VIRAL LOAD MONITORING COMPLIANCE AMONG WOMEN ATTENDING PMTCT SERVICES DURING COVID-19 PANDEMIC IN EHLANZENI DISTRICT, MPUMALANGA, SOUTH AFRICA

Thandiwe Elsie Mbira

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Sciences in Epidemiology and Biostatistics.

Witwatersrand, **Johannesburg, 2022.**

DECLARATION

I Thandiwe Elsie Mbira declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Sciences Epidemiology and Biostatistics at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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(Signature of candidate)

_____09_____day of____November_____20_22_____in__Pretoria_____

DEDICATION

In memory of my grandmother

Nomayeza Elisa Mbira

1950-2020

ABSTRACT

Background: Human Immunodeficiency Virus (HIV) viral load (VL) testing is the gold standard approach recommended by the World Health Organization (WHO) for monitoring the effectiveness of antiretroviral treatment (ART) in HIV-positive persons, including pregnant and breastfeeding women with HIV (PBWHIV). Progress towards the United Nations, Acquired Immunodeficiency Syndrome (UNAIDS) 2030 goals to eliminate vertical HIV transmission has been slow, and the 2025 interim target towards this goal is to have 95% of PBWHIV having suppressed VL to eliminate vertical HIV transmission (MTCT, EMTCT). Further delays towards EMTCT and UNAIDS 2030 goals were caused by the Coronavirus disease 2019 (COVID-19) pandemic, as access to HIV healthcare services was interrupted, including routine VL monitoring particularly during the early outbreak period.

Objectives: The objectives of this study were to:

(i) determine compliance to repeat VL testing schedule during the pre-COVID-19 period, transition period, and COVID-19 period, overall and by previous VL status (<50 copies/ml, 50-999 copies/ml and ≥1000 copies/ml) among PMTCT clients in Ehlanzeni district.

(ii) compare compliance to repeat VL testing schedule between pre-COVID-19, transition, and COVID-19 periods.

(iii) determine factors associated with timely VL testing among PMTCT clients in Ehlanzeni district over the course of the three periods, and during the COVID-19 period.

Methods: This was a secondary retrospective cohort analysis of repeat VL testing among PBWHIV using PMTCT services at Ehlanzeni district. Compliance to repeat VL testing schedule was determined as a proportion of participants with timely repeat VL tests in line with national PMTCT guidelines, during different time periods: pre-COVID-19 (1 April 2019- 25 March 2020), transition (VL test contact before start of lockdown on 26 March 2020 and expected repeat VL test on or after 26 March 2020), and COVID-19 (26 March 2020 -30 September 2021). Descriptive statistics were used to present participant characteristics and compliance to the repeat VL testing schedule during pre-COVID-19, transition, and COVID-19 periods. Partially overlapping z-test was used to compare proportions between pre-COVID-19 and transition periods, pre-COVID-19 and COVID-19 periods, and transition and COVID-19 periods. Multivariable Poisson regression (with robust error variance) analysis was conducted to determine factors associated with timely VL testing over the course of the three periods (combined) and during the COVID-19 period (sub-analysis).

Results: Of 405 women with ≥2 VL tests and included in the analysis, the overall median age was 30 years (Interquartile range (IQR): 26-35), 70% of them were in the postpartum period at baseline, and around 75% were diagnosed with HIV before their current or recent pregnancy and had initiated ART. During pre-COVID-19 period the proportion of women who were compliant to VL test schedule was 82.6% (233/282). Compliance during the transition period was 81.5% (172/211), while during COVID-19 was 86.0% (178/207). During pre-COVID-19, compliance was higher among women who had baseline VL<50 and VL=50-999 copies/ml compared to those with baseline VL≥1000 copies/ml, while during transition and COVID-19 compliance was higher among women with a baseline VL<50 copies/ml compared to women with baseline VL≥50 copies/ml. Compliance to repeat VL testing was not significantly different between periods.

Across all three periods, being compliant was significantly increased for the 25-34 years age-group (incidence-rate ratio (IRR)=1.12, [95% CI:1.01-1.23], p value=0.027) compared to younger age-group, and reduced among those with baseline VL=50-999 copies/ml (IRR=0.71, [95% CI: 0.61-0.82], p value<0.001) and VL≥1000 copies/ml (IRR=0.18, [95% CI:0.09-0.36], p value<0.001). Similarly, during the COVID-19 period, compliance was reduced by having baseline VL=50-999 copies/ml (IRR=0.40, [95% CI:0.23-0.67], p value=0.001) and VL≥1000 copies/ml (IRR=0.14, [95% CI:0.04-0.51], p value=0.003).

Conclusion: A slight decrease in compliance was observed during transition period, but overall compliance was over 80% and significantly reduced among PMTCT clients who previously had viraemia regardless of the pandemic. Young women compared to the mid-adult group were less likely to comply to VL testing schedule and to improve timely uptake of repeat VL testing especially among young women and those with detectable VL, there is a need to strengthen interventions such as short message service (SMS) reminders and other strategies such as young PBWHIV-targeted services, increasing educational efforts on its benefits, using point-of-care VL testing for short results turnaround times and access to VL testing in resource-limited settings, enhanced adherence counselling, and compensating patients, which have shown a potential to improve uptake and timeous linkage for appropriate treatment and care.

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ABBREVIATIONS

ANC	Antenatal care
ART	Antiretroviral Treatment
CHCs	Community Healthcare centers
COVID-19	Coronavirus Disease-2019
EMTCT	Elimination of vertical Transmission
HIV	Human Immunodeficiency Virus
NHLSCDW	National Health Laboratory Services central data warehouse
PBWHIV	Pregnant and Breastfeeding women with HIV
PEPFAR	President's Emergency Plan Aids Relief
PMTCT	Prevention of vertical HIV Transmission
PWH	People with HIV
SARS-COV-2	Severe acute respiratory syndrome-2 Viruses
UNAIDS	United Nations, Acquired Immunodeficiency Syndrome
VL	Viral Load
WHO	World Health Organization

1 CHAPTER 1: INTRODUCTION

1.1 Background

Human Immunodeficiency Virus (HIV) viral load (VL) testing is the gold standard approach recommended by the World Health Organization (WHO) for monitoring the effectiveness of antiretroviral treatment (ART) in HIV-positive persons [1]. Routine VL monitoring plays a vital role in following the individual response to antiretroviral treatment (ART), population-level effectiveness of ART, and community progress towards achieving the United Nations, Acquired Immunodeficiency Syndrome (UNAIDS) global targets for HIV epidemic control [2]. The UNAIDS's third target in its 95-95-95 goals to end Acquired Immunodeficiency Syndrome (AIDS) by 2030 is to ensure that 95% of people on ART are virally suppressed [3,4]. However, the progress towards meeting this third target has been slow. In 2019, 88% of people who were on treatment achieved viral suppression, and only 59% of people with HIV (PWH) regardless of their treatment status were virally suppressed globally [5], indicating slow progress towards the 95% targets by 2030.

To accelerate progress, UNAIDS has developed new interim set of targets for 2025 that will make 2030 goals possible if achieved. One of the main 2025 targets is to have 95% of pregnant and breastfeeding women with HIV (PBWHIV) having suppressed VL to eliminate HIV vertical transmission [5]. PBWHIV are a priority population for HIV VL monitoring, to ensure a decrease in the risk of HIV vertical transmission and promoting healthy living during pregnancy and postnatal periods in breastfeeding populations such as South Africa [6-9]. Progress towards the elimination of vertical HIV transmission (MTCT, EMTCT) has been slow due to new HIV infections during pregnancy (HIV incidence), late HIV diagnosis and initiation of ART, and lack

of retention in care [10-15]. Although, ART coverage among pregnant women was high (84%) in 2019 [16], VL monitoring in this population has been minimal, and in South Africa gaps in the prevention of vertical HIV transmission (PMTCT) program remain around repeat VL testing [17,18].

The PMTCT program outcomes were affected by the Coronavirus disease 2019 (COVID-19) pandemic and the restrictions on mobility and trade (the national lockdown restrictions) which were imposed to curb its spread. COVID-19 is a disease caused by severe acute respiratory syndrome-2 viruses (SARS-CoV-2) and spreads from one person to another by means of respiratory droplets produced when an infected person spits, coughs, or sneezes [19]. The lockdown restrictions and fear of getting COVID-19 made it difficult for people including PBWHIV to access healthcare services and conducting face-to-face encounters was near impossible [5,20]. HIV services were disrupted, particularly during the early outbreak period, as resources were shifted towards the pandemic, and healthcare workers were allocated to COVID-19 tasks.

The effect of COVID-19 on the scale-up of HIV VL testing was observed in all President's Emergency Plan for AIDS Relief (PEPFAR)-supported countries. In these 25 countries, VL testing coverage among PWH on ART decreased from 78% to 71% during the period of January-March 2020, despite high VL suppression rate (90%) in that same period [21,22]. In South Africa average weekly number of VL tests in PWH decreased by 22% during the level 5 lockdown from 26 March to the end of April 2020 [23]. Declines in HIV testing and treatment as part of PMTCT services were also experienced. Six countries (Jamaica, Nigeria, Rwanda, Mozambique, Cameroon, Sierra Leone, and Botswana) experienced a decline of 25% or more in pregnant women testing for HIV. South Africa was among five countries that experienced a decline in initiating ART from the period

of March to September 2020 [5]. With the existing gaps and effects of COVID-19, VL monitoring for timeous management of HIV infection among PBWHIV is likely to be affected further and the risk of vertical transmission increased.

1.2 Review of literature

VL monitoring compliance to scheduled repeat VL testing

While viral suppression among PMTCT clients is regularly monitored, few studies have considered the timing of repeat VL testing within the recommended schedules. Studies have reported contrasting uptake to repeat VL testing results. A study that included PWH from the general population of Mozambique (2017) reported 35% follow-up VL testing among those on ART for 6 months or more who had elevated VL [24]. While the general population of Swaziland (2015), reported 60% repeat VL testing of those with elevated VL and on ART for 6 months [25]. Resulting in about a 25%-point difference to repeat VL testing among those with elevated VL and on ART for 6 months between the two countries. In the South African national HIV cohort followed up between 2004 and 2014, about 87% of repeat VL testing was observed among those with elevated VL [26]. This shows that globally, VL testing uptake varies with examples of success varying by country. An increase in ART coverage in most countries led to an increase in demand for VL testing, which resulted in delayed monitoring of treatment failure for South Africa and other sub-Saharan African countries in 2018 [27].

Countries in sub-Saharan Africa are supported by the centers for disease control and prevention (CDC) and other United States government agencies and international partners to provide VL testing to those on ART. A report on VL testing scale-up in seven sub-Saharan African countries

(South Africa, Kenya, Malawi, Namibia, Côte d'Ivoire, Tanzania, and Uganda) in 2016 reported the progress of routine VL monitoring scale-up [26]. The report showed all these countries were routinely testing <50% of those on ART from January to June 2016 for VL. However, the percentage of those on ART with VL tests from 2015 to 2016 varied among countries from less than 25% (Malawi (19%), Tanzania (5%), Côte d'Ivoire (10%), and Uganda (23%)) to > 85% (Namibia (91%) and South Africa (87%)). South African VL testing coverage in this report was comparable to a national study by Fox and colleagues (2020) that indicated VL repeat testing in 84% of the South African HIV-positive population on ART between 2004 and 2014. However, the timing of this repeat test within the recommended schedule was only in 56% of the sample and there was a strong variation by province, Mpumalanga Province with the least guideline-adherent VL tests (38%) [28].

Delayed uptake of scheduled repeat VL tests has also been reported among PBWHIV who used public hospitals in Kenya for PMTCT services, where only 6% had a repeat VL test within the recommended schedule [29]. Attention to VL testing within recommended schedule among PMTCT clients has been minimal. Among PBWHIV in sub-Saharan Africa, VL monitoring according to recommended guidelines of >80% coverage was reported in South Africa, Kenya, and Zambia, while Malawi had 30-60% coverage. However, VL monitoring distinctly varied between pregnancy (range 14-100%) and breastfeeding (38-98%) [30]. Irrespective of the VL monitoring variation among PBWHIV, VL monitoring has proven to increase viral suppression and retention in care, resulting in reduced HIV transmission, maternal morbidity, and mortality [27,31]. Therefore, a late diagnosis of virological failure may result in maternal morbidity and mortality.

HIV vertical transmission

HIV services provision throughout pregnancy and breastfeeding for women at elevated risk of HIV infection and HIV-positive women is essential. VL monitoring indicates the risk of MTCT during pregnancy and breastfeeding. The MTCT rate of <5% at the end of breastfeeding in breastfeeding countries or <2% at 6 weeks postpartum in non-breastfeeding countries is a target for EMTCT [32]. In South Africa, the MTCT rate during pregnancy was 0.9% between April 2016-March 2017. As a result, there are still 240 cases per 100 000 live births, higher than the targeted 50 cases [32,33]. While the MTCT rate among women exclusively breastfeeding and receiving treatment was 2.2% in 2016, below the <5% target [34]. Given that the national antenatal HIV prevalence was 30% in 2019, remaining mostly unchanged since 2010 [34,35], it is vital to ensure women remain virally suppressed in order to sustain progress and reduce new infections over time [36]. Regular monitoring especially for PBWHIV population is essential as women on ART may not all remain suppressed and to monitor overall health and well-being of mothers and their infants [9,17,27,37].

SA PMTCT VL monitoring guidelines

The 2015 and 2019 South African National Department of Health PMTCT (SAPMTCT) guidelines for VL monitoring are outlined in Appendix A and B respectively [38,39]. The 2015 guidelines outlined recommendations and schedules for newly diagnosed mothers and known positives on ART. The 2015 guidelines recommended a repeat VL test in 1 month if VL≥1000 copies/ml and within 6 months when the VL is between 400 and 1000 copies/ml and 6 monthly VL testing if <400 copies/ml [38]. The 2019 guidelines added the following: targeted monitoring for mothers with interrupted ART exposure and who book late for antenatal care; universal VL

testing at delivery and six months postpartum for all women on ART; and six-monthly VL testing during breastfeeding [39]. Furthermore, the 2019 guidelines shortened the window period for repeat VL testing for different VL levels. That is, a PMTCT client should have a repeat VL test at 4 to 6 weeks if their current VL result is >1000 copies/ml, at 8 to 10 weeks if VL=50-999 copies/ml, and at 6 months if VL<50 copies/ml. Although these guidelines aim to improve VL monitoring outcomes and achieve the 95% target of viral suppression, whether adherence to these recommendations is achieved or not is unclear and the COVID-19 effect to repeat VL testing would not be apparent if adherence before and after is unknown.

Factors affecting VL testing compliance and the risk during pre-COVID-19 and COVID-19 periods

Factors associated with VL testing compliance are patient and health system related. Patient-related factors identified by studies include age and length of time on ART, tailored service delivery platforms, lack of knowledge on VL testing, education, costs, wage loss, and time constraints [40]. Age 16 to 30 years relative to older age >46 years and 15 years and younger, low education, travel costs, loss of wage, been on ART for <2 years compared to >4 years, and not attending tailored services delivery platforms were associated with non-uptake to VL testing [24,41]. Health system-related factors influencing non-uptake include lack of staff, testing capacity, prolonged sample storage times at clinics, lack of information, education, lack of communication materials for educating those living with HIV, and lack of training on VL testing [28,40,41]. However, one of these studies reported patient-related factors from the healthcare provider's perspective, data was not collected from PWH [28].

Factors influencing healthcare services uptake during COVID-19 included shortage of medication, lack of personal protective wear, lack of risk allowance for workers, perceived quality of care, restrictions, anxiety, and fear of getting COVID-19 [42]. Pregnant HIV-positive women from the Republic of Moldova reported fear of getting COVID-19, not knowing about the availability of HIV services, and canceled clinics visits as barriers to HIV care uptake, and also reported missing or delaying routine HIV-related lab tests during COVID-19 [43]. Nonetheless, whether factors related to HIV care non-uptake were health system or patient-related, they all increased the risk of missed opportunities for timely management of ART, adherence counseling support, and the risk of vertical HIV transmission [21] due to missing or delaying the uptake of scheduled visits for repeat VL testing.

1.3 Problem statement

Evidence shows that adherence to scheduled repeat VL testing in the South African HIV-positive population, particularly among pregnant and postpartum women is low and delays progress towards the 2030 targets [3]. In the context of the PMTCT program, repeat VL testing according to the SAPMTCT 2015 and 2019 recommended schedules has not been evaluated sufficiently [30]. The COVID-19 pandemic affected clinic visits and further disrupted VL testing completion and progress with its effect already observed in the early stages [21].

1.4 Justification

Evaluating compliance to repeat VL testing within the recommended schedule among the PMTCT clients before, and during the pandemic period, was essential because pregnant and postpartum women were at high risk of both maternal morbidity and mortality, and there was a risk of vertical HIV transmission if the viral suppression was not achieved. Monitoring VL suppression is necessary to improve suppression through enhanced adherence support or switching regimens when failure exists. Therefore, understanding the effect of the COVID-19 pandemic on routine health care services and identifying specific gaps to assist in planning for uninterrupted HIV care during any future/similar national disasters, was critical.

1.5 Research question

1. To what extent did the COVID-19 pandemic and lockdown restrictions affect compliance to recommended repeat VL testing schedules among PMTCT clients in Ehlanzeni District, a rural setting in Mpumalanga between March 2020 to September 2021 (i.e., COVID-19 period)?
2. What sociodemographic factors were associated with timely VL testing among PMTCT clients in Ehlanzeni District, during COVID-19 period?

1.6 Aim and Objectives

The study aim was to determine the extent to which COVID-19 and lockdown restrictions affected compliance to repeat VL testing, and factors associated with timely VL testing among PMTCT clients in Ehlanzeni District, a rural setting in Mpumalanga.

The specific objectives were:

I. To determine compliance to repeat VL test schedule during pre-COVID-19 period, transition period, and during COVID-19 period, overall and by baseline VL status (<50 copies/ml, 50-999 copies/ml and ≥1000 copies/ml) among PMTCT clients in Ehlanzeni district.

II. To compare compliance to repeat VL testing schedule between pre-COVID-19, transition, and COVID-19 periods, among PMTCT clients in the Ehlanzeni district.

III. To determine factors associated with timely VL testing among PMTCT clients in Ehlanzeni district over the course of three periods, and during the COVID-19 period.

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2 CHAPTER 2: SUBMISSIBLE DRAFT MANUSCRIPT

Compliance to viral load monitoring schedules among women attending PMTCT services before and during the COVID-19 pandemic in Ehlanzeni District, Mpumalanga, South Africa

Thandiwe E Mbira[1,2§], Tendesayi Kufa-Chakezha[2,3], Nobubelo K, Ngandu[1]

1. HIV and Other Infectious Disease Research Unit, South African Medical Research Council, Cape Town, South Africa
2. Division of Epidemiology and Biostatistics, School of Public Health, University of the Witwatersrand, Johannesburg, South Africa
3. Centre for HIV and STI, National Institute for Communicable Diseases, Johannesburg, South Africa.

§ Corresponding author: Thandiwe Mbira

Francie van Zyl Drive
Parrowvallei, Cape Town 7505, South Africa
012 339 8609
Thandiwe.Mbira@mrc.ac.za

E-mail addresses of authors:

TM: Thandiwe.Mbira@mrc.ac.za

TK: TendesayiKC@nicd.ac.za

NN: Nobubelo.Ngandu@mrc.ac.za

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2.1 Abstract

Introduction: Human immunodeficiency virus (HIV) viral load (VL) monitoring was interrupted during the Coronavirus disease 2019 (COVID-19) pandemic. This study determined compliance to repeat VL testing schedule and associated factors, among prevention of vertical HIV transmission (PMTCT) clients, before and during the COVID-19 pandemic.

Methods: This was a secondary retrospective cohort analysis of routine data for repeat VL testing among PMTCT clients (N=667) in Ehlanzeni district. Compliance (i.e., timely tests within guideline recommended number of weeks/months) to repeat VL testing schedule was determined during different time periods: pre-COVID-19 (1 April 2019- 25 March 2020), transition (VL test contact before start of lockdown on 26 March 2020 and expected repeat test on or after 26 March 2020), and COVID-19 (26 March 2020 -30 September 2021). Descriptive and inferential analyses were conducted.

Results: Of 405 women with ≥2 VL tests and included in the analysis, the overall median age was 30 years (interquartile range (IQR): 26-35). Compliance to repeat VL testing schedule was above 80% across different periods: pre-COVID-19 (82.6% (233/282)), transition (81.5% (172/211)), and COVID-19 periods (86.0% (178/207)). During pre-COVID-19, compliance was high among women aged ≥25 years compared to younger women (15-24 years), and among women who had baseline VL<50 copies/ml and VL=50-999 copies/ml compared to those with VL≥1000 copies/ml, while during transition and COVID-19 compliance was high among women with baseline VL<50 copies/ml, compared to women with VL≥50 copies/ml. Across all three periods, being compliant was significantly increased for the 25-34 years age-group (incidence-rate ratio (IRR)=1.12, [95% CI:1.01-1.23], p value=0.027) compared to younger age-group, and reduced among those with

baseline VL=50-999 copies/ml (IRR=0.71, [95% CI: 0.61-0.82], p value<0.001) and VL≥1000 copies/ml (IRR=0.18, [95% CI:0.09-0.36], p value<0.001). Similarly, during the COVID-19 period, compliance was reduced by having baseline VL=50-999 copies/ml (IRR=0.40, [95% CI:0.23-0.67], p value=0.001) and VL≥1000 copies/ml (IRR=0.14, [95% CI:0.04-0.51], p value=0.003).

Conclusions: A slight reduction in compliance was observed during transition period, but overall compliance was over 80% and significantly reduced among PMTCT clients who previously had viraemia regardless of the pandemic. Strengthening short message service (SMS) reminders and other strategies can potentially improve uptake and timeous linkage.

2.2 Introduction

The World Health Organization (WHO) recommended viral load (VL) testing for monitoring the effectiveness of antiretroviral treatment (ART) in human immunodeficiency virus (HIV) positive persons [1]. VL monitoring is vital to tracking individual responses to ART, population-level effectiveness of ART, and progress towards United Nations Acquired Immunodeficiency Syndrome (UNAIDS) global targets for combating the HIV epidemic [2]. The UNAIDS's third target in its 95-95-95 goals is to ensure that 95% of people on ART are virally suppressed by 2030 [3,4]. However, progress towards the third target has been slow. In 2019, only 59% of people with HIV (PWHIV) globally were virally suppressed [5]. New interim set of targets for 2025 were developed to accelerate progress towards the 2030 goals. One of the main 2025 targets is to have 95% of pregnant and breastfeeding women with HIV (PBWHIV) having suppressed VL to eliminate vertical HIV transmission (MTCT, EMTCT) [5-9]. South African Prevention of MTCT 2015 guidelines recommends a repeat VL test in 1 month if VL>1000 copies/ml and within 6 months when the VL<1000 copies/ml, while the 2019 guidelines shortened the window period for repeat VL testing for different VL levels [10,11].

Progress towards EMTCT has been slow and new infections still occur and are due to existing gaps in prevention of MTCT (PMTCT), new HIV infections during pregnancy, late HIV diagnosis and initiation of ART, and lack of retention in care [12-20]. VL monitoring in this population has been minimal, and gaps in the PMTCT program remain around repeat VL testing, e.g., only 6% of PBWHIV who use public hospitals in Kenya were reported to have a repeat VL test within the recommended schedule [21-23]. Additionally, PMTCT program outcomes were impacted by the Coronavirus disease 2019 (COVID-19) pandemic and the restrictions on mobility and trade that

were imposed to curb it. In the 2022 UNICEF report, pregnant women from the Republic of Moldova missed and delayed HIV-related lab tests during the COVID-19 pandemic [24].

In many countries, HIV services were interrupted, resources shifted towards the pandemic, and healthcare workers were allocated to COVID-19 tasks. This may explain the decline of 25% or more in testing for HIV in six countries (Jamaica, Nigeria, Rwanda, Mozambique, Cameroon, Sierra Leone, and Botswana) among pregnant women [5]. The lockdown restrictions and fear of getting COVID-19 further made it difficult for people including pregnant and breastfeeding women to access healthcare services, and conducting face-to-face encounters was near impossible [5,25]. This disruption resulted in delays in VL monitoring among PWHIV when clinics and labs were closed during COVID-19 [26]. Considering the existing gaps and effects of COVID-19, VL monitoring for timely management of HIV infection among pregnant and breastfeeding women was likely to be further affected, increasing the potential for vertical transmission. This study aimed to determine compliance to repeat VL testing schedule, and associated factors among PMTCT clients, before and during the COVID-19 pandemic in Ehlanzeni District.

2.3 Methods

Study design and setting

This study was a secondary retrospective cohort analysis, among pregnant women and postpartum mothers, who were previously included in a facility-based cross-sectional study (the PHANGISA study) that took place during September-December 2019 in the eight largest community healthcare centers (CHCs) of the Ehlanzeni District, Mpumalanga province of South Africa. Ehlanzeni district is among three districts located within the Mpumalanga province (mostly rural) of South Africa. The district HIV prevalence during pregnancy is the highest in the province and is among districts with the highest HIV prevalence (20%) in the general population nationally.

Description of primary study

The primary study was comprised of a cross-sectional and longitudinal follow-up component. The PHANGISA study took place from September-December 2019, and the study sample was designed to measure the prevalence of maternal VL non-suppression among pregnant or postpartum women with HIV and is described in detail in Ngandu *et al* [27].

The 667 HIV-positive mothers who were enrolled in the PHANGISA study were followed up virtually using routine VL testing data from the National Health Laboratory Services central data warehouse (NHLSCDW) for uptake of routine VL testing in the PHANGISA COVID study. Uptake of repeat VL testing was tracked retrospectively over a 30-month period starting from 1 April 2019 until 30 September 2021. Unique anonymized patient identifiers were used to longitudinally search for participants' lab test episodes (identified by unique numbers per test date) firstly within the study district and then nationally.

Sampling and sample size determination

Sample precision was calculated assuming that all participants (N=667) enrolled during the PHANGISA study would be included in the secondary analysis. Based on this, the study had 100% power to detect VL testing compliance of 38+/- 5% (based on the Mpumalanga province's known compliance) OR 90.2% power to detect compliance of 38+/- 3% OR 58.7% power to detect compliance of 38+/- 2% with 5% level of significance [28]. When considering the initial sample size being reduced by 30% to 480 due to the exclusion criteria, then at 5% level of significance the study had a power of 99.8% to detect 38+/- 5% compliance OR 84.3% power to detect compliance of 38+/- 3% OR 60.4% power to detect compliance of 38+/- 2%.

Inclusion criteria and exclusion criteria

The inclusion criteria for the secondary study were: all HIV-positive pregnant and postpartum mothers aged 15 years and above, who were enrolled in the primary study and had at least two VL testing data available in the NHLSCDW during the study period (1 April 2019 to 30 September 2021) and reached 24 months postpartum only after the start of COVID-19 lockdown period (i.e., after 25 March 2020). Mothers with no NHLSCDW data or insufficient NHLSCDW data i.e., only one VL test throughout the study period, and those who reached 24 months postpartum before COVID-19 period were excluded.

Variables and outcomes

Primary outcome

The primary outcome measure was compliance to repeat VL testing within each period (i.e., pre-COVID-19, transition, or COVID-19), and was defined as the proportion of participants with a timely test (i.e., within guideline recommended number of weeks/months) out of the sample expected to have a repeat test during that period. The samples for each period were determined as follows: pre-COVID-19 (Figure 1-A step 2): - all participants with the first VL test (pre-COVID-19 baseline) and expected repeat VL test falling before the start of lockdown (i.e., before 25 March 2020), were grouped as the pre-COVID-19 sample; Transition period (Figure 1-B step-2): - all participants with the latest observed VL test (transition baseline) in the pre-COVID-19 period and the expected repeat VL test falling during COVID-19 period were grouped as the transition sample; Covid-19 period (Figure 1-C step 2): - all participants with the earliest observed VL test (COVID-19 baseline) the expected repeat VL test in the COVID-19 period formed the COVID-19 sample.

The numerators for timing of repeat tests are defined in Figure 1- step 3. The difference between the calculated expected date and the actual observed VL test date was used to determine the timing of the VL test (on-time, delayed or missed), within each of the three COVID-19 periods. A VL test done on-time, hence compliant, was defined as a test conducted within a recommended timeframe and allowing a delay of half of the minimum recommended timeframe. That is, within 9 months (i.e., 6 months plus 3 months) if baseline VL<1000 copies/ml, and 4 weeks if VL≥1000 copies/ml using 2015 guidelines, or within 9 months if VL<50 copies/ml, 8-14 weeks if VL=50-999 copies/ml, and 4-6 weeks if VL≥1000 copies/ml using 2019 guidelines (**Appendix C**) [10,11]. Delayed VL testing was defined as a test done after the proposed on-time test period but before the next testing window period. A missed VL test was defined as a test conducted after a full recommended window period between tests had elapsed.

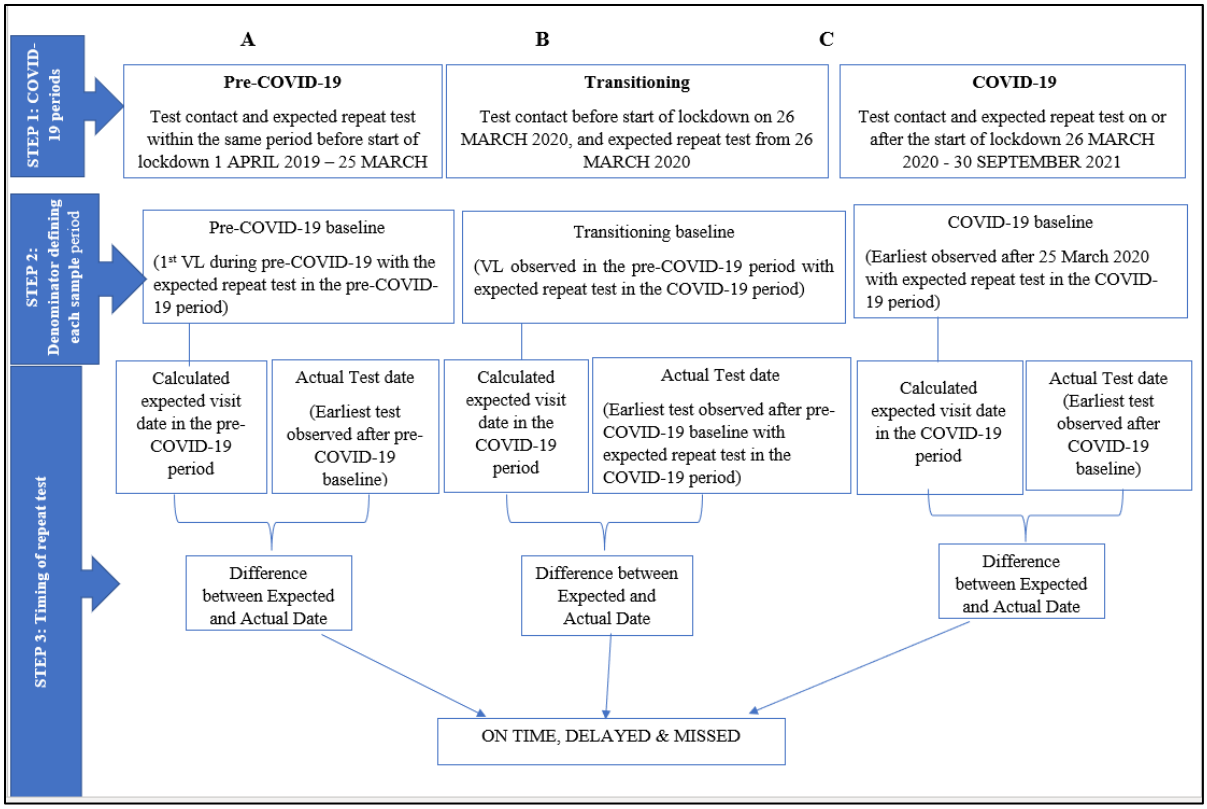

Figure 1: Baseline VL results and the actual VL tests to determine compliance during pre-COVID-19, Transition, and COVID-19 periods

Main exposures

The first main exposure variable was time periods pre-COVID-19, transition, and COVID-19, defined in Figure 1-Step 1 for the VL repeat test samples. The second main exposure variable was the COVID-19 lockdown levels (1 through to 5) at the repeat VL test which changed differentially over the course of the COVID-19 period.

Other independent (exposure) variables (defined in appendix D)

Sociodemographic factors collected during the cross-sectional component of the PHANGISA study, perceived to influence healthcare uptake and HIV indicators were evaluated, and included the participant's PMTCT stage at recruitment (pregnant or postpartum), maternal age in years (15-

24, 25-34, 35-49), level of education (ranging from no formal schooling to higher learning), marital status (never married or never lived with a partner, married or living together, widowed, divorced or separated), source of income (employed, spouse/partner, depend on others and government grant/no income), monthly income (≤R3200, and >R3200), Body mass index (BMI) (obese, overweight, normal, underweight), partner's HIV status (positive, negative, don't know), condom use frequency (Never, Sometimes, always), planned pregnancy (no/yes), gestation at first Antenatal care (ANC) visit (0-12weeks, 13-20weeks, 21-40 weeks), number of ANC visits (0-4 visits, 5-12 visits), timing of HIV diagnosis stage and ART initiation (before recent pregnancy, before 28 weeks gestation, after 28 weeks gestation, around labour/delivery, at postnatal before 6 months, at postnatal after 6 months), Current ART regimen (first line, second/third/ unknown), missed an ART dose last 7days (no/yes), and facing any ART adherence challenges (no/yes).

Data management and analysis

The primary outcome variable and exposure variables were generated using definitions explained earlier. Data were analyzed in Stata/BE-basic edition 17.0 [StataCorp, College Station, Texas USA] and R version 4.2.0 [2022-04-22 ucrt]. The socio-demographic data and the new longitudinal VL tests data were merged. Data were cleaned to exclude participants not meeting the inclusion criteria for this analysis. Proportions were used to describe population characteristics and to report compliance to repeat VL testing (on-time, delayed, and missed tests). The outcome variable was also presented as a binary of on-time versus delayed or missed for the rest of the analyses. The distribution of the outcome by various exposures was assessed using a Chi-square test, for the pre-COVID-19, transition, and COVID-19 periods, separately. A partially overlapping samples z-test which compares proportions for two dichotomous samples was used to compare

compliance to repeat VL testing between pre-COVID-19 and transition periods, pre-COVID-19 and COVID-19 periods, and transition and COVID-19 periods. Data in each comparison comprised a combination of paired (within patient) and unpaired observations [29]. Univariable and multivariable Poisson regression (with robust error variance) analyses were conducted to identify exposure factors associated with compliance to repeat VL testing across the three periods (including all repeat tests) and during the COVID-19 period separately (sub-analysis) and assumptions were tested (**Appendix F**) [30,31]. Exposure variables with an overall univariable p value<0.200 were selected for each multivariable model. Factors such as age, education level, and income were kept in both overall multivariable analysis and sub-analysis *a priori*. A significance level of 0.050 was used in the multivariable analysis to indicate a significant association with compliance to VL testing.

Ethical Considerations

The PHANGISA study ethical approval was obtained from the South African Medical Research Council (SAMRC) ethics committee (EC021-6/2020). For secondary data analysis ethical clearance was granted by the University of the Witwatersrand Human Research Ethics Committee (Medical) (M220268) (**Appendix G**). All participants gave consent in the during recruitment for their routine data to be accessed and used for other related research in the future.

2.4 Results

Sample size realization

Out of the target sample of 667, data for 526 (78.9%) participants were successfully extracted from the NHLSCDW using unique patient identifiers. A further 23% (121/526) of participants were excluded from the study using the study exclusion criteria, resulting in a final sample of 405 participants (**Figure 2**). With the achieved final sample size, the study had 89% power to detect VL testing compliance of 86+/- 3% with 5% level of significance. The number of participants included in the pre-COVID-19, transition, and COVID-19 exposure samples were 282, 211, and 207, respectively.

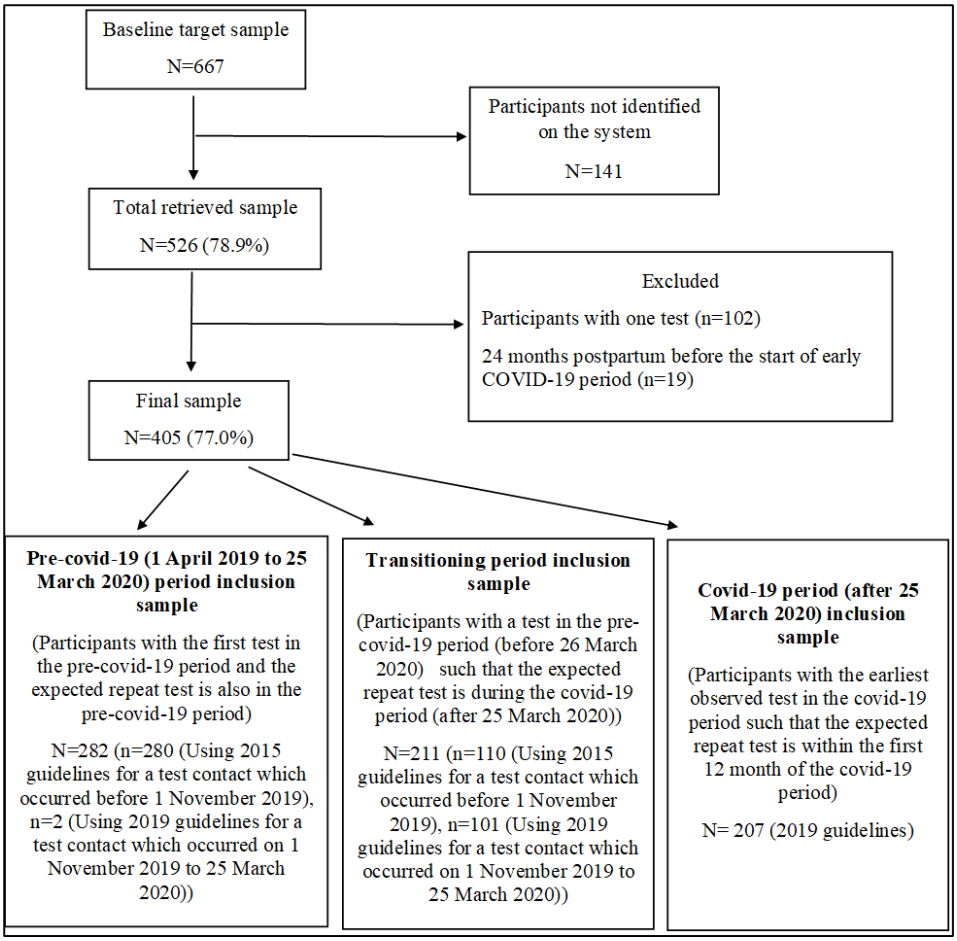

Figure 2: Final sample realization after exclusion and denominator for each period

Population Characteristics

Socio-demographics and PMTCT related factors

Of the 405 included in the analysis, the overall median age of study participants was 30 years (interquartile range (IQR): 26-35) (**Table S 1**). Over 90% of participants had at least grade 8 education level. Most (48.2%) had partners who were HIV positive, while approximately 35% did not know their partner's status. A majority (70%) of the participants were in the postpartum period at recruitment. Most (63.2%) attended their first ANC visit within 0-12 weeks of pregnancy, and 64.2% had more than 4 ANC visits. Around 75% were diagnosed with HIV before their current or recent pregnancy and had initiated ART.

Compliance to repeat VL testing during pre-COVID-19, transition, and COVID-19 period

Compliance to repeat VL testing guidelines during pre-COVID-19, transition period, and COVID-19 was determined, overall and by baseline VL status (**Figure 3**). During pre-COVID-19 period the proportion of women who were compliant to VL test schedule, i.e., on time, was 82.6% (233/282). Compliance during the transition period was 81.5% (172/211), while during COVID-19 was 86.0% (178/207). Compliance to repeat VL testing was compared between two periods at a time and there was no significant difference between periods (**Appendix E**).

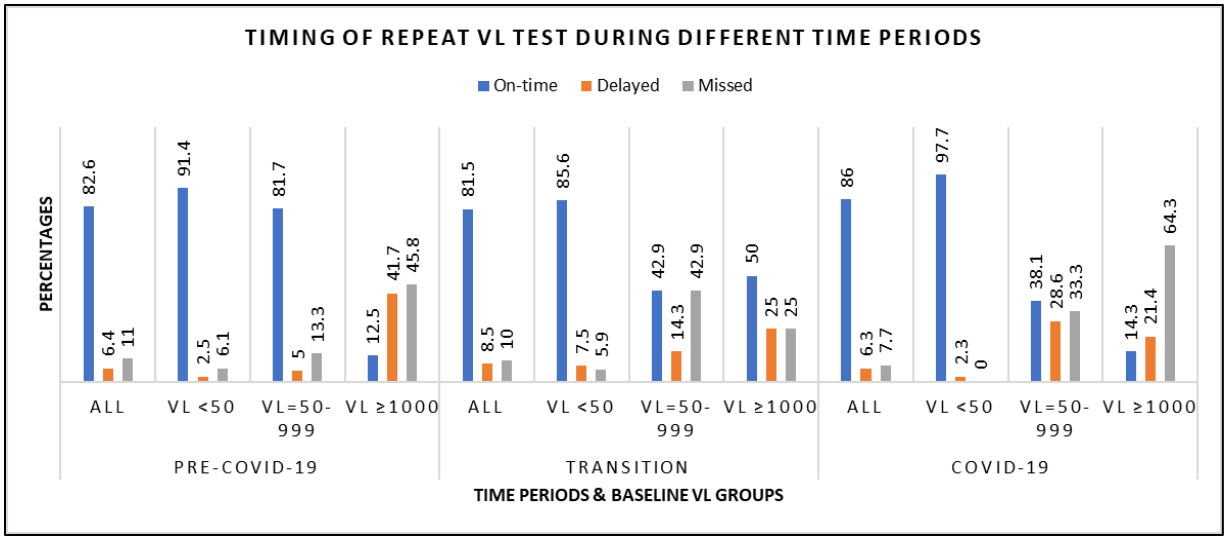

Figure 3: Compliance to repeat VL test during pre-COVID-19, transition, and COVID-19 periods, overall and by baseline VL.

Compliance to repeat VL testing by exposure variables during pre-COVID-19, transition, and COVID-19 periods

Tables S2 and S3 show the distribution of compliance to repeat VL testing by baseline socio-demographic and PMTCT-related factors during pre-COVID-19, transition, and COVID-19 periods. During pre-COVID-19 compliance to repeat VL testing recommended schedule was high among: older age groups (25-34 years (87.1%, [95% CI: 81.0-91.5]) and 35-46 years (81.3%, [95% CI: 70.9-88.6]), compared to the younger group (15-24 years (68.2%, [95% CI: 53.1-80.2])), and the difference was statistically significant (p value=0.012); and those who had baseline VL<50 copies/ml (91.4%, [95% CI: 86.6-94.6]) and VL=50-999 copies/ml (81.7%, [95% CI: 67.8-89.6]), compared to 12.5% [95% CI:4.1-32.5] of those with VL≥1000 copies/ml, p value<0.001. During the transition and COVID-19 periods, compliance was high among those with baseline VL<50 copies/ml, compared to those with baseline VL≥50 copies/ml (both p values<0.001).

Factors associated with compliance to repeat VL testing

Independent variables with an overall p value <0.200 were included in the multivariable Poisson regression model (**Table S4 and S5**). The likelihood of being compliant across all three periods was significantly increased among the 25-34 years age-group (incidence-rate ratio (IRR)=1.12, [95% CI:1.01-1.23], p value=0.027) compared to younger (15-24 years) age-group and reduced among those with baseline VL=50-999 copies/ml (IRR=0.71, [95% CI: 0.61-0.82], p value<0.001) and VL≥1000 copies/ml (IRR=0.18, [95% CI:0.09-0.36], p value<0.001) compared to VL<50 copies/ml. Similarly, during the COVID-19 period (sub-analysis), compliance was reduced when baseline VL=50-999 copies/ml (IRR=0.39, [95% CI:0.23-0.67], p value=0.001) and VL≥1000 copies/ml (IRR=0.14, [95% CI:0.04-0.51], p value=0.003) compared to VL<50 copies/ml.

2.5 Discussion

This study determined and reported compliance to repeat VL testing schedule before and during COVID-19 period in a rural district in South Africa, in line with the PMTCT guidelines used during April 2019- September 2021. Compliance to repeat VL testing was not optimal, ranging 81.5%-86%, and lowest during transition period. High compliance was observed among those with low-level viraemia baseline VL=50-999 copies/ml during pre-COVID-19, compared to other periods. Compliance to repeat VL testing was not significantly different between periods. The likelihood of being compliant was significantly increased among the mid-adulthood age-group (25-34 years) and reduced among those with a detectable baseline VL≥50 copies/ml across the three study periods. When looking at the COVID-19 period alone, compliance was also reduced by having a detectable VL≥50 copies/ml.

This study had a higher (82.6%) compliance to repeat VL testing among PMCT clients before the initiation of the national lockdown compared to what was reported for the general population in South Africa (47.7-56.4%) [28], and what was seen among PMTCT clients in Kenya (only 6% of repeat VL testing within recommended schedule) [21]. The estimates from this study were also higher than what was reported in the Republic of Moldova during the COVID-19 pandemic among PWHIV (28.6%) [24], but comparable to observations of PWHIV in southwestern Uganda (with compliance of 80.3%) [32]. Nonetheless, compliance to repeat VL testing was still sub-optimal, highlighting the gaps that existed around VL testing among PMTCT clients before COVID-19 pandemic in South Africa. Compliance to repeat VL testing during the transition period was reduced slightly from 82.6% to 81.5%, yet it increased to 86.0% as the pandemic continued. Although these differences were not statistically significant, the slight decrease of timely VL testing during the transition period (where repeat tests were during the first six months of the

pandemic with strictest lockdown restrictions) indicates that the COVID-19 pandemic did influence delayed VL monitoring. This observed reduction is supported by the study conducted by El-Nahal et al. which reported delayed VL monitoring when clinics and laboratories were closed during COVID-19 period (March 16–July 12, 2020) [26].

The slight decrease could also be the result of PMTCT guidelines changes at the end of 2019, which may overestimate the delayed testing especially among those with low-level viraemia during the transition and COVID-19 periods, as clinics would not have implemented the recent guidelines used in this analysis which had a short eight to ten weeks window (2019 guidelines) versus a six-month window (2015 guidelines). Therefore, our results might reflect a slow transition to the recent guidelines and supports a country-wide survey now that the 2019 policy is in effect. However, the observed compliance of less than 90% and the significantly reduced likelihood in compliance among all those with detectable VL, regardless of the COVID-19 pandemic compliance is comparable to what was reported in the national South African study that found delayed repeat VL testing in patients with detectable VL [28]. The reduced likelihood in compliance further point to a gap in the system in supporting clients to adhere to more frequent testing when they have presented with viraemia previously. Therefore, continuous evaluation and strengthening of the existing interventions, such as short message service (SMS) appointment reminders is vital. SMS reminders have previously been shown to improve retention and viral suppression among PMTCT clients, early infant diagnosis follow-up testing, and uptake of repeat HIV testing, and the currently ongoing initiative called eLABS solutions, aiming to improve VL monitoring systems, is promising to close the gap of delayed repeat VL testing [33-36]. Continuous evaluation will also help in understanding the gaps that exist around implementation of guidelines.

Compliance to repeat VL testing likelihood was increased among women in the age group of 25-34 years, which agrees to what other studies have reported on VL testing uptake during the study periods [28,37,38]. Services targeted at young PBWHIV are needed to increase timely uptake due to their lower likelihood of receiving VL testing. Furthermore, some previously proposed interventions that have shown potential to improve and encourage VL testing include educational efforts on the benefits of VL testing, using point-of-care VL testing for quick results turnaround times and access to VL testing in resource-limited settings, enhanced adherence counselling, and compensating patients [37-41]. None of the participant sociodemographic factors (education, and income) influenced repeat VL testing as reported in previous studies [32,37,38,42]. However, these previous studies examined factors associated with uptake rather than the timing of repeat testing.

This study had limitations and strengths. As a secondary analysis, we were limited by the data collected at the primary study, also, the issue of missing data in the primary study extended to our study as well. The study did not consider deaths that may have occurred, given the high death rate during COVID-19, which could have overestimated missed repeat VL tests. However, VL test episodes were searched within the district and nationally during the primary study to account for women mobility in and out of the Ehlanzeni district. Our study used the 2019 guidelines (released in December 2019) with a shortened window period for contact tests that took place from January 1st, 2020, which could have further overestimated delayed/missed repeat VL tests in cases where there was slower shift to the new guidelines. However, using the new guidelines will be important to highlight the efforts required to meet the new recommendations. The sociodemographic factors were collected once only prior to the COVID-19 pandemic (during the PHANGISA study), and time-changing factors could have changed during COVID-19. Therefore, another study exploring potential factors over time is required to understand existing gaps outside of the pandemic and help

to effectively strengthen gaps. Ehlanzeni district is a peri-urban setting with large rural population, hence there could be limited external validity of our results to different settings. Given that there have been extremely limited assessments of this kind for PBWHIV, it is essential to conduct a similar evaluation across different settings in South Africa to obtain an accurate status of the guideline's implementation.

2.6 Conclusions

Compliance to repeat VL testing schedule among PMTCT clients was slightly reduced during the peak lockdown restrictions but was not optimal regardless of the time-period and was significantly reduced among those with detectable baseline VL. To improve compliance to repeat VL testing, especially among those with detectable VL and young women, there is a need to strengthen interventions such as short message service (SMS) reminders and other strategies targeted at young PBWHIV, which have shown a potential to improve uptake and timeous linkage for appropriate treatment and care.

2.7 Competing interests

All authors have no competing interests.

2.8 Authors' contributions

TEM, NKN, and TK conceptualized and designed the study. TEM prepared the initial manuscript draft after analyzing the data. Further drafts were critiqued and revised by TEM, NKN, and TK.

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Disclaimer: Opinions, findings, conclusions, or recommendations expressed are those of the authors, not of the funders or organizations.

2.10 Additional files

Table S 1: Characteristics of the PBWHIV included in the study (N=405)

Table S 2: Distribution of compliance to repeat VL tests during pre-COVID-19 (N=282), transition (N=211), and COVID-19 (N=207) periods using 2015 or 2019 guidelines by demographic and socioeconomic factors

Table S 3: Distribution of compliance to repeat VL tests during pre-COVID-19 (N=282), transition (N=211), and COVID-19 (N=207) periods using 2015 or 2019 guidelines by PMTCT factors

Table S 4: Factors associated with timely repeat VL testing among PMTCT clients across the three time periods (N=700 repeat tests)

Table S 5: Factors associated with timely repeat VL testing among PMTCT clients during COVID-19 period (N=207)

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Table S 1: Characteristics of the PBWHIV included in the study (N=405)

Variables	Categories	N	%
Maternal age (years)	Median (IQR)		30 (26.0-35.0)
	15-24 years	65	16.1
	25-34 years	234	57.8
	35-46 years	106	26.2
BMI	Median (IQR)		27 (23.4-32.0)
	Obese	141	34.8
	Overweight	115	28.4
	Normal	130	32.1
	Underweight	17	4.2
	Missing	2	0.5
Level of Education	No formal school	2	0.5
	Grade 1-7	26	6.4
	Grade 8-12	231	57.0
	Certificate with grade12)	103	25.4
	Diploma with grade12)	41	10.1
	Postgrad certificate/diploma/honours degree	1	0.3
	Masters or PhD	1	0.3
Marital status	Never married/not cohabit	239	59.0
	Married/cohabiting	153	37.8
	Widowed	4	1.0
	Divorced/separated	8	2.0
	Other	1	0.3
Source of income	Employed	119	29.4
	Spouse/partner	115	28.4
	Depend on others	61	15.1
	Government grant/no income	110	27.2

Monthly income	No income- R3200	235	58.0
	>R3200	170	42.0
Partner's HIV status	Positive	195	48.2
	Negative	69	17.0
	Don't know	141	34.8
Condom use frequency	Never	37	9.1
	Sometimes	156	38.5
	Always	210	51.9
	Missing	2	0.5
Planned pregnancy	No	217	53.6
	Yes	188	46.4
PMTCT stages	Pregnant	121	30.0
	Postpartum	284	70.0
Gestation at first ANC visit	0-12weeks	256	63.2
	13-20weeks	112	27.7
	21-40 weeks	37	9.1
Number of ANC visits	0-4 visits	145	35.8
	5-12 visits	260	64.2
HIV diagnosis stage	Before current/ recent pregnancy	304	75.1
	Before 28 weeks gestation	88	21.7
	After 28 weeks gestation	10	2,5
	Around labour/delivery	1	0.3
	At PNC before 6mnths	1	0.3
	At PNC after 6mnths	1	0.3
ART initiation	Before current/recent pregnancy	303	74.8
	Before 28 weeks gestation	85	21.0
	After 28 weeks gestation	8	2.0
	Around labour/delivery	1	0.3
	At PNC before 6mnths	3	0.7
	At PNC after 6mnths	4	1.0

	Missing	1	0.3
Current ART regimen	First line	332	82.0
	2nd/3rd line/unknown	71	17.5
	Missing	2	0.5
Missed an ART dose last 7days	No	386	95.3
	Yes	19	4.7
Facing any ART adherence challenges	No	131	32.4
	Yes	274	67.7

n=number of cases per category; BMI, Body mass index; IQR, Interquartile range; ART, Antiretroviral treatment; PMTCT, Prevention of vertical HIV transmission; ANC, antenatal care; PNC, Postnatal care

Table S 2: Distribution of compliance to repeat VL tests during pre-COVID-19 (N=282), transition (N=211), and COVID-19 (N=207) periods using 2015 or 2019 guidelines by demographic and socioeconomic factors

	Pre-COVID-19				Transitional Period				COVID-19			
		On-time	Delayed/ Missed	Chi-sq p-value		On-time	Delayed/ Missed	Chi-sq p-value		On-time	Delayed/ Missed	Chi-sq p-value
	N	% [95% CI]	% [95% CI]		N	% [95% CI]	% [95% CI]		N	% [95% CI]	% [95% CI]	
All	282	82.6 [77.8, 86.6]	17.4 [13.4, 22.2]		211	81.5 [75.7, 86.2]	18.5 [13.8, 24.3]		207	86.0 [80.5, 90.1]	14.0 [9.9, 19.5]	
Maternal Age groups				**0.012**				0.523				0.181
15-24 years	44	68.2 [53.1, 80.2]	31.8 [19.8, 46.9]		32	78.1 [60.6,89.2]	21.9 [10.8, 39.4]		33	75.8 [58.4, 87.4]	24.2 [12.6, 41.6]	
25-34 years	163	87.1 [81.0, 91.5]	12.9 [8.5, 19.0]		120	84.2 [76.5, 89.7]	15.8 [10.3, 23.5]		123	87.8 [80.7, 92.5]	12.2 [7.5, 19.3]	
35-46 years	75	81.3 [70.9, 88.6]	18.7 [11.4, 29.1]		59	78.0 [65.6, 86.8]	22.0 [13.2, 34.4]		51	88.2 [76.1, 94.6]	11.8 [5.4, 23.9]	
BMI groups				0.636				0.362				**0.022**
Obese	99	82.8 [74.2, 90.5]	17.2 [10.9, 25.9]		74	87.8 [78.2, 93.6]	12.2 [6.4, 21.8]		74	86.5 [76.6, 92.6]	13.5 [7.4, 23.4]	
Overweight	81	84.0 [74.2, 90.5]	16.0 [9.5, 25.8]		61	78.7 [66.6, 93.6]	21.3 [12.8, 33.4]		55	80.0 [67.3, 88.6]	20.0 [11.4, 32.7]	
Normal	88	79.5 [69.8, 86.7]	20.5 [13.3, 30.2]		64	76.9 [65.1, 85.6]	23.1 [14.4, 34.9]		66	93.9 [84.9, 97.7]	6.1 [2.3, 15.1]	
Underweight	14	92.9 [62.8, 99.0]	7.1 [1.0, 37.2]		11	81.8 [49.1, 95.5]	18.2 [4.5, 50.9]		11	63.6 [33.7, 85.8]	36.4 [14.2, 66.3]	
Level of Education				0.198				0.303				0.962
None-Grade 7	19	68.4 [45.1, 85.1]	31.6 [14.9, 54.9]		13	84.6 [54.7, 96.2]	15.4 [3.8, 45.3]		12	83.3 [52.1, 95.8]	16.7 [4.2, 47.9]	

Grade 8-12	160	82.5 [75.8, 87.7]	17.5 [12.3, 24.2]		123	78.0 [69.8, 84.5]	22.0 [15.5, 30.2]		122	86.1 [78.7, 91.2]	13.9 [8.8, 21.3]	
Over high school	103	85.4 [77.2, 91.0]	14.6 [9.0, 22.8]		75	86.7 [76.9, 92.7]	13.3 [7.3, 23.1]		73	86.3 [76.3, 92.5]	13.7 [7.5, 23.7]	
Marital status				0.932				0.478				0.649
Never married/ not cohabiting	161	82.6 [75.9, 87.7]	17.4 [12.3, 24.1]		132	79.5 [71.8, 85.6]	20.5 [14.4, 28.2]		115	84.3 [76.5, 89.9]	15.7 [10.1, 23.5]	
Married/cohabiting	113	82.3 [74.1, 88.3]	17.7 [11.7, 25.9]		71	85.9 [75.7, 92.3]	14.1 [7.7, 24.3]		87	88.5 [79.9, 93.7]	11.5 [6.3, 20.1]	
Widowed/divorced/separate	8	87.5 [46.0, 98.3]	12.5 [1.7, 54.0]		8	75.0 [37.5, 93.8]	25.0 [6.2, 62.5]		5	80.0 [30.6, 97.3]	20.0 [2.7, 69.4]	
Source of income				0.992				0.871				0.954
Employed	82	81.7 [71.8, 88.7]	18.3 [11.3, 28.2]		52	80.8 [67.7, 89.4]	19.2 [10.6, 32.3]		59	84.7 [73.1, 91.9]	15.3 [8.1, 26.9]	
Spouse/partner	81	82.7 [72.9, 89.5]	17.3 [10.5, 27.1]		58	79.3 [66.9, 87.9]	20.7 [12.1, 33.1]		63	87.3 [76.5, 93.5]	12.7 [6.5, 33.5]	
Depend on others	40	82.5 [67.5, 91.4]	17.5 [8.6, 32.5]		36	86.1 [70.6, 94.1]	13.9 [5.9, 29.4]		31	83.9 [66.5, 93.2]	16.1 [6.8, 33.5]	
Government grant/no income	79	83.5 [73.6, 90.2]	16.5 [9.8, 26.4]		65	81.5 [70.2, 89.2]	18.5 [10.8, 29.8]		54	87.0 [75.1, 93.7]	13.0 [6.3, 24.9]	
Monthly income				0.169				0.725				0.970
No income- R3200	163	85.3 [78.9, 89.9]	14.7 [10.1, 21.1]		135	82.2 [74.8, 87.8]	17.8 [12.2, 25.2]		85	85.9 [76.7, 91.8]	14.1 [8.2, 23.3]	
>R3200	119	79.0 [70.7, 85.4]	21.0 [14.6, 29.3]		76	80.3 [69.7, 87.8]	19.7 [12.2, 30.3]		122	86.1 [78.7, 91.2]	13.9 [8.8, 21.3]	
Partner's HIV status				0.503				0.240				0.672
Positive	141	80.1 [72.7, 85.9]	19.9 [14.1, 27.3]		97	77.3 [67.9, 84.6]	22.7 [15.4, 32.1]		101	88.1 [80.2, 93.2]	11.9 [6.8, 19.8]	
Negative	46	87.0 [73.8, 94.0]	13.0 [6.0, 26.2]		42	81.0 [66.2, 90.2]	19.0 [9.8, 33.8]		35	82.9 [66.6, 92.1]	17.1 [7.9, 33.4]	

Don’t know	95	84.2 [75.4, 90.3]	15.8 [9.7, 24.6]		72	87.5 [77.6, 93.4]	12.5 [6.6, 22.4]		71	84.5 [74.1, 91.2]	15.5 [8.8, 25.9]	
Condom use frequency*				0.998				0.900				0.984
Never	23	82.6 [61.7, 93.3]	17.4 [6.7, 38.3]		20	80.0 [57.1, 92.3]	20.0 [7.7, 42.9]		15	86.7 [59.2, 96.7]	13.3 [3.3, 40.8]	
Sometimes	110	82.7 [74.5, 88.7]	17.3 [11.3; 25.5]		88	83.0 [73.6, 89.5]	17.0 [10.5, 26.4]		81	86.4 [77.1, 92.3]	13.5 [7.7, 22.9]	
Always	147	83.0 [76.0, 88.3]	17.0 [11.7, 24.0]		103	80.6 [71.7, 87.1]	19.4 [12.9, 28.3]		111	85.6 [77.7, 91.0]	14.4 [9.0, 22.3]	
Planned pregnancy				0.542				0.812				0.333
No	150	81.3 [74.3, 86.8]	18.7 [13.2, 25.7]		110	80.9 [72.4, 87.2]	19.1 [12.8, 27.6]		110	88.2 [80.7, 93.0]	11.8 [7.0, 19.3]	
Yes	132	84.1 [76.8, 89.4]	15.9 [10.6, 23.2]		101	82.2 [73.4, 88.5]	17.8 [11.5, 26.6]		97	83.5 [74.7, 89.7]	16.5 [10.3, 25.3]	
Lockdown levels at a repeat test												0.832
Level 1									42	88.1 [74.3, 95.0]	11.9 [5.0, 25.7]	
Level 2									22	81.8 [60.2, 93.0]	18.2 [7.0, 39.8]	
Level 3									72	88.9 [79.3, 94.4]	11.1 [5.6, 20.7]	
Level 4									30	83.3 [65.6, 92.9]	16.7 [7.1, 34.4]	
Level 5									41	82.9 [68.2, 91.7]	17.1 [8.3, 31.8]	

* Variables with missing data, Bolded p values= statistically significant. n=number of cases per category; BMI, Body mass index; ART, Antiretroviral treatment; ANC, Antenatal Care; PMTCT, Prevention of vertical HIV transmission

Table S 3: Distribution of compliance to repeat VL tests during pre-COVID-19 (N=282), transition (N=211), and COVID-19 (N=207) periods using 2015 or 2019 guidelines by PMTCT factors

	Pre-COVID-19				Transitional Period				COVID-19			
		On-time	Delayed/ Missed	Chi-sq p-value		On-time	Delayed/ Missed	Chi-sq p-value		On-time	Delayed/ Missed	Chi-sq p-value
	N	% [95% CI]	% [95% CI]		N	% [95% CI]	% [95% CI]		N	% [95% CI]	% [95% CI]	
PMTCT stages at baseline				0.161				0.656				0.389
Pregnant	87	87.4 [78.5, 92.9]	12.6 [7.1, 21.5]		75	80.0 [69.4, 87.6]	20.0 [12.4, 30.6]		51	82.4 [69.3, 90.6]	17.6 [9.4, 30.7]	
Postpartum	195	80.5 [74.3, 85.5]	19.5 [14.5, 25.7]		136	82.4 [75.0, 87.9]	17.6 [12.1, 25.0]		156	87.2 [80.9, 91.6]	12.8 [8.4, 19.1]	
Baseline or previous VL				**<0.001**				**<0.001**				**<0.001**
VL<50 copies/ml	198	91.4 [86.6, 94.6]	8.6 [5.4, 13.4]		186	86.6 [80.8, 90.8]	13.4 [9.2, 19.2]		172	97.7 [93.9, 99.1]	2.3 [0.9, 6.1]	
VL=50-999 copies/ml	60	81.7 [69.8, 89.6]	18.3 [10.4, 30.2]		21	42.9 [23.9, 64.2]	57.1 [35.8, 76.1]		21	38.1 [20.2, 59.9]	61.9 [40.1,79.7]	
VL≥1000 copies/ml	24	12.5 [4.1, 32.5]	87.5 [67.5, 95.9]		4	50.0 [12.2, 87.8]	50.0 [12.2, 87.8]		14	14.3 [3.6, 42.9]	85.7 [57.1,96.4]	
Gestation at first ANC visit				0.619				0.854				0.860
0-12 weeks	178	84.3 [78.1, 88.9]	15.7 [11.1, 21.9]		124	83.1 [75.4, 88.7]	16.9 [11.3,24.6]		137	85.4 [78.4, 90.4]	14.6 [9.6, 21.6]	
13-20 weeks	81	80.2 [70.1, 87.6]	19.8 [12.4, 29.9]		69	79.7 [68.5, 87.6]	20.3 [12.4, 31.5]		51	88.2 [76.1, 94.6]	11.8 [5.4, 23.9]	
21-40 weeks	23	78.3 [57.1, 90.7]	21.7 [9.3, 42.9]		18	77.8 [53.4, 91.5]	22.2 [8.5, 46.6]		19	84.2 [60.7, 94.9]	15.8 [5.1, 39.3]	
Number of ANC visits				0.181				0.995				0.658
0-4 visits	103	78.6 [69.6, 85.5]	21.4 [14.5, 30.4]		76	81.6 [71.2, 88.8]	18.4 [11.2, 28.8]		78	84.6 [74.8, 91.1]	15.4 [8.9, 25.2]	
5-12 visits	179	84.9 [78.9, 89.5]	15.1 [10.5, 21.1]		135	81.5 [74.0, 87.2]	18.5 [12.8, 26.0]		129	86.8 [79.8, 91.7]	13.2 [8.3, 20.2]	
HIV diagnosis stage				0.418				0.504				0.244
Before pregnancy	225	81.3 [75.7, 85.9]	18.7 [14.1, 24.3]		160	80.0 [73.0, 85.5]	20.0 [14.5, 27.0]		146	88.4 [82.0, 92.7]	11.6 [7.3, 18.0]	
During pregnancy, before 28 weeks	53	86.8 [74.7, 93.6]	13.2 [6.4, 25.3]		46	84.8 [71.3, 92.6]	15.2 [7.4, 28.7]		54	81.5 [68.8, 89.8]	18.5 [10.2, 31.2]	

During pregnancy, after 28 weeks or during delivery or postnatal	4	100	0		5	100	0		7	71.4 [32.4, 92.9]	28.6 [7.1, 67.6]	
ART initiation				0.670				0.476				0.338
Before pregnancy	223	81.6 [76.0, 86.2]	18.4 [13.8, 24.0]		160	80.0 [73.0, 85.5]	20.0 [14.5, 27.0]		145	88.3 [81.9, 92.6]	11.7 [7.4, 18.1]	
During pregnancy, before 28 weeks	50	86.0 [73.4, 93.2]	14.0 [6.8, 26.6]		44	84.1 [70.1, 92.3]	15.9 [7.7, 29.9]		53	81.1 [68.3, 89.6]	18.9 [10.4, 31.7]	
During pregnancy, after 28 weeks or during delivery or postnatal	9	88.9 [49.8, 98.5]	11.1 [1.5, 50.2]		7	100	0		9	77.8 [41.9, 94.4]	22.2 [5.6, 58.1]	
Current ART regimen*				0.438				**0.014**				0.784
First line	227	83.7 [78.3, 88.0]	16.3 [12.0, 21.7]		177	78.5 [71.8, 84.0]	21.5 [16.0, 28.2]		174	86.2 [80.2, 90.6]	13.8 [9.4, 19.8]	
2nd/3rd line/unknown	53	79.2 [66.2, 88.1]	20.8 [11.9, 33.8]		33	97.0 [81.2, 99.6]	3.0 [0.4, 18.8]		32	84.4 [67.4, 93.3]	15.6 [6.6, 32.6]	
Missed an ART dose last 7days				0.476				0.736				0.576
No	270	83.0 [78.0, 87.0]	17.0 [13.0, 22.0]		203	81.8 [75.8, 86.5]	18.2 [13.5, 24.2]		197	86.3 [80.7, 90.5]	13.7 [9.5, 19.3]	
Yes	12	75.0 [44.7, 91.8]	25.0 [8.2, 55.3]		8	75.0 [37.5, 93.8]	25.0 [6.2, 62.5]		10	80.0 [45.7, 95.0]	20.0 [5.0, 54.3]	
Facing any ART adherence challenges				0.504				0.545				0.935
No	81	80.2 [70.1, 87.6]	19.8 [12.4, 29.9]		70	82.9 [72.1, 90.0]	17.1 [10.0, 27.9]		70	85.7 [75.4, 92.2]	14.3 [7.8, 24.6]	
Yes	201	83.6 [77.8, 88.1]	16.4 [11.9, 22.2]		141	80.9 [73.5, 86.6]	19.1 [13.4, 26.5]		137	86.1 [79.2, 91.0]	13.9 [9.0, 20.8]	

* Variables with missing data, Bolded p values= statistically significant. n=number of cases per category; ART, Antiretroviral treatment; ANC, Antenatal Care; PMTCT, Prevention of vertical HIV transmission

Table S 4: Factors associated with timely repeat VL testing among PMTCT clients across the three time periods (N=700 repeat tests)

	Number with on-time repeat VL tests (row %)	Unadjusted		Adjusted	
		IRR (95% CI)	P Value	IRR (95% CI)	P Value
COVID-19 stages			0.348		
Pre-COVID-19	233 (82.6)	Ref			
Transition	172 (81.5)	0.99 [0.1, 1.07]	0.752		
COVID-19	178 (86.0)	1.04 [0.96, 1.12]	0.308		
Maternal Age groups			0.216		
15-24 years	80 (73.4)	Ref		Ref	
25-34 years	351 (86.5)	1.18 [1.05, 1.33]	0.007	1.12 [1.01, 1.23]	**0.027**
35-46 years	152 (82.2)	1.12 [0.98, 1.28]	0.093	1.08 [0.97, 1.21]	0.176
BMI groups			0.404		
Obese	2111 (85.4)	Ref			
Overweight	160 (81.2)	0.95 [0.87, 1.03]	0.243		
Normal	182 (83.1)	0.97 [0.90, 1.05]	0.494		
Underweight	29 (80.6)	0.94 [0.80, 1.12]	0.495		
Level of Education			**0.097**		
None-Grade 7	34 (77.3)	Ref		Ref	
Grade 8-12	333 (82.2)	1. 06 [0.90, 1.26]	0.465	1.00 [0.86, 1.15]	0.958
Over high school	216 (86.1)	1.11 [0.94, 1.32]	0.209	1.03 [0.89, 1.20]	0.681
Marital status			0.432		
Never married/ not cohabiting	335 (82.1)	Ref			
Married/cohabiting	231 (85.2)	1.04 [0.97, 1.11]	0.275		
Widowed/divorced/separated	17 (81.0)	0.99 [0.80, 1.22]	0.896		
Source of income			0.677		
Employed	159 (82.4)	Ref		Ref	
Spouse/partner	168 (83.2)	1.01 [0.92, 1.10]	0.837	0.98 [0.91, 1.06]	0.623
Depend on others	90 (84.1)	1.02 [0.92, 1.13]	0.699	1.04 [0.95, 1.13]	0.448
Government grant/no income	166 (83.8)	1.02 [0.93, 1.11]	0.701	1.01 [0.93, 1.09]	0.831
Monthly income			0.292		
>R3200	228 (81.4)	Ref		Ref	

No income- R3200	355 (84.5)	1.04 [0.97, 1.11]	0.292	1.05 [0.99, 1.12]	0.106
Partner's HIV status			0.247		
Positive	277 (81.7)	Ref			
Negative	103 (83.7)	1.02 [0.93, 1.12]	0.604		
Don't know	203 (85.2)	1.04 [0.97, 1.12]	0.249		
Condom use frequency*			0.919		
Never	48 (82.8)	Ref			
Sometimes	234 (83.9)	1.01 [0.89, 1.15]	0.838		
Always	300 (83.1)	1.00 [0.88, 1.14]	0.949		
Planned pregnancy			0.975		
No	308 (83.2)	Ref			
Yes	275 (83.3)	1.00 [0.94, 1.07]	0.975		
PMTCT stages			0.894		
Pregnant	178 (83.6)	Ref			
Postpartum	405 (83.2)	1.00 [0.93, 1.07]	0.894		
Baseline or previous VL			**<0.001**		
VL<50 copies/ml	510 (91.7)	Ref		Ref	
VL=50-999 copies/ml	66 (64.7)	0.78 [0.61, 0.82]	0.000	0.71 [0.61, 0.82]	**<0.001**
VL≥1000 copies/ml	7 (16.7)	0.16 [0.09, 0.36]	0.000	0.18 [0.09, 0.36]	**<0.001**
Gestation at first ANC visit			0.342		
0-12 weeks	370 (84.3)	Ref			
13-20 weeks	165 (82.1)	0.97 [0.90, 1.05]	0.498		
21-40 weeks	48 (80.0)	0.95 [0.83, 1.08]	0.442		
Number of ANC visits			0.301		
0-4 visits	209 (81.3)	Ref			
5-12 visits	374 (84.4)	1.04 [0.97, 1.11]	0.301		
ART initiation			0.548		
Before pregnancy	438 (83.0)	Ref			
During pregnancy, before 28 weeks	123 (83.7)	1.01 [0.93, 1.09]	0.835		
During pregnancy, after 28 weeks or during delivery or postnatal	22 (88.0)	1.06 [0.91, 1.23]	0.440		
Current ART regimen*			0.445		
First line	479 (82.9)	Ref			

2nd/3rd line/unknown	101 (85.6)	1.03 [0.95, 1.12]	0.445
Missed an ART dose last 7days			0.398
No	560 (83.6)	Ref	
Yes	23 (76.7)	0.92 [0.75, 1.12]	0.398
Facing any ART adherence challenges			0.819
No	183 (82.8)	Ref	
Yes	400 (83.5)	1.01 [0.94, 1.08]	0.819

*Variables with missing data, Factors with overall univariate p-value<0.2 bolded, Bolded multivariate significant p-value<0.05. IRR, Incident rate ratios; CI, Confidence Interval; n=number of cases per category; BMI, Body mass index; ART, Antiretroviral treatment; ANC, Antenatal Care; PMTCT, Prevention of vertical HIV transmission

Table S 5: Factors associated with timely repeat VL testing among PMTCT clients during COVID-19 period (N=207)

	Number with on-time repeat VL tests (row%)	Unadjusted		Adjusted	
		IRR (95% CI)	P Value	IRR (95% CI)	P Value
Maternal Age groups			**0.193**		
15-24 years	25 (75.8)	Ref		Ref	
25-34 years	108 (87.8)	1.16 [0.94, 1.42]	0.157	1.06 [0.93, 1.20]	0.388
35-46 years	45 (88.2)	1.16 [0.94, 1.45]	0.170	1.10 [0.94, 1.29]	0.233
BMI groups			0.995		
Obese	64 (86.5)	Ref			
Overweight	44 (80.0)	0.93 [0.79, 1.09]	0.340		
Normal	62 (93.9)	1.09 [0.98, 1.21]	0.133		
Underweight	7 (63.6)	0.74 [0.47, 1.16]	0.188		
Level of Education			0.851		
None-Grade 7	10 (83.3)	Ref		Ref	
Grade 8-12	105 (86.1)	1.03 [0.79, 1.34]	0.810	1.03 [0.80, 1.32]	0.819
Over high school	63 (86.3)	1.04 [0.79, 1.36]	0.799	1.03 [0.81, 1.32]	0.801
Marital status			0.570		
Never married/ not cohabiting	97 (84.4)	Ref			
Married/cohabiting	77 (88.5)	1.05 [0.94, 1.17]	0.389		
Widowed/divorced/separated	4 (80.0)	0.95 [0.61, 1.48]	0.816		
Source of income			0.834		
Employed	50 (84.8)	Ref		Ref	
Spouse/partner	55 (87.3)	1.03 [0.89, 1.19]	0.686	1.04 [0.95, 1.14]	0.395
Depend on others	26 (83.9)	0.99 [0.82, 1.20]	0.914	1.01 [0.91, 1.12]	0.852
Government grant/no income	47 (87.0)	1.03 [0.88, 1.19]	0.727	1.05 [0.94, 1.18]	0.358
Monthly income			0.970		
>R3200	73 (85.9)	Ref		Ref	
No income- R3200	105 (86.1)	1.00 [0.90, 1.12]	0.970	0.96 [0.88, 1.05]	0.356
Partner's HIV status			0.478		
Positive	89 (88.1)	Ref			
Negative	29 (82.9)	0.94 [0.80, 1.11]	0.471		

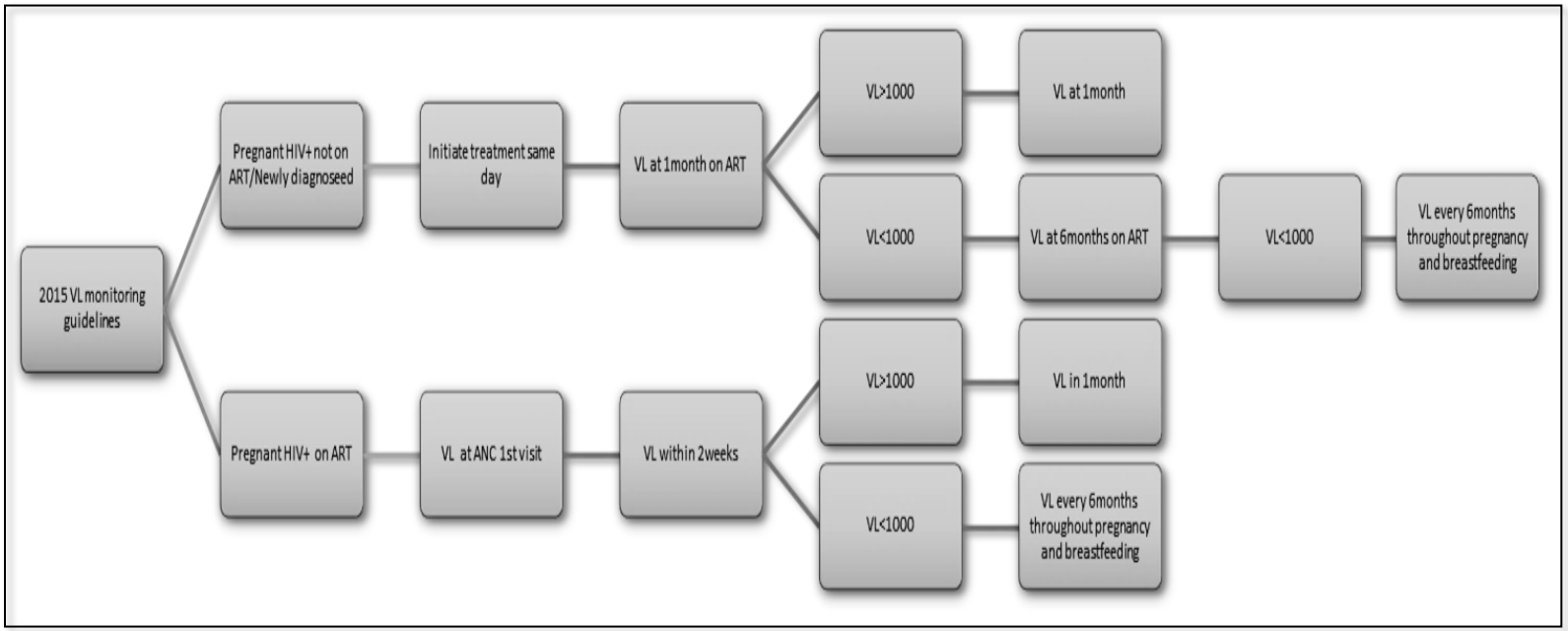
Don't know	90 (84.5)	0.96 [0.85, 1.08]	0.505		
Condom use frequency*			0.860		
Never	13 (86.7)	Ref			
Sometimes	70 (86.4)	1.00 [0.80, 1.24]	0.979		
Always	95 (85.6)	0.99 [0.80, 1.22]	0.908		
Planned pregnancy			0.341		
No	97 (88.2)	Ref			
Yes	81 (83.5)	0.95 [0.85, 1.06]	0.341		
Lockdown levels at repeat test			**0.173**		
Level 1		Ref			
Level 2		1.04 [0.91, 1.20]	0.558	1.02 [0.89, 1.18]	0.750
Level 3		0.95 [0.84, 1.08]	0.447	0.95 [0.88, 1.02]	0.133
Level 4		0.82 [0.61, 1.10]	0.184	0.81 [0.65, 1.01]	0.057
Level 5		1.13 [1.05, 1.11]	0.001	0.97 [0.91, 1.04]	0.428
PMTCT stages					
Pregnant	42 (82.4)	Ref			
Postpartum	136 (87.2)	1.06 [0.92, 1.22]	0.428		
Baseline or previous VL			**<0.001**		
VL<50 copies/ml	168 (97.7)	Ref		Ref	
VL=50-999 copies/ml	8 (38.1)	0.39 [0.23, 0.67]	0.001	0.40 [0.23, 0.67]	**0.001**
VL≥1000 copies/ml	2 (14.3)	0.15 [0.04, 0.53]	0.003	0.14 [0.04, 0.51]	**0.003**
Gestation at first ANC visit			0.888		
0-12 weeks	117 (85.4)	Ref			
13-20 weeks	45 (88.2)	1.03 [0.91, 1.17]	0.600		
21-40 weeks	16 (84.2)	0.99 [0.80, 1.21]	0.894		
Number of ANC visits			0.665		
0-4 visits	66 (84.6)	Ref			
5-12 visits	112 (86.8)	1.02 [0.91, 1.15]	0.665		
ART initiation			**0.207**		
Before pregnancy	128 (88.3)	Ref		Ref	
During pregnancy, before 28 weeks	43 (81.1)	0.92 [0.80, 1.06]	0.248	0.95 [0.86, 1.06]	0.352
During pregnancy, after 28 weeks or during delivery or postnatal	7 (77.8)	0.88 [0.62, 1.26]	0.485	0.96 [0.75, 1.23]	0.727

Current ART regimen*			0.794
First line	150 (86.2)	Ref	
2nd/3rd line/unknown	27 (84.4)	0.98 [0.83, 1.15]	0.794
Missed an ART dose last 7days			0.638
No	170 (86.3)	Ref	
Yes	8 (80.0)	0.93 [0.68, 1.27]	0.638
Facing any ART adherence challenges			0.935
No	60 (85.7)	Ref	
Yes	118 (86.1)	1.00 [0.89, 1.13]	0.935

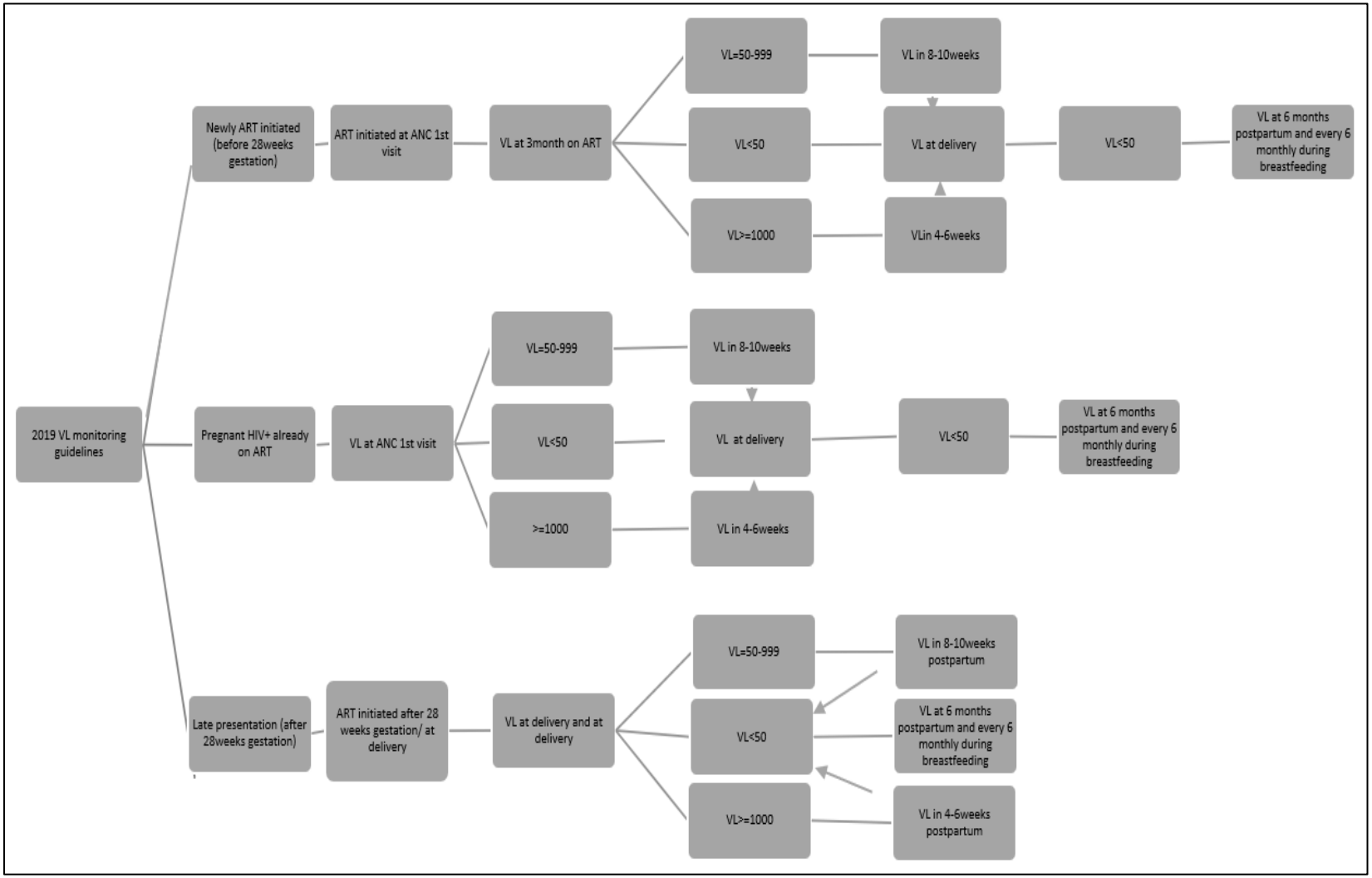
* Variables with missing data, Factors with overall univariate p-value<0.2 bolded, Bolded multivariate significant p-value<0.05. IRR, Incident rate ratios; CI, Confidence Interval; n=number of cases per category; BMI, Body mass index; ART, Antiretroviral treatment; ANC, Antenatal Care; PMTCT, Prevention of vertical HIV transmission

APPENDICES

Appendix A: 2015 SAPMTCT VL monitoring guidelines for pregnant and breastfeeding mothers



Appendix B: 2019 SAPMTCT VL monitoring guidelines for pregnant and breastfeeding women



Appendix C: Calculation of compliance to repeat VL tests during COVID-19 periods using 2015 and 2019 guidelines

Guidelines	Baseline or previous VL	Expected time period to next visit as per the PMTCT guidelines	Proposed time window for 'on-time' VL test	Proposed time window for 'delayed' VL test	Proposed time window for 'missed' VL test
2015 guidelines	<1000 copies/ml	6 months	6-9 months (i.e., plus half of 6)	>9 – 12 months (i.e., until next due date)	>12 months
	>=1000	4 weeks	4 weeks (unchanged)	7-8 weeks (i.e., until just before next due date)	>8 weeks
2019 guidelines	<50 copies/ml	6 months	6-9 months (i.e., plus half of 6)	>9 – 12 months (i.e., until next due date)	>12 months
	50-999 copies/ml	8 to 10 weeks	8-14 weeks (i.e., plus half of 8)	15 - 20 weeks (i.e., until next due date)	>20 weeks
	>=1000	4 to 6 weeks	4-6 weeks (unchanged)	7-10 weeks (i.e., until just before next due date)	>10 weeks

Appendix D: Other exposure variables

Factor	Level	Definition
Maternal age	15-24 years	Mother's age on the day of enrollment day (in years)
	25-34 years	
	35-49 years	
PMTCT stages	Pregnant	In the 3rd trimester
	Post-partum	From birth up to 24 months
Level of education	No formal school	
	Primary	Grade 1-7
	High school	Grade 8-12
	Over high school	Certificate with grade 12, diploma, degree, and postgraduate
Marital status	Never married/never lived with a partner	
	Married/lived together	
	Widowed/divorced/separated	
Source of income	Employed	Paid employee (not family/domestic worker)/ Paid family/domestic worker
	Self-employed	
	Depend on others	Depend on spouse/partner/parents/relatives
	Government grant	
	No stable income	
Income/month		Self-reported monthly income
	no income- R3200	
	>R3200	
Body mass index (BMI)	Obese	≥30 kg/m^2
	Overweight	25.0–29.9 kg/m^2
	Normal	18.5–24.9 kg/m^2
	Underweight	13.0–18.4 kg/m^2
Partner's HIV status	Positive	
	Negative	
	Don't know	
Condom use frequency*	Never	
	Sometimes	
	Always	
Planned pregnancy	No	
	Yes	
Lockdown levels at baseline	Level 5	Baseline tests done in the period of 26 March to 30 April 2020
	Level 4	Baseline tests done in the period of 1 to 31 May 2020 and 28 June to 25 July 2021
	Level 3	Baseline tests done in the period of 1 June to 17 August 2020, 29 December 2020 to 28 February 2021, 16 June to 27 June 2021, and 26 July to 12 September 2021
	Level 2	Baseline tests done in the period 18 August to 20 September 2020, 31 May

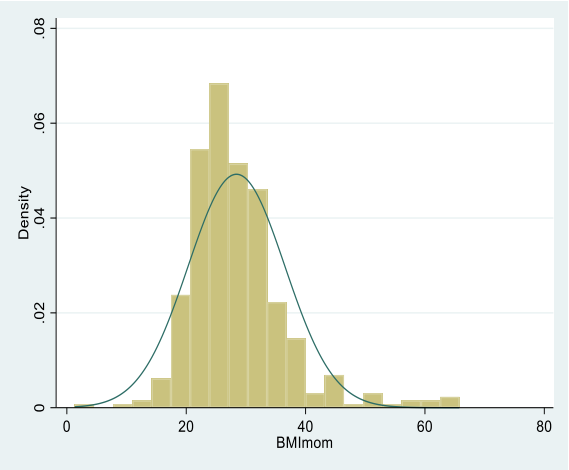
		to 15 June 2021 and 13th September to 30 September 2021
	Level 1	Baseline tests done in the period of 21 September to 28 December 2020 and 1 March 2021 to 30 May 2021.
PMTCT stages	Pregnant	
	Postpartum	
Baseline or previous VL	VL <50 copies/ml	VL at baseline
	VL=50-999 copies/ml	
	VL>=1000 copies/ml	
Gestation at first ANC visit	0-12 weeks	
	13-20 weeks	
	21-40 weeks	
Number of ANC visits	0-4 visits	
	5-12 visits	
HIV diagnosis stage	Before pregnancy	
	During pregnancy, before 28 weeks	
	During pregnancy, after 28 weeks or during delivery or postnatal	
ART initiation	Before pregnancy	
	During pregnancy, before 28 weeks	
	During pregnancy, after 28 weeks or during delivery or postnatal	
Current ART regimen*	First line	
	2nd/3rd line/unknown	
Missed an ART dose last 7days	No	
	Yes	
Facing any ART adherence challenges	No	
	Yes	

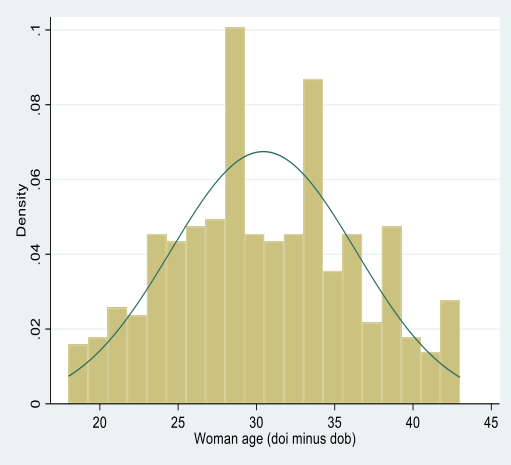
Appendix E: The pairwise comparison of compliance to repeat VL testing between pre-COVID-19 and transition, pre-COVID-19 and COVID-19, and transition and COVID-19 was conducted using partially overlapping sample z-test in R.

Periods	**Difference in proportions (DIP)**	**95% confidence interval (CI)**	**P value**
Pre-COVID-19 and transition	1.1%	-5.5 to 7.7	0.742
Pre-COVID-19 and COVID-19	-3.4%	-9.8 to 3.1	0.305
Transition and COVID-19	-4.5%	-11.7 to 2.8	0.228

Appendix F: Poisson regression assumption tests

Normality test, the data was normally distributed





Poisson distribution: mean= variance

Variable	Obs	Mean	Std. dev.	Min	Max
timing	700	.8328571	.3733702	0	1

Variance= $(.3733702)^2$ =0.1394053, which is less than the mean.

Estimating a simple model with constant-only

Iteration 0: log likelihood = -689.62671

Iteration 1: log likelihood = -689.62671

Poisson regression Number of obs = 700

LR chi2(0) = 0.00

Prob > chi2 = .

Log likelihood = -689.62671 Pseudo R2 = 0.0000

timing	Coefficient	Std. err.	z	P>z	[95% conf.	interval]
_cons	-.1828931	.0414158	-4.42	0.000	-.2640666	-.1017197

The exponent of the coefficient= mean observed earlier of 0.8328571

Testing model goodness of fit, the model is of good fit for our data the observed distribution is the same with the distribution predicted by a Poisson distribution

Deviance goodness-of-fit = 213.2534

Prob > chi2(699) = 1.0000

Pearson goodness-of-fit = 117

Prob > chi2(699) = 1.0000

Appendix G: Ethic's clearance certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Ms T Mbira

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220268

NAME: (Principal Investigator)	Ms T Mbira
DEPARTMENT:	School of Public Health Division of Epidemiology and Biostatistics Medical School University
PROJECT TITLE:	*Viral load monitoring compliance amongst women attending PMTCT services during COVID-19 pandemic in Ehlanzeni District, Mpumalanga, South Africa*
DATE CONSIDERED:	2022/02/25
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Drs T Kufa-Chakezha and N Ngandu
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2022/04/12

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **February** and therefore reports and re-certification will be due in the month of **February** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

14 April 2022
Date

PLAGIARISM DECLARATION

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Thandiwe Elsie Mbira (Student number: 2479369) am a student registered for the degree of MSc Epidemiology and Biostatistics in the academic year 2021.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

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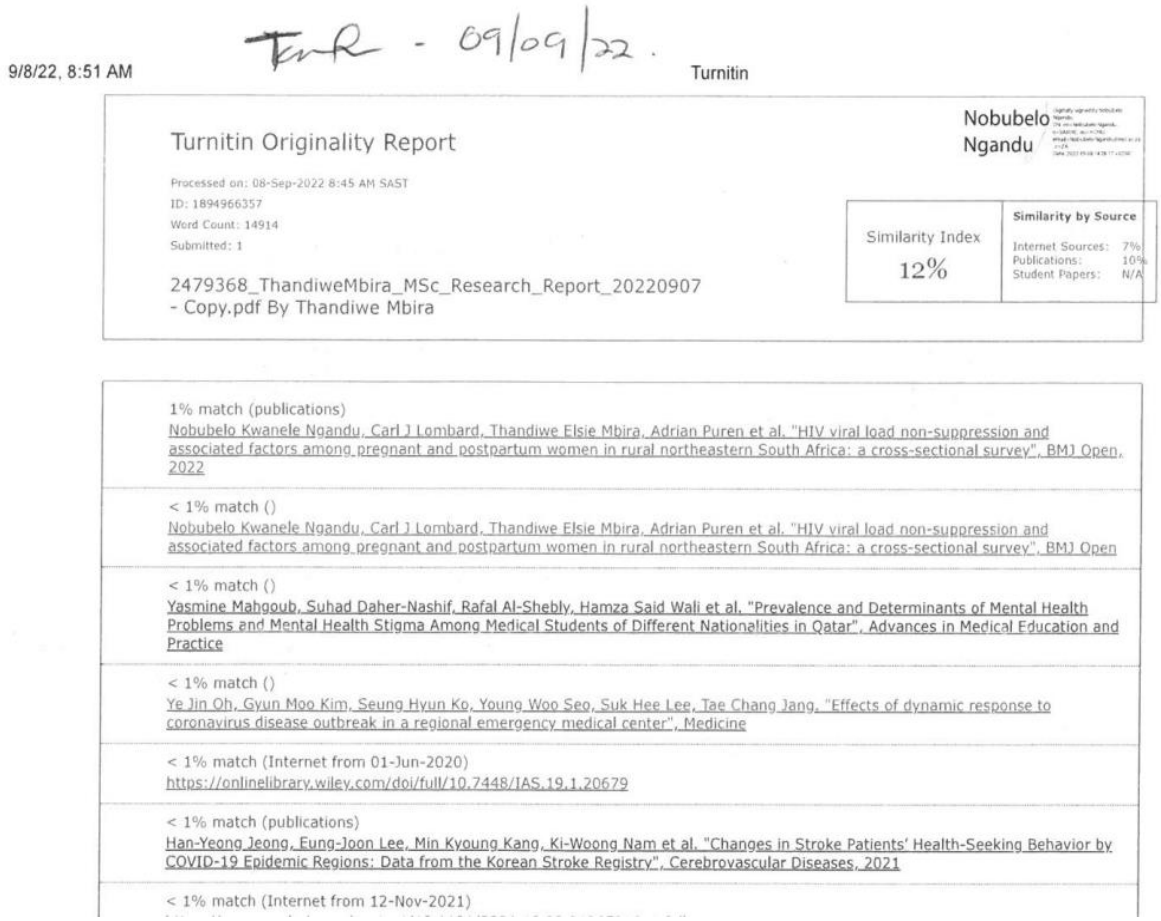

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