
3.	What is your role in implementing the Universal Test and Treat program?	Doctor NIMART trained Professional Nurse Professional Nurse Enrolled Nurse Phlebotomist Testing Counsellor Data Capturer Filing Clerk Pharmacist Pharmacist Assistant Other	1 2 3 4 5 6 7 8 9 10 11
4.	In your clinics, on average, how long after patients HIV diagnosis do they commence ART?	Same day Within 1 weeks Within 2 weeks within 1 month	1 2 3 4
5.	How long does a reactive patient last in the facility for all the ART initiation processes to be complete?	1 hour 2 hours 3 hours 4 hours 5 hours	0 1 2 3 4
6.	Who is/are in charge of implementing Universal Test and Treat policy in the clinic?	NIMART Professional Nurse Doctor Professional Nurse	1 2 3
7.	Do you see the need for Universal Test and Treat policy in this clinic?	Yes No Sometimes	1 2 3

8.	What are the Structural / System factors affecting rapid ART initiation?	HIV testing/diagnosis occurs off site poor linkage to care (referrals to clinic) Limited NIMART trained Nurses to initiate patients No available Doctors to initiate patients Limited space for rapid ART initiation Delays in receiving TB results for TB symptomatic patients Long waiting time at different service points Other	1 2 3 4 5 6 7
9.	What is your attitudes towards rapid ART initiation	I think it's beneficial because it saves time by not seeing the same patient twice within the same week I think it's beneficial because it gives an opportunity to quickly suppress viral load I don't think it's beneficial because it is time consuming having all processes are done in a day. I don't think it's beneficial because it doesn't give the patient's time to process the results and decide on starting ART. Other	1 2 3 4 5
10	Are resources and trainings available in order to learn about and how to implement the Universal Test and Treat policy?	Yes No Sometimes	1 2 3
11	What are some of the challenges you have encountered, if any, when implementing the Universal Test and Treat/ rapid ART initiation policy in this clinic?	Denial of reactive patients to initiate ART Patients not ready to start ART TB symptomatic patients awaiting results Other	1 2 3 4
12	What are some of the successes you have witnessed with rapid ART initiations?	Patients presenting with virally suppressed results Reduction in HIV coinfections Reduced patient's clinic visits	1 2 3

		Other	4
13	What might assist strengthening the implementation of rapid ART initiation in this clinic?	Increasing the number of NIMART trained nurses Skills development of Testing Counsellors in offering quality pre and post HIV counselling Availability of Point of Care TB Genexpert machines Other	1 2 3 4
	Patient Factors		
14	What factors do you think influence patients to accept rapid ART initiation?	Desire to live longer Available strong support system Having an HIV positive partner Adequate knowledge and information on ART Reduction in the number of clinic visits Patient feeling sick Positive healthcare worker's attitudes Desire to be healthy Other	1 2 3 4 5 6 7 8 9
15	What factors do you think influence patients to delay ART initiation?	Stigma Fear of disclosing to significant others Fear of poor adherence to treatment Fear of potential treatment side effects Lack of social support system Substance abuse Religion beliefs Food insecurities Patient feeling healthy Negative healthcare attitude Other	1 2 3 4 5 6 7 8 9 10 11

Closing

Is there anything else that you think of to tell us about the Universal Test and Treat / rapid ART initiation policy?

Acceptability and effectiveness of rapid ART initiation in the era of Universal Test and Treat: evaluating the impact on patient and healthcare workers.

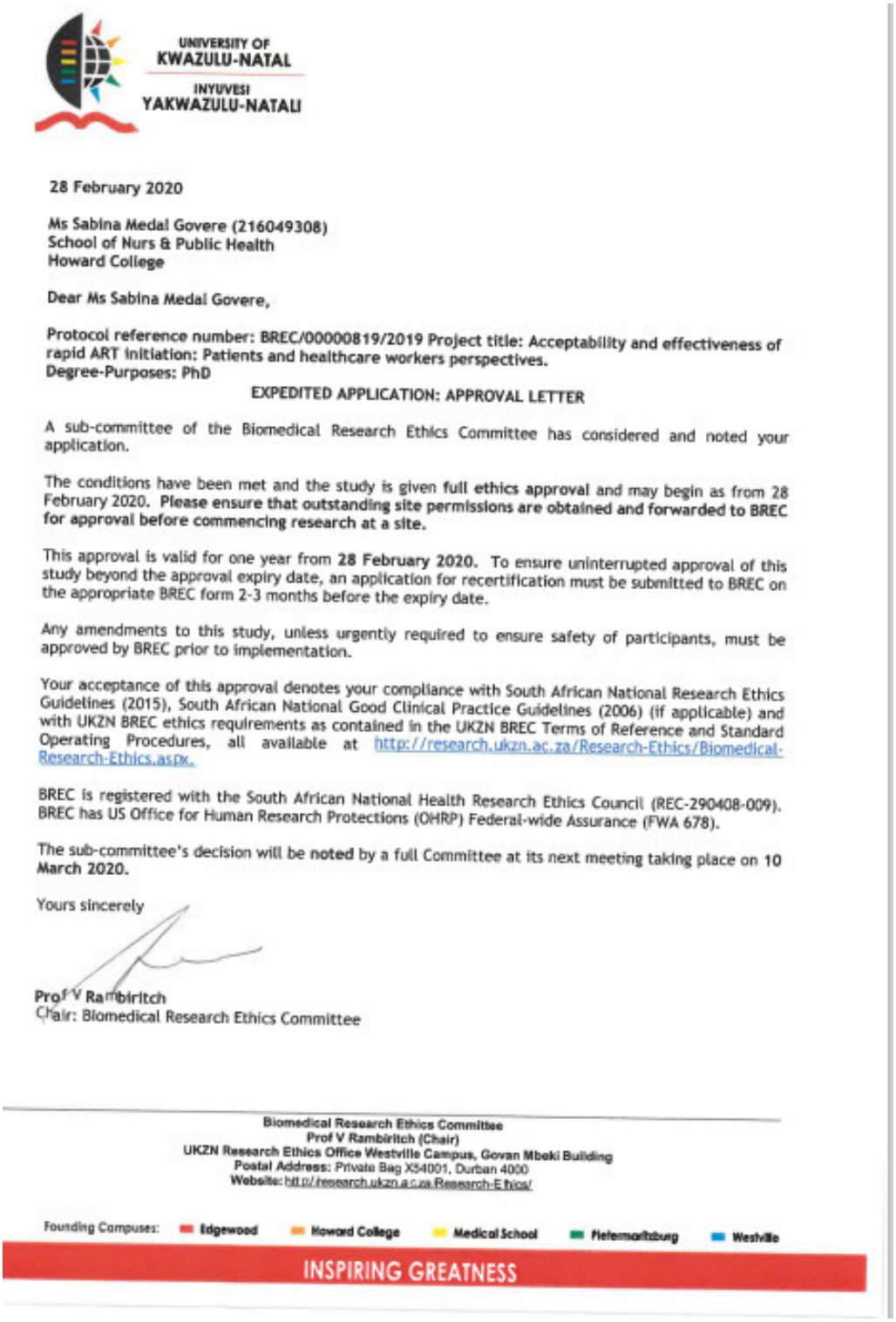
Appendix F: Clinic Profile form

Clinic Profile Form

Number	Questions	Responses	Coding Category
A1	Type of clinic	□ Municipal □ Department of Health □ NGO	1 2 3
A2	Location of clinic	□ Urban □ Rural	1 2
A3	Affiliations with a supporting partner organizations?	□ No □ Yes, one NGO □ Yes, more than one NGO	1 2 3
A4	List of Affiliated organizations assisting with ART initiation.		
A5	Number of headcount serviced by the clinic monthly *(estimate)*		
A6	Number of professional nurses staff in the clinic during a typical day		
A7	How frequently is there at least one doctor in the clinic?	Daily not daily, but at least weekly not weekly but at least monthly not at all	1 2 3 4

ARV PROGRAM			
B1	Number of adults tested for HIV each day *(estimate)*		
B2	Number of new adults diagnosed with HIV per day *(estimate)*		
B3	Number of new adult HIV diagnosed per month *(approximate)*		
B4	Number of adult patients initiating on ART per month *(estimate)*		
B5	Total number of adult patients on ART		
B6	Current number of patients lost to follow-up that need to be traced		
B7	Number of clinic staff members involved in ART initiation		

Appendix G: 2020 Ethics clearance letter from Biomedical Research Ethics Committee (BREC)



UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

28 February 2020

Ms Sabina Medal Govere (216049308)
School of Nurs & Public Health
Howard College

Dear Ms Sabina Medal Govere,

Protocol reference number: BREC/00000819/2019 Project title: Acceptability and effectiveness of rapid ART initiation: Patients and healthcare workers perspectives.
Degree-Purposes: PhD

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application.

The conditions have been met and the study is given **full ethics approval** and may begin as from 28 February 2020. **Please ensure that outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.**

This approval is valid for one year from **28 February 2020.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **noted** by a full Committee at its next meeting taking place on **10 March 2020.**

Yours sincerely

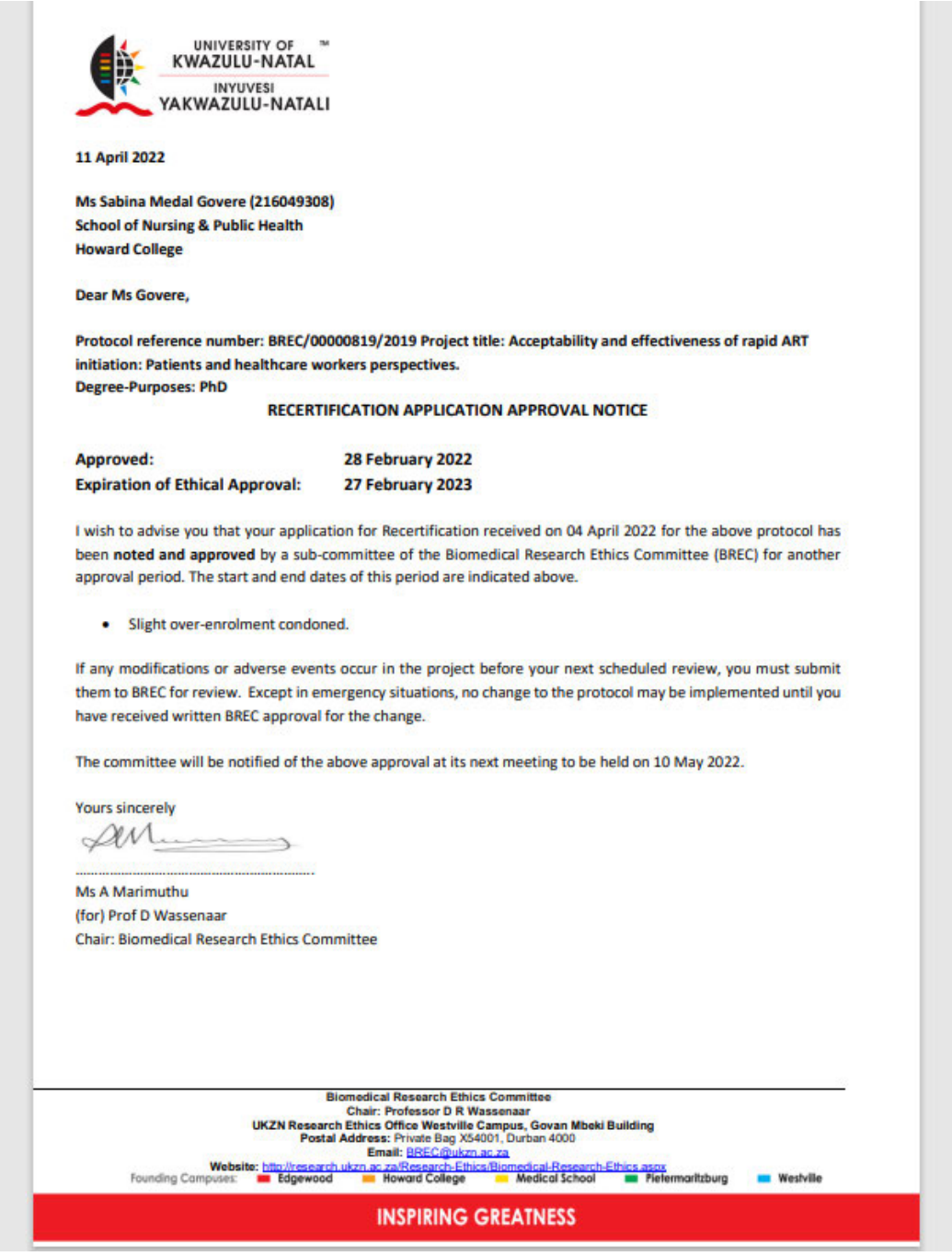
Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee
Prof V Rambiritch (Chair)
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Website: http://research.ukzn.ac.za/Research-Ethics/

Founding Campuses: Edgewood Howard College Medical School Pietermaritzburg Westville

INSPIRING GREATNESS

Appendix H: 2022 Ethics clearance letter from Biomedical Research Ethics Committee (BREC)



UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

11 April 2022

Ms Sabina Medal Govere (216049308)
School of Nursing & Public Health
Howard College

Dear Ms Govere,

Protocol reference number: BREC/00000819/2019 Project title: Acceptability and effectiveness of rapid ART initiation: Patients and healthcare workers perspectives.
Degree-Purposes: PhD

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved: **28 February 2022**
Expiration of Ethical Approval: **27 February 2023**

I wish to advise you that your application for Recertification received on 04 April 2022 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

- Slight over-enrolment condoned.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

The committee will be notified of the above approval at its next meeting to be held on 10 May 2022.

Yours sincerely

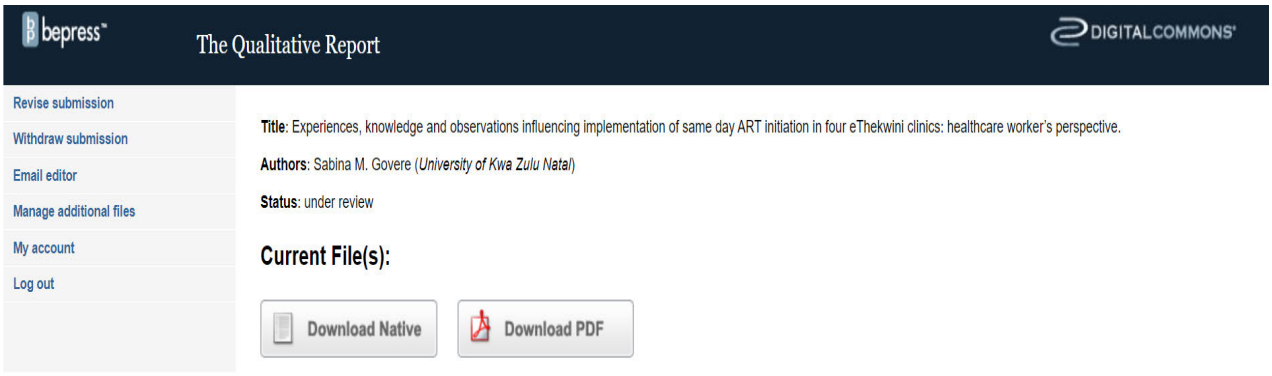
.....

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee
Chair: Professor D R Wassenaar
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx
Founding Campuses: Edgewood Howard College Medical School Pietermaritzburg Westville

INSPIRING GREATNESS

Appendix I**: Proof of manuscript 4 submission**



Summary

Abstract

World Health Organisation (WHO) recommends that individuals should be offered same day Antiretroviral therapy ART after a positive HIV diagnosis. South Africa commenced implementation of the Universal-Test-and-Treat (UTT) and same day antiretroviral therapy initiation (SDI) policies in September 2016, striving to achieve the UNAIDS 95-95-95 targets by 2030. We assessed experiences, knowledge and observations made by a diverse group of healthcare workers on the implementation of Universal-Test-and-Treat (UTT) to strengthen and improve the policy implementation. A cross-sectional qualitative study was conducted in four health facilities of eThekwini municipality KwaZulu-Natal Province in South Africa. Key informant semi-structured interviews were conducted with 20 diverse healthcare workers. Interviews were conducted in English or IsiZulu depending on preference of interviewee and responses were recorded on Kobo collect. Major themes were identified and categorised using the Health Belief Model stages. Healthcare workers demonstrated detailed knowledge of the Universal Test and Treat and same day ART initiation policy and its importance as an HIV prevention measure for reducing morbidity and mortality. Healthcare workers experienced episodes of medication stock shortages, frequent changes in reporting tools and increase in workload during the inception stages of policy implementation. Healthcare workers observed that newly HIV diagnosed individuals who accepted ART on the same day made the decision because they were feeling sick, not rushing to go back home or work, had better knowledge of HIV as well as ART, were willing to leave longer and with some feeling it was mandatory. Denial, Fear of disclosure, fear of side effects, limited knowledge on ART, structural and system factors and limitations of healthcare worker's expertise were cited as some of the factors affecting SDI. Our findings identified extensive knowledge presented by HCW about same day ART initiation as an HIV prevention measure and crucial gaps impeding the attainment of the UNAIDS second 95% intended to ensure that HIV diagnosed individuals are initiated on ART on the same day. The study results illustrate the strain experienced by HCW in implementing the SDI policy, particularly work overload, skills development and facility readiness. Community awareness on the importance of SDI of ART is needed to increase patient understanding for early ART.

Appendix J: Proof of manuscript 5 submission

Global Health Research and Policy

The impact of Same-day Antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa.

--Manuscript Draft--

Manuscript Number:	GHRP-D-22-00242
Full Title:	The impact of Same-day Antiretroviral therapy initiation on retention in care and clinical outcomes at four eThekwini clinics, KwaZulu-Natal, South Africa.
Article Type:	Research
Funding Information:	Inyuvesi Yakwazulu-Natali (CU90) Ms Sabina Govere
Abstract:	Background Same-day initiation (SDI) of antiretroviral therapy (ART) increases ART uptake, however retention in care after ART initiation remains a challenge. Public health behaviours, such as retention in HIV care and adherence to antiretroviral therapy (ART) pose major challenges to reducing new Human Immunodeficiency Virus (HIV) transmission and improving health outcomes among HIV patients. Methods We evaluated 6-month retention in care, and clinical outcomes of an ART cohort comprising of SDI and delayed ART initiators. We conducted a 6 months' observational prospective cohort study of 403 patients who had been initiated on ART. A structured questionnaire was used to abstract data from patient record review which comprised the medical charts, laboratory databases, and Three Interlinked Electronic Registers.Net (TIER.Net). Treatment adherence was ascertained by patient visit constancy for the clinic scheduled visit dates. Retention in care was determined by status at 6 months after ART initiation. Results Among the 403 participants enrolled in the study and followed up, 286 (70.97%) and 267 (66.25%) complied with scheduled clinics visits at 3 months and 6 months, respectively. Seventeen (4.22%) participants of those that defaulted after six months had died, 6 (1.49%) had been transferred to other health facilities and 113 (28.04%) had been lost to follow-up. Among those that had been lost to follow-up, 30 (33.63%) deferred SDI while 75 (66.37%) initiated ART under SDI. One hundred and eighty-nine (70.79%) participants who had remained in care were SDI patients while 78 (29.21%) were SDI deferred patients. In the multivariate analysis results showed that among those remaining in care (aOR: 2.44; 95% CI: 1.614–3.872) and contraction of other diseases during the period of the study (aOR: 1.212; 95% CI: 1.031–1.425) were the predictors of viral load detection. Furthermore, SDI patients who defaulted treatment were 2.4 (95% CI: 1.165–4.928) times more likely to have increased viral load than those who had been returned in care. Conclusion Viral suppression under SDI proved higher but with poor retention in care. However, the results also emphasise a vital need, to not only streamline processes to increase immediate ART uptake further, but also to ensure retention in care.
Corresponding Author:	Sabina KwaZulu Govere University of KwaZulu-Natal College of Health Sciences Durban, kzn SOUTH AFRICA
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University of KwaZulu-Natal College of Health Sciences
Corresponding Author's Secondary	

Appendix K: Proof of publication 3 acceptance

Notifications ×

JPHIA - Journal of Public Health in Africa [paper 2179] - Editorial Decision - Acceptance

16-05-2022 12:02 PM

Dear Sabina Hwenje,

We are pleased to inform you that your paper entitled "AN An assessment on the implementation of Same Day Antiretroviral Therapy initiation in eThekwini clinics, KwaZulu-Natal, South Africa: Facility implementation level" has been accepted for publication in Journal of Public Health in Africa.

Please, take in account the following referee's comments and suggestions to improve your article.

The Corresponding Author is now required to download, fill in and sign the Copyright and License form (http://www.pagepressjournals.org/public/License_Agreement.pdf).
Each Author of the paper has to download and fill in the Conflict of Interest form (pagepress.org/public/COI_disclosure.docx).
All the forms must be sent to: emanuela.fusinato@pagepress.org
Please note that these documents are necessary prior to publication.

Appendix L: Plagiarism Declaration

Plagiarism:

DECLARATION

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