PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Factors associated with viral load non-suppression in people living with HIV on ART in Nigeria: cross-sectional analysis from 2017 to 2021
AUTHORS	Tomescu, Silviu; Crompton, Thomas; Adebayo, Jonathan; Akpan, Francis; Dauda, Dauda; Allen, Zola; Ondura, Evans; Kinge, Constance W.; Chasela, Charles; Pisa, Pedro

VERSION 1 – REVIEW

REVIEWER	Ngandu, Nobubelo South African Medical Research Council, Health Systems Research Unit
REVIEW RETURNED	13-Jul-2022

GENERAL COMMENTS	The authors present a large national level study of over 500 000 patient data collected in Nigeria cross-sectionally, covering a 20-year period between 2001 and 2021. They investigate factors associated with a high non-suppressed HIV viral load above 1000 copies/ml. Males, younger age, shorter period (<3 months) of 'take-home' refill antiretroviral therapy, secondary/tertiary healthcare facilities, shorter duration (1-3 years) since ART initiation & some geo-political local areas were identified as associated with non-suppressed viral load. They point out that this study adds new knowledge by co-investigating the contribution of geographic local areas and type of facilities to population level prevalence of HIV viral non-suppression. I think the important contribution this paper makes is the difference in viral load non-suppression between the geo-political areas. It therefore, raises a need for the Nigeria health department to investigate the possible socio-cultural bottlenecks in access to HIV care and put in place acceptable interventions to make sure all PLHIV have unrestricted access to viral load monitoring services. The paper is written well and publishable. Minor Essential Revisions: ABSTRACT: MMD abbreviation not explained INTRUDUCTION: Line 46 "..undetectable VL makes HIV untransmissible.." This is not entirely true, what is true is that it reduces the risk of transmission significantly. RESULTS: Line 162-163: This sentence is not clear: "Both the adult second-line and paediatric first-line ART regimens had 2% of the clients, with 80% and 78% of clients on these regimens being virally suppressed, respectively. Line 165-166: Using 'more likely' is inappropriate for a chi-squared

	test result given it does not give relative comparisons of likelihood or odds but simply compares the distribution of proportions. “Clients receiving treatment at a tertiary or secondary health facility were more likely to be virally non-suppressed compared with clients receiving ART at a primary health facility.” DISCUSSION: Line 244-246 In your regression model your reference group is ART for more than 3 years. SO this statement might require revision: “244 ART clients who had their last VL test conducted within less than 1 year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested conducted within 1 to 3 years of being on ART.” Line 267: The abbreviation ‘IIT’ is not explained.

REVIEWER	Nabukeera , Sarah Makerere University
REVIEW RETURNED	19-Jul-2022

GENERAL COMMENTS	I thank the author for choosing a topic of great public health importance, to help Nigeria streamline the HIV programming to ensure virological suppression for HIV control. This paper is worth publication if the authors can address the comments below. Plus, let them ensure that they correct all the grammatical and typographical errors in the document. <u>Title</u> 1. The authors need to clarify the study population here, and throughout the manuscript. I think it should be people living with HIV on ART. If you say just people living with HIV, then the denominator includes those diagnosed/not, and those on treatment/not. <u>Abstract</u> 1. The objective is incongruent with the study title. The study populations differ. Which is which? The authors need to rectify this. The abstract can be better written with the objective part of the background, and the methods section to include design, setting, participants, and variables. 2. We don’t have to have the strengths and limitations of the study, as part of the abstract unless the journal specifies so. But rather in the main body just before the conclusion. Plus, please explain the implication of each of these limitations/strengths to the study findings. <u>Introduction</u> 1. If you used data from 20 years, why not give us a picture of the evolution of HIV and ART in Nigeria for the last 20 years, instead of just 2020 and now. This would in a way justify the need to analyze data for 2 decades. The authors also need to clarify what “currently”, means. 2. 20 years is a big time to just bring us to 2019-2022. What happened before the VL suppression movement? The

	introduction doesn't go 20 years back. Show us the evolution of HIV programming as far as 2000. Maybe in segments of 2000-2005, 2005-2010, 2010-2015, and 2015-2020. Bundling the years introduces confounding that needs to be addressed. Especially for the time-varying covariates in HIV treatment and care. 3. The authors need to clarify why 20 years back? What is the analysis trying to dig from the 20-years of HIV programming in relation to these factors of interest? This needs to come out clearly. How have the factors evolved over the 20-year period? Why the need to study these specific factors? Aren't there any studies in Nigeria that have studied this? Kindly justify. 4. In the same regard, what has the government of Nigeria done to control the epidemic over the last 20 years? How has this evolved? Why is it important to study these factors, as far as 20 years back? 5. The authors need to have had "year of ART initiation", as a variable. We need to know this was a contributing factor to the viral non-suppression/suppression over the 20 years. Meaning, the non/suppression rate and factors in 2000, to a certain degree will be different from those of 2020. This helps us control for the various interventions (an example of a time-varying covariate) in the HIV programing in Nigeria, that have been under taken over years, as a confounder. <u>Methods</u> 1. It is important that we have ART regimen as a factor, based on the evolution of ART treatment and care over the decades. Unless there is a justification for not including this, which needs to be clearly stated. I think this will also speak to the "year of initiation" variable, since different years of initiation, may have had different ART regimens/ regimen changes. Which may also speak to managing opportunistic infections/side effects among HIV patients in care. The presence of opportunistic infections or side effects among those on treatment, may not be necessarily variables. But, maybe tied together for a comprehensive discussion of the findings over the 20-year period. Adherence level is a key factor in viral load suppression, invariably, the authors may tell us why it is not part of the study variables. Adherence, ART regimens are mandatory indicators for tracking in all HIV care programs/projects. why not included? 2. The authors may have to provide a little more information on the HIV data collection tools, for example, tell us a bit of what kind of data do they collect, within which period. Need to elaborately talk about the data source. 3. "Clients with a date of birth earlier than 194089 (n=961) or an ART start date earlier than 1990 (n=2) were also excluded from the analysis". What was the justification for this? Did you have an exclusion by age and date of ART initiation? 4. "An 90 additional 2,314 clients with a VL test result date earlier than the ART start date were likewise 91

	removed.". Why so? 5. Dropping participants gives us a reason to have "year of initiation" as a variable. What if the people dropped at this stage were different on some characteristics compared to those retained? Could have introduced an unknown degree of selection bias. If we had a "year of initiation", it would show us which year was affected the most by the elimination at this stage. And then we would have year-specific programmatic explanations for the unavailability of VL data. but also, see if this is a significant variable in the model or not. 6. Refer to lines 101-107: "Variables like Sex and MDD are mentioned in the background, but not here. I thought this was a section to show the definition/measurement of each of the predictor variables. Authors need to align this. 7. In the background you say; "The Nigeria National Guidelines for HIV Prevention, Treatment, and Care define virologic suppression as having a viral load (VL) below 1,000 HIV ribonucleic acid copies per mL of plasma [3] (viral load non-suppression is defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL 46 of plasma).". Now, for this study, what was the definition of the outcome variable. Which I suppose was virological non-suppression. How was it measured. This should come out in the methods section where you talk about the varibles. 8. Refer to line 134, Current ART status seems not have been a factor. At least according to the preceding sections. But maybe as an inclusion criterion. How was it then excluded for modelling as a factor and also appears in the results? 9. Plus, how did you ensure that all those deceased, IIT and stopped treatment, for all the 20 years, prior to the analysis, were dropped from the study. Since this was secondary data. Authors need to elaborate on this. 10. Refer to line 136, Since this is a prevalence study and not, measuring incidence. Is it right that we include the deceased and those not on treatment (especially, if your study population is PLHIV on ART). Authors need to clarify what exactly the study population was. Plus, the statement in this line and those that follow, maybe an indication of a bias that needs to be acknowledged. 11. Refer to lines 136 to138, "Similarly, 137 the regimen line was excluded from the regression analysis because other regimen lines, aside 138 from the first-line regimen, are prescribed in the case of a non-suppressed VL.". But ART regimen was not part of the descriptive analysis either. Plus, I think regimen line can still be used as a variable associated with VL non-suppression, because, we want to know, for the 20 years, how have the different regimens (regardless of being used for treatment failure or not) have contributed to VL suppression. This may indicate the need for targeted interventions across different treatment groups, to avoid treatment failure, or even modification of ART regimens. Thinking that this is a 20-year data set, a lot of changes have been made in ART treatment to ensure suppression over the years, we may need to see the

evolution of regimens, treatment failure and VL suppression. By having a variable on ART regimen. Besides, some ART regimens had dire side effects between the 2000-2010, which may have contributed to non-suppression around that time. Corroborating the need for "year of initiation variable". We need to tie these pieces together to make sense of the data set for the good of HIV treatment and care, for Nigeria going forward.

12. How exactly was the selection of variables to be included in the model done? what was the basis? Explain this in detail.
13. Refer to line 144, Why not <0.05, Did the authors want to consider only factors highly significant? if so may briefly tell us why they eliminated the other "significant variables. If this was the criteria for inclusion into the model but not the statistical significance of the variables, then state it clearly
14. Plus, this section should also include the descriptive analysis done. but as is now, only tells us about inferential analysis. In my opinion, it is always good to also consider logic and literature when building a model, for the variables in the analysis may already be confounded, that the variables of importance will be eliminated if only statistical significance is considered.
15. What was the cutoff for multicollinearity of the variables? The authors didn't mention this.

<u>Results</u>

1. Refer to line 159, "The ART status of 87% of the clients was recorded as active on treatment".
2. You need to restate this; it doesn't come out right. Plus, you didn't have ART status described as a variable in the methods. Now how come it appears in the results? You did not have ART regimen as a variable, how come you have results on ART regimen. (Methods-Results discordance)
3. Table 1. Is this variable current ART status or ART status? The authors need to be consistent with the names of the variables. Plus, in the methods section you say, you didn't consider regimen as a variable. Now why the results on it?
4. Did you consider literature and logic when including the variables in the model? Because, these usually support the variables that may not be significant but are of importance. For example, ART regimen, is a salient variable, per literature. Also, results on Facility ownership are not included in Table 2. Is there a reason why?
5. Lines 197-198, 2. "All factors used in the adjusted logistic regression model were statistically significant, with a p-value of <0.000001" Justify why you included Sex that was not significant at bivariate. This should have come out well in the methods section.
6. Create a paragraph in the results section, that mentions and explains the factors that were found to be associated with VL non-suppression, all together. For now, they are

written in isolation, and bivariate and multivariable findings for each, combined together. Have bivariate results paragraph/s, and one/s for multivariable. Precisely, we need a summary of the variables that were found to be associated or not associated with VL non-suppression.

Discussion

1. Line 231, kindly mention the age groups, specifically. And the writing should be; "Being in a younger age group and on MDD 1-2 months were highly associated". (Showing the strength of the association of the variable, not as an adjective).
2. "We also found that males, clients who received 233 treatment at tertiary health facilities, at small or medium facilities, or in the North-Central or North 234 East zones were associated with a higher risk of VL non-suppression. Other studies have found 235 similar results for the risk of viral non-suppression in younger age groups in Cambodia, Uganda, 236 and South Carolina (USA) [6,8,16], and among males [17–19]". What do these findings imply, in terms of HIV care and programming? What do they mean in terms of HIV programming? How do we consider the age group and the other significant variables, going forward in HIV programming in Nigeria?

3. "The increased odds of viral non-suppression among ART clients who received treatment at tertiary health facilities were unlike the higher odds reported for primary health facilities in Ethiopia [20]. Small and medium facilities were identified as having greater odds for viral non-suppression; this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [21]." Authors need to make this statement clear, as is, it is unclear. Plus, avoid using odds. this is an interpretive section where the results are supposed to be broken down for

understanding/comprehension. What exactly do you want to mean?

4. "Small and medium facilities were identified as having greater odds for viral non-suppression; this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [21]." What is the implication of this finding in terms of HIV programming for Nigeria?
5. "ART clients who had their last VL test conducted within less than 1 year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested conducted within 1 to 3 years of being on ART. Our finding was consistent with the Center for Disease Control and Prevention's finding that PLHIV on ART could be virally suppressed within six months of

initiation provided that they adhered to their medication [22]. Moreover, a greater likelihood of viral suppression was found among PLHIV who were initiated on treatment for less than one year compared with those on ART for more than one year [23]." What do these findings imply, in terms of HIV care and programming in Nigeria?

6. "Also, 254 elucidating that clients more engaged in care can have more opportunities for non-suppressed viral load test results, though this does not necessarily mean that this population is more likely to be 256 non-suppressed.". How then in Nigeria, should this be taken into consideration to ensure viral suppression among HIV clients on ART? What is the implication of this?
7. Avoid using odds and the language of univariate/ multivariable in the discussion section.
8. "Shorter MMD is initially prescribed to new clients and longer MMD is prescribed to virally stable clients to reduce the number of clinic visits. Because of non-adherence, clients may become virally non-suppressed and be placed on shorter duration treatment, requiring more frequent check-ups and clinical support to become stable. It is apparent that MMD is dependent on the VL status of clients; however, that is not 265 necessarily the case for new clients.". Break this into two sentences.
9. "A possible explanation for the North-Central zone having the highest odds of viral non-suppression could be linked to health-seeking behaviour such as non-use of the service, poor adherence to treatment, and possibly religious affiliation (for example Islamic religion predominant in northern where in certain circumstances women require permission to leave the premises of a household which can reduce access to healthcare [27,28]." What can be done to solve the problem in this region? Authors should make succinct recommendations on the key findings across this section.
10. "One of the limitations of our study was the inaccessibility of the longitudinal data set, leaving us

unable to conduct a longitudinal study to explore the factors affecting viral non-suppression over time. We were therefore restricted to conducting a cross-sectional study. The inclusion of MMD as an independent variable is a limitation of the study because a shorter MMD can be applied based on a non-suppressed VL, in which case MMD would be a proxy for IIT". Authors need to state what the implication of this limitation to the study findings' accuracy and precision was. Plus, how did they minimize the impact of this limitation `on the findings?

11. "It is likely that some of the nearly 40% of client records (eliminated from analysis) without a VL

test on record are a consequence of poor adherence to treatment which could lead to viral load non-suppression that is not tested/recorded." The authors need to state the basis of this assumption, since you didn't consider adherence levels as a variable?

	12. “Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, marital status, and education level. The absence of VL suppression data for adolescents and recently initiated clients may have also had an impact on the study, suggesting that these findings may not necessarily apply to those subpopulation groups.”. 13. Were these unavailable or not considered? You mention not considering ART regimen for some reasons in the methods section, but then state it as just data on this was unavailable. Authors may need to make us understand clearly, how an HIV treatment and care program may have no records of salient variables like a regimen. 14. Also, you have 15-24 age group category. (what is the definition of adolescents in your setting). You also have those initiated on treatment <1 year ago. You may have to restate this and reflect exactly what you wanted to mean. There is a discrepancy between this section and the study methods. 15. Avoid repeating results in the discussion section, and focus on the key messages from the key results, and provide the implication of each. Authors also need to make sure that there is a congruency across all the sections, for now there is some significant discrepancy between the sections. 16. For study limitations, the authors need to acknowledge the type of bias this kind of design/methodology introduces and its implication to the findings.

REVIEWER	Bailey , Lauren US Agency for International Development, Office of HIV/AIDS
REVIEW RETURNED	21-Jul-2022

GENERAL COMMENTS	Thank you for the opportunity to review this paper. This is a well-written analysis that adds to the growing literature around barriers/strategies for achieving virologic suppression and larger epidemic control of HIV. The analysis also expands on the critical role MMD can play in supporting virologic suppression and will hopefully encourage more countries to adopt and expand MMD as a person-centered approach to achieving improved treatment outcomes for PLHIV. However, a few key revisions are recommended to strengthen the analysis and clarify some confusion around including MMD as an independent variable. Variables Explored as Predictors of a non-suppressed viral load You do not include MMD and how it is defined/calculated in this section (which is very important per my comments below); however, you list it in line 141 as one of the variables included in the models. Statistical Analysis Line 136-140: You note that the regimen line was dependent on the VL outcome investigated and therefore could not be used as an

	independent variable associated with VL non-suppression; but isn't this the same case with MMD? Do clients need to be virally suppressed in order to be enrolled on MMD? I think it's critical that you note the eligibility criteria for MMD; additionally, I recommend you define what is considered MMD. PEPFAR defines MMD as dispensing of 3 months or greater; anything less than 3 months is not considered MMD. With this in mind, a client that is virally non-suppressed could receive 2MMD but they would not be eligible for 3MMD. If the USAID-supported sites are following the guidelines, the virally non-suppressed clients would be placed on 1-2 month dispensing and transition to 3MMD or greater once clinically stable (which includes virologic suppression). Discussion Lines 259-260: The study you are referencing analyzed outcomes associated with multi-month prescribing, which can be different from multi-month dispensing. In many scenarios clients receive a multi-month prescription but can only be dispensed one month of ARVs at a time. I recommend rephrasing this sentence or using another source to support this statement. Lines 260-261: When you reference shorter MMD and longer MMD, are you referring to Nigeria-specific MMD policy or global MMD policy in general? Again, I recommend clarifying MMD eligibility in Nigeria and what is technically considered MMD as this could affect your analysis. Line 262-264: This statement is a bit confusing. This is implying that the client is already receiving MMD or some duration of extended dispensing if they have become non-adherent and subsequently virally non-suppressed and placed on shorter dispensing. Do we know what dispensing interval the client was receiving when they became non-adherent and virally non-suppressed? Is it common practice in Nigeria for clients with documented adherence challenges and subsequent non-suppression to be placed on a shorter dispensing interval? Line 264: Please clarify, is MMD dependent on the VL status of the client because virologic suppression is a requirement for enrollment on MMD; or is this statement the result of your logistic regression model? Why is this not the case for new clients? Again, it would be good to clarify MMD eligibility criteria. Line 266-268: Can you please more clearly explain how you arrived at MMD being a confounding factor that possibly represented interruption in treatment? Are you suggesting that clients were receiving shorter MMD because of a history of treatment interruption, and that was leading to non-suppression? What do you mean by "misadministration" of MMD? Line 274: Can it be suggested that longer dispensing intervals support treatment adherence and virologic suppression? There are several non-inferiority studies demonstrating that continuity of treatment and virologic suppression remain high among clients on 6MMD. It might be worth citing these studies in your discussion and noting how your research adds to the current body of literature on MMD and viral load suppression. Line 287: Is the lack of a VL test the consequence of poor adherence or treatment interruption (i.e. retention challenges). While

	treatment adherence and treatment interruption/retention are related, be careful not to conflate them. Line 282-284: I'm glad you note here the limitation with including MMD as an independent variable; however, the issue remains that virally non-suppressed individuals are technically not eligible for MMD and PEPFAR does not consider ARV dispensing < 3 months to be MMD – so one could assume all clients receiving 1-2 month dispensing have likely not yet achieved virologic suppression. It is possible, though, especially during COVID, that many clients who had not yet attained virologic suppression were placed on MMD as a protective measure. It would be worth looking into this and citing if this did, indeed, occur across the sites included in this analysis.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Nobubelo Ngandu, South African Medical Research Council
Comments to the Author:
The authors present a large national level study of over 500 000 patient data collected in Nigeria cross-sectionally, covering a 20-year period between 2001 and 2021. They investigate factors associated with a high non-suppressed HIV viral load above 1000 copies/ml. Males, younger age, shorter period (<3 months) of 'take-home' refill antiretroviral therapy, secondary/tertiary healthcare facilities, shorter duration (1-3 years) since ART initiation & some geo-political local areas were identified as associated with non-suppressed viral load.
They point out that this study adds new knowledge by co-investigating the contribution of geographic local areas and type of facilities to population level prevalence of HIV viral non-suppression.
I think the important contribution this paper makes is the difference in viral load non-suppression between the geo-political areas. It therefore, raises a need for the Nigeria health department to investigate the possible socio-cultural bottlenecks in access to HIV care and put in place acceptable interventions to make sure all PLHIV have unrestricted access to viral load monitoring services.
The paper is written well and publishable.
Because the reviewer found most value in geo-political areas, we have expanded the study to State level.

Minor Essential Revisions:
ABSTRACT:
MMD abbreviation not explained
INTRUDUCTION:
Line 46 "..undetectable VL makes HIV untransmissible.." This is not entirely true, what is true is that it reduces the risk of transmission significantly.

Amended to reflect as: "… an undetectable VL significantly reduces the transmission risk of HIV".

RESULTS:
Line 162-163: This sentence is not clear: "Both the adult second-line and paediatric first-line ART regimens had 2% of the clients, with 80% and 78% of clients on these regimens being virally suppressed, respectively.

Amended: “The adult second-line and paediatric first-line ART regimens each accounted for 2% of the clients in the study, with 80% and 78% of clients on the two regimen lines being virally suppressed, respectively.”

Line 165-166: Using ‘more likely’ is inappropriate for a chi-squared test result given it does not give relative comparisons of likelihood or odds but simply compares the distribution of proportions. “Clients receiving treatment at a tertiary or secondary health facility were more likely to be virally non-suppressed compared with clients receiving ART at a primary health facility.”

Amended: “Clients receiving treatment at a tertiary or secondary health facility were non-suppressed in higher proportions compared with clients receiving ART at a primary health facility.”

DISCUSSION:
Line 244-246 In your regression model your reference group is ART for more than 3 years. SO this statement might require revision: “244 ART clients who had their last VL test conducted within less than 1 year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested conducted within 1 to 3 years of being on ART.”

Revised as: “ART clients who had their last VL test conducted within less than one year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested after one year on ART.”

Line 267: The abbreviation ‘IIT’ is not explained.

IIT was defined under the statistical analysis section: “…interruption in treatment (IIT) defined as missing a drug-pickup appointment for longer than 28 days …”

Reviewer: 2
Sarah Nabukeera , Makerere University
Comments to the Author:
I thank the author for choosing a topic of great public health importance, to help Nigeria streamline the HIV programming to ensure virological suppression for HIV control.
This paper is worth publication if the authors can address the comments in the attached document. Plus, let them ensure that they correct all the grammatical and typographical errors in the document.

Contents from attached document from Reviewer 2.

Title
1. The authors need to clarify the study population here, and throughout the manuscript. I think it should be people living with HIV on ART. If you say just people living with HIV, then the denominator includes those diagnosed/not, and those on treatment/not.

Amended the title: “…in people living with HIV on ART in Nigeria…”

Abstract
1. The objective is incongruent with the study title. The study populations differ. Which is which? The authors need to rectify this. The abstract can be better written with the objective part of the background, and the methods section to include design, setting, participants, and variables.

The Objectives were revised to align with the title.
The structure of the abstract was written in accordance to the guidelines of the Journal, therefore the Objectives, Design, Setting Participants were not included as part of the Background section of the Abstract.

2. We don't have to have the strengths and limitations of the study, as part of the abstract unless the journal specifies so. But rather in the main body just before the conclusion. Plus, please explain the implication of each of these limitations/strengths to the study findings.

Strengths and limitations are requirements of the journal. In addition, in the strengths and limitations section: "The novelty, aims, results or expected impact of the study should not be summarised here."

Introduction
1. If you used data from 20 years, why not give us a picture of the evolution of HIV and ART in Nigeria for the last 20 years, instead of just 2020 and now. This would in a way justify the need to analyze data for 2 decades. The authors also need to clarify what "currently", means.

After revisions recommended by the reviewers, the study was focused on the 2017-2021 period. This better defines the current situation.

2. 20 years is a big time to just bring us to 2019-2022. What happened before the VL suppression movement? The introduction doesn't go 20 years back. Show us the evolution of HIV programming as far as 2000. Maybe in segments of 2000-2005, 2005-2010, 2010-2015, and 2015-2020. Bundling the years introduces confounding that needs to be addressed. Especially for the time-varying covariates in HIV treatment and care.

As recommended by the reviewer, the timeline included in the cross-sectional study was 2017-2021, i.e. since the beginning of change in Nigerian policy on viral load testing for PLHIV on ART.

3. The authors need to clarify why 20 years back? What is the analysis trying to dig from the 20-years of HIV programming in relation to these factors of interest? This needs to come out clearly. How have the factors evolved over the 20-year period? Why the need to study these specific factors? Aren't there any studies in Nigeria that have studied this? Kindly justify.

Considerations were given to the reviewer's emphasis that a 20-year period is not necessarily reflecting the current situation in Nigeria, we therefore restricted the period of the study to 2017-2021 to reflect more recent times and policy changes regarding VL testing in Nigeria. In that regard, the study updates the situation with respect to some of the factors such as sex, age, and time on ART. The study also focuses on other distal factors such as facility level, size, ownership, and the geographical location of the facilities where clients receive treatment. Literature does not cover viral load suppression with respect to the distal factors to our knowledge.

4. In the same regard, what has the government of Nigeria done to control the epidemic over the last 20 years? How has this evolved? Why is it important to study these factors, as far as 20 years back?

No longer conducting the study over the 20 years period.

5. The authors need to have had "year of ART initiation", as a variable. We need to know this was a contributing factor to the viral non-suppression/suppression over the 20 years. Meaning, the non/suppression rate and factors in 2000, to a certain degree will be different from those of 2020. This helps us control for the various interventions (an example of a time-varying covariate) in the HIV programing in Nigeria, that have been under taken over years, as a confounder.

The year of ART initiation was included in the study.

Methods

1. It is important that we have ART regimen as a factor, based on the evolution of ART treatment and care over the decades. Unless there is a justification for not including this, which needs to be clearly stated. I think this will also speak to the “year of initiation” variable, since different years of initiation, may have had different ART regimens/ regimen changes. Which may also speak to managing opportunistic infections/side effects among HIV patients in care. The presence of opportunistic infections or side effects among those on treatment, may not be necessarily variables. But, maybe tied together for a comprehensive discussion of the findings over the 20-year period. Adherence level is a key factor in viral load suppression, invariably, the authors may tell us why it is not part of the study variables. Adherence, ART regimens are mandatory indicators for tracking in all HIV care programs/projects. why not included?

We included the year of ART initiation. The ART regimen was not included because the ART regimen at the time of the VL test cannot be determined from the cross-sectional dataset, that is only the current regimen can be determined; nor can it be determined how many times a regimen was switched by a client. Further, the regimen switch was not included because that is a result of a non-suppressed viral load, therefore it is not an independent factor associated with VL non-suppression. Regarding adherence to treatment, it is not possible to determine the adherence level or how many times a patient interrupted treatment historically, only if the patient’s most recent status is active, dead, stopped treatment, transferred out or interrupted treatment (IIT). However, this variable cannot be included in the logistic regression analyses because at the time of the VL test, the patient must have been active to attend a clinic for VL sample collection.

Opportunistic infections like TB or side-effects were not recorded in the dataset.

Co-morbidities were only recorded for 0.4% of clients which is considerably below the global prevalence of comorbidities in PLHIV, therefore, the variable was omitted. More specifically, it was estimated that 9 percent of PLHIV globally had hypertension, and more than 59 percent of them lived in sub-Saharan Africa.[1] Other studies indicated that 29.5 percent of PLHIV in South Africa may have had other comorbidities or infections,[2] whereas in Zimbabwe, 19.6 percent of PLHIV were diagnosed with at least one noncommunicable disease (NCD) and 4.6 percent with more than one NCD.[3]. Moreover, co-morbidities may be a result of a of a non-suppressed VL and cannot be used as an independent factor to associate with the outcome.

2. The authors may have to provide a little more information on the HIV data collection tools, for example, tell us a bit of what kind of data do they collect, within which period. Need to elaborately talk about the data source.

We have revised and elaborated on the data collection and the data source.

3. “Clients with a date of birth earlier than 194089 (n=961) or an ART start date earlier than 1990 (n=2) were also excluded from the analysis”. What was the justification for this? Did you have an exclusion by age and date of ART initiation?

We no longer excluded patients born before 1940 as it is reasonable to include those of 80 years of age and above in the study. Further, we only excluded patients that started ART before 2002 when the ART program rolled out in Nigeria.

4. “An 90 additional 2,314 clients with a VL test result date earlier than the ART start date were likewise 91 removed.”. Why so?

We no longer excluded patients with a VL test result before the ART start date, because although those may be exceptional cases, they may nevertheless be possible.

5. Dropping participants gives us a reason to have “year of initiation” as a variable. What if the people dropped at this stage were different on some characteristics compared to those retained? Could have introduced an unknown degree of selection bias. If we had a “year of initiation”, it would show us which year was affected the most by the elimination at this stage. And then we would have yearspecific programmatic explanations for the unavailability of VL data. but also, see if this is a significant variable in the model or not.

“Year of ART initiation” was included and it was a significant variable to include.

6. Refer to lines 101-107: “Variables like Sex and MDD are mentioned in the background, but not here. I thought this was a section to show the definition/measurement of each of the predictor variables. Authors need to align this.

This section details variables engineered as predictors of VL non-suppression. Whereas the variables that were readily provided in the dataset were listed in the statistical analysis section. We have revised the section heading to reflect as “Variables engineered as predictors of a non-suppressed viral load” instead of “Variables explored as predictors of a non-suppressed viral load”.

7. In the background you say; “The Nigeria National Guidelines for HIV Prevention, Treatment, and Care define virologic suppression as having a viral load (VL) below 1,000 HIV ribonucleic acid copies per mL of plasma [3] (viral load non-suppression is defined as having a VL of at least 1,000 HIV ribonucleic acid copies per mL 46 of plasma).”. Now, for this study, what was the definition of the outcome variable. Which I suppose was virological non-suppression. How was it measured. This should come out in the methods section where you talk about the variables.
We have specified the definition of a non-suppressed VL in the statistical analysis section:
“Unadjusted and adjusted logistic regression models were run to explore the association of variables with a non-suppressed VL (a VL above 1,000 ribonucleic acid copies per mL of plasma).”

8. Refer to line 134, Current ART status seems not have been a factor. At least according to the preceding sections. But maybe as an inclusion criterion. How was it then excluded for modelling as a factor and also appears in the results?

We included the variable as part of the chi-square distribution table which does not imply causation of VL non-suppression by the current ART status. However, the current ART status was not included within logistic regression models because then we would assume that the variable may cause VL non-suppression.

9. Plus, how did you ensure that all those deceased, IIT and stopped treatment, for all the 20 years, prior to the analysis, were dropped from the study. Since this was secondary data. Authors need to elaborate on this.

We did not drop clients based on their current ART status because at the time of their VL test, those clients (dead/IIT/stopped treatment/transferred out) must have been active on treatment and present at the clinic to have their VL sample collected and tested.

10. Refer to line 136, Since this is a prevalence study and not, measuring incidence. Is it right that we include the deceased and those not on treatment (especially, if your study population is PLHIV on ART). Authors need to clarify what exactly the study population was. Plus, the statement in this line and those that follow, maybe an indication of a bias that needs to be acknowledged.

Like we mentioned prior to this, all clients with a VL test must have been alive, and active on treatment when being tested.

11. Refer to lines 136 to138, “Similarly, 137 the regimen line was excluded from the regression analysis because other regimen lines, aside 138 from the first-line regimen, are prescribed in the case of a non-suppressed VL.”. But ART regimen was not part of the descriptive analysis either. Plus, I think regimen line can still be used as a variable associated with VL non-suppression, because, we want to know, for the 20 years, how have the different regimens (regardless of being used for treatment failure or not) have contributed to VL suppression. This may indicate the need for targeted interventions across different treatment groups, to avoid treatment failure, or even modification of ART regimens. Thinking that this is a 20-year data set, a lot of changes have been made in ART treatment to ensure suppression over the years, we may need to see the evolution of regimens, treatment failure and VL suppression. By having a variable on ART regimen. Besides, some ART regimens had dire side effects between the 2000-2010, which may have contributed to non- suppression around that time. Corroborating the need for "year of initiation variable". We need to tie these pieces together to make sense of the data set for the good of HIV treatment and care, for Nigeria going forward.

“Regimen line” is a different variable than the “ART regimen” itself. The regimen line is a standard prescription with optimal doses of a particular ART regimen. 2nd and 3rd regimen lines have modified doses of the ART regimens, and possibly a different ART regimen altogether. Nevertheless, we have now also included the ART regimen as part of the descriptive statistics of the cohort, however, we have not included this variable in logistic regression analyses either because, the ART regimen itself can be changed as a result of a non-suppressed VL, as such, the ART regimen is not an independent predictor of VL non-suppression.

The regimen line cannot be used in logistic regression analyses, or any regression, because the explanatory/predictive variables of regressions cannot be cause by the outcome to add any value to the regression. More specifically, correlation between a variable and the outcome does not imply causation. However, for the reason to present a distribution of the prevalence of VL non-suppression stratified by regimen line, the regimen line was included in the chi-square distribution table.

Indeed, if the dataset would have been longitudinal, the inclusion of the regimen line and the ART regimen at the time of the VL tests would have been valuable variables to include. However, we only have the most recent regimen line and ART regimens of the clients, and we cannot assume those were the same/unchanged at the time of VL testing. Especially, because regimens are switched dynamically for clients to improve their VL outcomes.

12. How exactly was the selection of variables to be included in the model done? what was the basis? Explain this in detail.

After excluding the variables that are not independent of the outcome (VL non-suppression). Variables that improved the model were retained in the analysis. Likewise, multicollinearity of the included variables was tested for, and none of the variables showed multicollinearity. We have explained this in the statistical analysis section and have revised it for further clarification:
“Model selection was done using forward addition and backward elimination of variables where the Akaike’s information criterion (AIC) was used to evaluate variable inclusion in the final model. The

model with the lowest AIC value was retained. Multicollinearity was tested using the generalized variance inflation factor (GVIF) for the set of variables used in the logistic regression model, and none of the variables exhibited multicollinearity."

13. Refer to line 144, Why not <0.05, Did the authors want to consider only factors highly significant? if so may briefly tell us why they eliminated the other "significant variables. If this was the criteria for inclusion into the model but not the statistical significance of the variables, then state it clearly

We have revised to use p-value of 0.05 to define statistical significance.

14. Plus, this section should also include the descriptive analysis done. but as is now, only tells us about inferential analysis. In my opinion, it is always good to also consider logic and literature when building a model, for the variables in the analysis may already be confounded, that the variables of importance will be eliminated if only statistical significance is considered.

Variables were not only included by statistical significance. The variables were selected first if they could not logically be affected by the VL status of the clients. Thereafter, the shortlisted variables were tested for statistical significance to be included in the model.

15. What was the cutoff for multicollinearity of the variables? The authors didn't mention this.

We have specified that the maximum GVIF for any of the variables was 1.4, which is well under the 5 GVIF threshold.

Results

1. Refer to line 159, "The ART status of 87% of the clients was recorded as active on treatment". You need to restate this; it doesn't come out right. Plus, you didn't have ART status described as a variable in the methods. Now how come it appears in the results? You did not have ART regimen as a variable, how come you have results on ART regimen. (Methods-Results discordance)
The ART status variable was mentioned in the statistical analysis section. And it was mentioned that it was excluded from the logistic regression analyses. However, it was not mentioned in the "Variables explored as predictors of a non-suppressed viral load" section, we have renamed the section as "Variables engineered as predictors of a non-suppressed viral load" for specificity.

2. Table 1. Is this variable current ART status or ART status? The authors need to be consistent with the names of the variables. Plus, in the methods section you say, you didn't consider regimen as a variable. Now why the results on it?

The variable is Current ART status. We have revised the labels in the table and in text. The regimen line was not mentioned in the "Variables explored as predictors of a non-suppressed viral load" section, we have renamed the section as "Variables engineered as predictors of a non-suppressed viral load" for specificity. The regimen line variable was mentioned in the statistical analysis section. And it was mentioned that it was excluded from "modelling", the chi-square distribution table is not part of modelling, it is just a distribution table.

3. Did you consider literature and logic when including the variables in the model? Because, these usually support the variables that may not be significant but are of importance. For example, ART

regimen, is a salient variable, per literature. Also, results on Facility ownership are not included in Table 2. Is there a reason why?

We did consider literature as well as the limitations of the data. We included now the ART regimen as part of the distribution table, however, this variables was excluded from modelling because we only have a record of the regimen at the last drug pickup date and there no certainty that the same regimen was in use by clients at the time of VL testing. Aside from that, the ART regimen can be change in response to a non-suppressed VL test result or side-effects. Therefore, because we only have the last ART regimen on record, it is possible that the regimen was changed and it is not an independent explanatory variable of the VL outcome. The facility ownership variable was excluded from the model by backwards elimination as it did not improve the model. Nevertheless, after adjusting the cohort to the 2017-2021 range, the ownership variable was retained in the model and it is presented now.

4. Lines 197-198, 2. “All factors used in the adjusted logistic regression model were statistically significant, with a p-value of <0.000001” Justify why you included Sex that was not significant at bivariate. This should have come out well in the methods section.

The reason why Sex was retained is because it is a core demographic variable and it was not excluded by backwards elimination either. We did specify in the statistical analysis section now the variables that were eliminated from the multivariate model. The bivariate or univariable model does not adjust for other variables, and its inclusion in the multivariable model was guided by the univariate results. We have used backwards and forwards elimination to select the explanatory variables best suited for the model.

5. Create a paragraph in the results section, that mentions and explains the factors that were found to be associated with VL non-suppression, all together. For now, they are written in isolation, and bivariate and multivariable findings for each, combined together. Have bivariate results paragraph/s, and one/s for multivariable. Precisely, we need a summary of the variables that were found to be associated or not associated with VL non-suppression.
The outline of our results presented here follows a logical sequence and describes the risks associated with variables in their groups. Splitting into two paragraphs for univariable and multivariable specifically would make the results section too verbose. We chose to focus on key results and presenting the reference groups as well seeing that the major conclusions are based on those results. Aside from that univariable results are mainly presented so that other researchers that do not have access to all the variables used here can refer to our univariable findings. Nevertheless, the conclusions are largely based on the adjusted multivariable results. We believe the current format is reasonable and common in literature.

Discussion
1. Line 231, kindly mention the age groups, specifically. And the writing should be; “Being in a younger age group and on MDD 1-2 months were highly associated”. (Showing the strength of the association of the variable, not as an adjective).

We have adhered to the stile suggested by the reviewer. To note, we have excluded the MMD variable from the multivariable model because as reviewer 3 pointed out, longer MMD is a consequence of having a suppressed VL, therefore the variable is not an independent explanatory variable of the VL outcome.

2. “We also found that males, clients who received 233 treatment at tertiary health facilities, at small or medium facilities, or in the North-Central or North 234 East zones were associated with a higher risk of VL non-suppression. Other studies have found 235 similar results for the risk of viral

nonsuppression in younger age groups in Cambodia, Uganda, 236 and South Carolina (USA) [6,8,16], and among males [17–19]". What do these findings imply, in terms of HIV care and programming? What do they mean in terms of HIV programming? How do we consider the age group and the other significant variables, going forward in HIV programming in Nigeria?

We have mentioned implications of the findings here for HIV care and programming. "Our findings suggest that in some Nigerian states, the health seeking behavior of certain demographics can be improved or given more attention to by HIV care programs, specifically for younger-aged males. In that same regard, the quality of HIV healthcare programs can be improved across several states in Nigeria with consideration the facility types, size, and public ownership."

3. "The increased odds of viral non-suppression among ART clients who received treatment at tertiary health facilities were unlike the higher odds reported for primary health facilities in Ethiopia [20]. Small and medium facilities were identified as having greater odds for viral non-suppression; this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [21]." Authors need to make this statement clear, as is, it is unclear. Plus, avoid using odds. this is an interpretive section where the results are supposed to be broken down for understanding/comprehension. What exactly do you want to mean?

We have revised the paragraph for clarification, and we avoided using terms like odds. We have revised the paragraph as follows:
"The increased risk of viral non-suppression among ART clients who received treatment at tertiary health facilities have not been observed in Ethiopia where higher risk of viral non-suppression was associated with primary health facilities in Ethiopia [4]. Small and medium facilities were identified to be associated with viral-non-suppression of HIV clients on treatment and this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities. This could be due to smaller clinics being located within smaller communities, as a result, patients may avoid stigmatisation within their community and may not pick-up treatment as routinely as patients that attend clinics that are outside of their communities [5]. Such clients that would miss their drug pickup appointments more frequently, are reasonably expected to have non-suppressed viral loads."

4. "Small and medium facilities were identified as having greater odds for viral non-suppression; this was consistent with findings that clients were more likely to miss consecutive visits at lower volume facilities [21]." What is the implication of this finding in terms of HIV programming for Nigeria?

We have stipulated possible implications of these findings as follows:
"A possible circumvention of the stigmatisation within communities would be to offer clients that live within communities a referral to HIV care facilities that are located outside of their communities. However, consideration should be given to the distance needed for travel as well because although a distance less than one kilometre to the clinic was associated with higher IIT [5], mean distances above 4.7 km to clinics were associate with higher IIT [6]."

5. "ART clients who had their last VL test conducted within less than 1 year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested conducted within 1 to 3 years of being on ART. Our finding was consistent with the Center for Disease Control and Prevention's finding that PLHIV on ART could be virally suppressed within six months of initiation provided that they adhered to their medication [22]. Moreover, a greater likelihood of viral suppression was found among PLHIV who were initiated on treatment for less than one year compared with those on ART for more than one year [23]." What do these findings imply, in terms of HIV care and

programming in Nigeria?

We have stipulated the implication as follows: “This could suggest that greater attention to patients enrolled on ART for less than one year could be given to perhaps cultivate a habit of adhering to the treatment, which could result to better viral load outcomes.”

6. “Also, 254 elucidating that clients more engaged in care can have more opportunities for non-suppressed viral load test results, though this does not necessarily mean that this population is more likely to be 256 non-suppressed.”. How then in Nigeria, should this be taken into consideration to ensure viral suppression among HIV clients on ART? What is the implication of this?

We have substantiated as follows: “…this advocates for support of newly enrolled clients into developing treatment-adherence habits because it is possible that in some clinical settings adherence habits are better developed earlier on due to more attentive healthcare programs. Therefore, improving HIV care may ultimately result in better treatment-adherence habits and consequential VL suppression.”

7. Avoid using odds and the language of univariate/ multivariable in the discussion section.

We avoided using technical terms such as odds or univariate/multivariable terminology in the discussion section.

8. “Shorter MMD is initially prescribed to new clients and longer MMD is prescribed to virally stable clients to reduce the number of clinic visits. Because of non-adherence, clients may become virally non-suppressed and be placed on shorter duration treatment, requiring more frequent check-ups and clinical support to become stable. It is apparent that MMD is dependent on the VL status of clients; however, that is not 265 necessarily the case for new clients.”. Break this into two sentences.

We have removed MMD from the model because it is not an independent explanatory variable of the VL suppression outcome. Consequently we have removed this from the discussion section as well.

9. “A possible explanation for the North-Central zone having the highest odds of viral non-suppression could be linked to health-seeking behaviour such as non-use of the service, poor adherence to treatment, and possibly religious affiliation (for example Islamic religion predominant in northern where in certain circumstances women require permission to leave the premises of a household which can reduce access to healthcare [27,28].” What can be done to solve the problem in this region? Authors should make succinct recommendations on the key findings across this section.

We have made recommendations: “…Community refills (door-to-door) could be implemented in such communities, perhaps staffed by female health workers. On the other hand, in Borno and Yobe states in the North-East zone of Nigeria, the incessant insecurity in the region has largely led to people often been displaced and this has largely impacted on the health-seeking behavior,
.”

10. “One of the limitations of our study was the inaccessibility of the longitudinal data set, leaving us unable to conduct a longitudinal study to explore the factors affecting viral non-suppression over time. We were therefore restricted to conducting a cross-sectional study. The inclusion of MMD as an independent variable is a limitation of the study because a shorter MMD can be applied based on a non-suppressed VL, in which case MMD would be a proxy for IIT”. Authors need to state what the implication of this limitation to the study findings' accuracy and precision was. Plus, how did they minimize the impact of this limitation `on the findings?

We have excluded the MMD variable from the model and from discussions and conclusion.

11. “It is likely that some of the nearly 40% of client records (eliminated from analysis) without a VL test on record are a consequence of poor adherence to treatment which could lead to viral load non-suppression that is not tested/recorded.” The authors need to state the basis of this assumption, since you didn’t consider adherence levels as a variable?

We have mentioned the basis for this assumption as follows:
“This assumption is based on the concept that patients need to attend clinic visits to either receive treatment or have their VL samples collected and tested.”

12. “Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, marital status, and education level. The absence of VL suppression data for adolescents and recently initiated clients may have also had an impact on the study, suggesting that these findings may not necessarily apply to those subpopulation groups.”. Were these unavailable or not considered? You mention not considering ART regimen for some reasons in the methods section, but then state it as just data on this was unavailable. Authors may need to make us understand clearly, how an HIV treatment and care program may have no records of salient variables like a regimen.

Some of these variables were available, though, not in a longitudinal manner in which they could be associated with the VL suppression outcome. That is, the ART regimen was only available at the last point of clinic visit of the client and it cannot be assumed that the same regimen was in use at the time of the VL test because the ART regimen is subject to change based on the VL suppression result as well as other healthcare policy and drugs made available. For example, DTG (dolutegravir) regimens were only introduced since 2018 and before that patients must have been on other regimens. While the data we have indicates that almost 95% of the clients were on DTG based regimens at their last clinical visit, many patients were tested before that and DTG based regimens cannot be associated with VL outcomes.

13. Also, you have 15-24 age group category. (what is the definition of adolescents in your setting). You also have those initiated on treatment <1 year ago. You may have to restate this and reflect exactly what you wanted to mean. There is a discrepancy between this section and the study methods.

We have revised the paragraph to reflect as: “Other unavailable variables that could be explored in future studies to identify their association with viral suppression are tuberculosis status, adherence level, ART drug regimen, side-effects, IIT, marital status, and education level, however, these variables would need to be provided and analysed longitudinally. The absence of VL suppression data for recently initiated clients may have also had an impact on the study seeing that they had to be excluded, therefore only the results of tested patients could be analysed, leaving out the results of those without a test.“

14. Avoid repeating results in the discussion section, and focus on the key messages from the key results, and provide the implication of each. Authors also need to make sure that there is a congruency across all the sections, for now there is some significant discrepancy between the sections.

We have attempted to avoid repeating the results in the discussion, however, some context had to be given here and there to serve as a point of reference for the discussion and comparisons with other studies.

15. For study limitations, the authors need to acknowledge the type of bias this kind of design/methodology introduces and its implication to the findings.

We have addressed this as follows: “The study cohort was composed of clients that received care at USAID-supported facilities, therefore, it may not be a true representation of the risk of VL suppression throughout the country. In facilities that support is better, the results here could overestimate the contribution of some of the factors to VL non-suppression. Vice-versa, where support is lacking, the contribution of some of the factors presented here on VL non-suppression could be underestimated.”

Reviewer: 3
Ms. Lauren Bailey , US Agency for International Development
Comments to the Author:
Thank you for the opportunity to review this paper. This is a well-written analysis that adds to the growing literature around barriers/strategies for achieving virologic suppression and larger epidemic control of HIV. The analysis also expands on the critical role MMD can play in supporting virologic suppression and will hopefully encourage more countries to adopt and expand MMD as a person-centered approach to achieving improved treatment outcomes for PLHIV. However, a few key revisions are recommended to strengthen the analysis and clarify some confusion around including MMD as an independent variable.

Variables Explored as Predictors of a non-suppressed viral load
You do not include MMD and how it is defined/calculated in this section (which is very important per my comments below); however, you list it in line 141 as one of the variables included in the models.

We have changed the label of the “Variables explored as predictors of a non-suppressed viral load” to “Variables engineered as predictors of a non-suppressed viral load” because in the section we only mentioned the variables that were engineered and the method of engineering the variables. The variables that were readily available were mentioned in the statistical analysis section.

Statistical Analysis
Line 136-140: You note that the regimen line was dependent on the VL outcome investigated and therefore could not be used as an independent variable associated with VL non-suppression; but isn’t this the same case with MMD? Do clients need to be virally suppressed in order to be enrolled on MMD? I think it’s critical that you note the eligibility criteria for MMD; additionally, I recommend you define what is considered MMD. PEPFAR defines MMD as dispensing of 3 months or greater; anything less than 3 months is not considered MMD. With this in mind, a client that is virally non-suppressed could receive 2MMD but they would not be eligible for 3MMD. If the USAID-supported sites are following the guidelines, the virally non-suppressed clients would be placed on 1-2 month dispensing and transition to 3MMD or greater once clinically stable (which includes virologic suppression).

We have given careful consideration to the comment made by the reviewer and the implications of including the variable in our analyses. We agree with the comment made by the reviewer and decided to remove MMD / months of dispensation from the analysis for the following reasons: For clients to be placed on longer MMD dispensation (3+ months), the clients need to be virally suppressed. Therefore, the variable is not independent of the outcome. Secondly, the number of dispensation months is only

available at the last clinic visit of clients and it cannot be assumed that the same prescription length was applied at the time of VL testing of clients.

Discussion
Lines 259-260: The study you are referencing analyzed outcomes associated with multi-month prescribing, which can be different from multi-month dispensing. In many scenarios clients receive a multi-month prescription but can only be dispensed one month of ARVs at a time. I recommend rephrasing this sentence or using another source to support this statement.

To our knowledge the MMD variable we used, was strictly referring to multi-month dispensation. And we would have made the distinction. Though, we have removed the paragraph because we are no longer including MMD as part of the model.

Lines 260-261: When you reference shorter MMD and longer MMD, are you referring to Nigeria-specific MMD policy or global MMD policy in general? Again, I recommend clarifying MMD eligibility in Nigeria and what is technically considered MMD as this could affect your analysis.

To meet MMD eligibility criteria in Nigeria, clients must be virally suppressed. We acknowledge that the inclusion of the variable in the model introduced bias and we have removed it from the model.

Line 262-264: This statement is a bit confusing. This is implying that the client is already receiving MMD or some duration of extended dispensing if they have become non-adherent and subsequently virally non-suppressed and placed on shorter dispensing. Do we know what dispensing interval the client was receiving when they became non-adherent and virally non-suppressed? Is it common practice in Nigeria for clients with documented adherence challenges and subsequent non-suppression to be placed on a shorter dispensing interval?

We have discarded the text because we acknowledge that MMD is not a suitable variable to include in the model. Further, we can tell what dispensation length a client was receiving when they became IIT but we cannot tell what dispensation length a client was receiving when they had a VL test done.
In Nigeria it is common practice to minimize the length of dispensation for non-adhering clients in order to facilitate enhanced adherence counselling and increasing the number of clinic visits.

Line 264: Please clarify, is MMD dependent on the VL status of the client because virologic suppression is a requirement for enrollment on MMD; or is this statement the result of your logistic regression model? Why is this not the case for new clients? Again, it would be good to clarify MMD eligibility criteria.

We have discarded MMD variable from the model and the text referring to it. Lengthier drug dispensation is dependent on virological suppression.

Line 266-268: Can you please more clearly explain how you arrived at MMD being a confounding factor that possibly represented interruption in treatment? Are you suggesting that clients were receiving shorter MMD because of a history of treatment interruption, and that was leading to non-suppression? What do you mean by “misadministration” of MMD?

We have discarded the text. Regardless, to clarify, non-adherence to treatment does prompt shorter drug dispensation. By “misadministration” we meant poor adherence.

Line 274: Can it be suggested that longer dispensing intervals support treatment adherence and virologic suppression? There are several non-inferiority studies demonstrating that continuity of treatment and virologic suppression remain high among clients on 6MMD. It might be worth citing

these studies in your discussion and noting how your research adds to the current body of literature on MMD and viral load suppression.

We agree that longer dispensation periods are not necessarily the causative factors of viral suppression. With the data available we cannot investigate whether the longer dispensation is associated with VL suppression outcomes, moreover, VL suppression prompts lengthier MMD, and not necessarily vice-versa. We have removed the text.

Line 287: Is the lack of a VL test the consequence of poor adherence or treatment interruption (i.e. retention challenges). While treatment adherence and treatment interruption/retention are related, be careful not to conflate them.

Define treatment adherence as routine, daily administration of ARTs whereas IIT is missing clinical visits for longer than 28 days.

Line 282-284: I'm glad you note here the limitation with including MMD as an independent variable; however, the issue remains that virally non-suppressed individuals are technically not eligible for MMD and PEPFAR does not consider ARV dispensing < 3 months to be MMD – so one could assume all clients receiving 1-2 month dispensing have likely not yet achieved virologic suppression. It is possible, though, especially during COVID, that many clients who had not yet attained virologic suppression were placed on MMD as a protective measure. It would be worth looking into this and citing if this did, indeed, occur across the sites included in this analysis.

We agree that it is possible that clients that were non-suppressed could have received longer dispensations of ARVs during COVID. Nevertheless, the inclusion of the MMD variable in a model that explains VL non-suppression introduces considerable bias. We have removed the variable from the model and the text referring to it.

VERSION 2 – REVIEW

REVIEWER	Ngandu, Nobubelo South African Medical Research Council, Health Systems Research Unit
REVIEW RETURNED	18-Nov-2022

GENERAL COMMENTS	ABSTRACT CONCLUSION: "Targeting male clients within the younger age groups, receiving care for less than 3 28 years at tertiary and secondary health facilities, small and medium facilities, and in the Edo, Borno and Niger states for interventions could lead to improvements in VL suppression in Nigeria." This sentence implies that the investigators conducted an interaction analysis between the 'male' variable and all the other independent variables (age, timing of ART treatment etc). My understanding of their analyses is that each predictor variable was treated as independent. Clarity in the RESULTS section as suggested below is necessary, else kindly consider revising this concluding statement. DISCUSSION: Line 246-248 "Our study found that male clients in younger age

	groups (0-24) who started treatment before 2020 and have been on treatment for less than one year, receiving care at small and medium facilities…..". This sentence implies that the investigators conducted an interaction analysis between the 'male' variable and all the other independent variables (age, timing of ART treatment etc). My understanding of their analyses is that each predictor variable was treated as independent. Could this interpretation in the discussion as well as in the ABSTRACT be revised or the interaction analyses be included in the RESULTS section. Line 281-287 It would be useful for the authors to point out which results they are discussing in this section. Their discussion is not consistent with the OR/RR results in Table 3. The discussion says "ART clients who had their last VL test conducted within less than one year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested after one year on ART." However, in Table 3, Time on ART for <3 years had higher odds of being virally non-suppressed compared to those with 3++ years on ART.

REVIEWER	Nabukeera , Sarah Makerere University
REVIEW RETURNED	12-Dec-2022

GENERAL COMMENTS	The authors did a tremendous job in addressing the initial set of comments. Now let them focus and address the issues i raise this time, and the manuscript will be ready for publication. 1. Title reads; "*Factors associated with viral load non-suppression in <u>people living</u> with HIV on ART in Nigeria: A cross-sectional analysis from 2017 to 2021*", the objective in the abstract: "*Identify factors (demographic and clinical) associated with a non-suppressed viral load of <u>patients</u> on antiretroviral therapy in Nigeria*.", and "*Participants "585,632 people living with HIV (PLHIV) on antiretroviral therapy (ART).*". PLHIV are not necessarily patients; some are actually healthily living with HIV. Which one are you looking at? 2. In the abstract, the authors need to provide a small background to the study (3 sentences –what is known, what is unknown and what the study is going to do, which is the objective) before delving into other sections like the design, setting and so on.). Let the abstract be structured with

	sections such as; background, methods (setting, design, population etc.), results and conclusion) 3. Get the Limitations and strengths out of the abstract and have them well explained in the discussion section right after discussing the findings, before the conclusion and recommendations. 4. You cannot use ORs/RRs as a measure of association with a cross-sectional study design (a prevalence study). Besides, if Nigeria has a suppression rate of 78% among PLHIV on ART, the non-suppression rate is 22%, which makes ORs not an appropriate measure of the association since the outcome (non-suppression is not rare >10%). The authors ought to use Prevalence ratios with a modified posion regression model. The model will give Rate Ratios, but these are interpreted PRs. If they say they converted the ORs to RRs, then they should interpret these as PRs and also provide a reference which indicates this can be done for cross-sectional designs rather than choosing another regression model. 5. Strengths and limitations of the study these need to be well explained; for example, if the authors say, *"The study uses data from over 500,000 PLHIV enrolled on ART across 16 Nigeria states over four years between 2017 and 2021"*, how is this a strength? *"Variables such as education level and marital status/cohabiting, adherence to treatment, opportunistic infections and side effects were not available"*. What was done to circumvent the effect of this on the validity of the findings? 6. In the introduction, Line 46, *"people were living with HIV," is not "people living with HIV"* (PLHIV). This needs to be rectified to bring out the acronym correctly. 7. What is the estimate of PLHIV in Nigeria before you tell us how many are virally

		suppressed? This comes out globally but doesn't for Nigeria. *"Nigeria, a country with one of the highest global HIV infection rates"*. Give us the magnitude of this. 8. Line 68 reads, "*The objective of this analysis is to guide HIV programs to target population groups at the highest risk."* To distinguish this from the objective of the study mentioned in the same paragraph, the authors would rather state that; "*The findings from the analysis will be used to guide HIV programs to target population groups at the highest risk."* or otherwise as they see fit. 9. Study design, setting and population; can the authors list the 16 states in Nigeria that were supported by the United States Agency for International Development (USAID) that were considered for the analysis? It is also essential that the authors mention the age of the clients, e.g. 0-above 60 years, under this section in line 73. 10. Line 97; *"with a lasat drug pickup date between January 1st, 2017, and December 31st, 2021".* I think the authors meant to write last instead of lasat. 11. Lines 98-100 "for downstream analysis to isolate a cohort that was active during the latest VL suppression policy rolled out in Nigeria, whereby every client on treatment for 6 months is due for a VL test, and VL tests should be repeated every 12 months" I suggest the authors use **"which is**" instead of "**whereby**" as they describe the policy. **Whereby** makes it come off as part of what they did and not the policy description itself. 12. Line 104, …. number is captured instead. Shouldn't the tense be past? (was instead of is)

		13. Line 218; "*Akwa Ibom state has the highest proportion of clients in the record (36.8%)*" The tense in the results section has to be past. Please correct this throughout the document. Use the appropriate tense for each section. Plus, since the outcome is Viral non-suppression, for consistency, the authors need to interpret the proportions of non-suppression and not suppression throughout the results section. The relative measures were correctly interpreted in this regard. 14. Lines 244-256 need to be in the methods section. If there are any results that the authors want to state, let them do so without necessarily repeating the methodology in this paragraph. Stick to the results in this section. 15. The authors must interpret the RRs as PRs based on the study design. 16. Line 297 "who started treatment before 2020 and have been on treatment for less than one year". Authors should stick to the past tense whenever giving or stating any results. The present tense is for sentences that discuss the results. Let them do this in the entire document. 17. Line 310 "The increased risk of viral non-suppression among ART clients". Cross-sectional designs can't measure risk. The authors need to change this language with regard to my earlier comment on the appropriate measure of association. This should be rectified throughout. 18. In Line 320, the authors talk about how stigmatization can possibly be circumvented. They, however, don't tell us earlier how stigma is part of the problem. Could they please make a brief statement on this in the earlier lines for consistency? 19. Lines 325-329 are inconsistent. "Clients that received care at privately owned facilities have a lower risk of a non-suppressed VL seeing that there are fewer clients represented in the private sector. However, clients receiving care at privately owned facilities were non-suppressed in higher proportion than those receiving care at public facilities….." The authors need to rectify this. 20. Line 341-343; authors need to explicitly point out some of the recommended strategies that can be emphasised as great attention, like Intensified adherence counselling and others. 21. Line 349, authors should change 'this

	advocates" to include a noun (someone or group or an organization) that should advocate. Findings only indicate or highlight the need for advocacy, but they don't advocate. 22. Lines 371-381, authors may need to consider recommending attitudinal change interventions for such communities. Community refills alone may not suffice if a person still has no good social support to use the ART. 23. The authors indicate the limitation of the study design very well in lines 382-391, but they inconsistently use "risk in their write-up. This study design cannot measure risk; it is only giving us a snapshot for a particular period (period prevalence). 24. Lines 403-408, what then does this do to the validity of the results? The authors need to acknowledge that the factors reflected in this study maybe not be exhaustive.

REVIEWER	Bailey , Lauren US Agency for International Development, Office of HIV/AIDS
REVIEW RETURNED	28-Nov-2022

GENERAL COMMENTS	The main issues regarding MMD that I outlined in my initial review have all been addressed in the revised version. MMD has essentially been eliminated from the paper (except for a listing of months of ART dispensed in Table 2, do you want to keep that in the Table?); and while it is unfortunate to not include ART dispensing intervals in the analysis, it is necessary due to the fact that virologically non-suppressed individuals are not technically eligible for 3MMD or greater. It might be worth noting in the methods and/or discussion, however, why dispensing intervals were not included.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Dr. Nobubelo Ngandu, South African Medical Research Council
Comments to the Author:
ABSTRACT CONCLUSION:
"Targeting male clients within the younger age groups, receiving care for less than 3
28 years at tertiary and secondary health facilities, small and medium facilities, and in the Edo, Borno and Niger states for interventions could lead to improvements in VL suppression in Nigeria." This sentence implies that the investigators conducted an interaction analysis between the 'male' variable and all the other independent variables (age, timing of ART treatment etc). My understanding of their analyses is that each predictor variable was treated as independent. Clarity in the RESULTS section as suggested below is necessary, else kindly consider revising this concluding statement.

The reviewer's interpretation is accurate, in that the variables were treated as independent. We have revised the conclusion section of the abstract to reflect that the variables were treated as independent and corrected phrasing to avoid possible misinterpretation that the results were based on interaction analysis.

DISCUSSION:
Line 246-248 "Our study found that male clients in younger age groups (0-24) who started treatment before 2020 and have been on treatment for less than one year, receiving care at small and medium facilities…..". This sentence implies that the investigators conducted an interaction analysis between the 'male' variable and all the other independent variables (age, timing of ART treatment etc). My understanding of their analyses is that each predictor variable was treated as independent. Could this interpretation in the discussion as well as in the ABSTRACT be revised or the interaction analyses be included in the RESULTS section.

We have revised the discussion section to indicate that the variables were treated as independent and corrected phrasing to avoid possible misinterpretation that the results were based on interaction analysis.

Line 281-287 It would be useful for the authors to point out which results they are discussing in this section. Their discussion is not consistent with the OR/RR results in Table 3.
The discussion says "ART clients who had their last VL test conducted within less than one year on treatment were less likely to be virally non-suppressed compared with clients who had their VL tested after one year on ART."
However, in Table 3, Time on ART for <3 years had higher odds of being virally non-suppressed compared to those with 3++ years on ART.

We have specified what results the discussion is based on. We have also addressed the discrepancy between the unadjusted and adjusted models in text and we have added Table 4 to assist with the interpretation of the discrepancy. Table 4 highlights that in some states VL non-suppression of patients on ART for less than a year is considerably higher. Thus, when adjusting for other variables, such as state, the PR (replacing OR/RR based on reviewer's 2 suggestions) does change to account for the higher prevalence of virally non-suppressed individuals under 1 year on ART in some states.
Reviewer: 2
Sarah Nabukeera , Makerere University
Comments to the Author:
The authors did a tremendous job in addressing the initial set of comments. Now let them focus and address the issues i raise this time, and the manuscript will be ready for publication.

*Please see attached document with further comments from this reviewer

1. Title reads; "Factors associated with viral load non-suppression in people living with HIV on ART in Nigeria: A cross-sectional analysis from 2017 to 2021", the objective in the abstract: "Identify factors (demographic and clinical) associated with a nonsuppressed viral load of patients on antiretroviral therapy in Nigeria.", and
"Participants "585,632 people living with HIV (PLHIV) on antiretroviral therapy (ART).". PLHIV are not necessarily patients; some are actually healthily living with HIV. Which one are you looking at?

We have corrected the objectives of the abstract to reflect as:
"Identify factors (demographic and clinical) associated with a non-suppressed viral load of PLHIV on

antiretroviral therapy in Nigeria."

2. In the abstract, the authors need to provide a small background to the study (3 sentences –what is known, what is unknown and what the study is going to do, which is the objective) before delving into other sections like the design, setting and so on.). Let the abstract be structured with sections such as; background, methods (setting, design, population etc.), results and conclusion)

The journal's prescribed structure for the abstract does not include a "background" section. In accordance, we have omitted a background section from the abstract.

3. Get the Limitations and strengths out of the abstract and have them well explained in the discussion section right after discussing the findings, before the conclusion and recommendations.

It is the journal's requirement to present a strengths and limitations section under the abstract in bullet form.

4. You cannot use ORs/RRs as a measure of association with a cross-sectional study design (a prevalence study). Besides, if Nigeria has a suppression rate of 78% among PLHIV on ART, the non-suppression rate is 22%, which makes ORs not an appropriate measure of the association since the outcome (non-suppression is not rare >10%). The authors ought to use Prevalence ratios with a modified posion regression model. The model will give Rate Ratios, but these are interpreted PRs. If they say they converted the ORs to RRs, then they should interpret these as PRs and also provide a reference which indicates this can be done for cross-sectional designs rather than choosing another regression model.

We have upheld the recommendation made by the reviewer and have conducted a modified Poisson regression model and, interpreted the results as prevalence ratios since the rate ratio was based on prevalence of the outcome of interest (VL non-suppression).

5. Strengths and limitations of the study these need to be well explained; for example, if the authors say, "The study uses data from over 500,000 PLHIV enrolled on ART across 16 Nigeria states over four years between 2017 and 2021", how is this a strength? "Variables such as education level and marital status/cohabiting, adherence to treatment, opportunistic infections and side effects were not available". What was done to circumvent the effect of this on the validity of the findings?

We have revised the strengths and limitations section of the study to elaborate further, reflecting as follows:
• The study used data from over 500,000 PLHIV enrolled on ART across 16 Nigeria states over four years between 2017 and 2021 which can allow the results to cover a broad portion of HIV healthcare in Nigeria in recent times.
• The data used was routinely collected by clinics, reflecting the actual state of HIV healthcare in Nigeria during the period of the study.
• The study included distal factors such as state, facility level, size and, ownership which can guide intervention at an infrastructural level.
• Variables such as education level and marital status/cohabiting, adherence to treatment, opportunistic infections and side effects were not available, and some of these factors could have

been confounders of the predictors used in this study.

6. In the introduction, Line 46, “people were living with HIV,” is not “people living with HIV” (PLHIV). This needs to be rectified to bring out the acronym correctly.

We have revised the phrase as follows:
“…there were 37.7 million people living with HIV (PLHIV)…”

7. What is the estimate of PLHIV in Nigeria before you tell us how many are virally suppressed? This comes out globally but doesn’t for Nigeria. “Nigeria, a country with one of the highest global HIV infection rates”. Give us the magnitude of this.

We have indicated the estimated number of PLHIV, as well as prevalence rate and incidence rate in Nigeria, alongside more recent estimates of PLHIV on ART that are virally suppressed, phrased as follows:
“Nigeria is a country with one of the highest numbers of PLHIV in the world (1.9 million), with a prevalence rate of 1.4% and an incidence rate of 0.34 per 1,000 capita with approximately 74,000 individuals newly infected as estimated in 2021. It was also estimated that 86% of the PLHIV on ART in Nigeria were virally suppressed in 2021”

8. Line 68 reads, “The objective of this analysis is to guide HIV programs to target population groups at the highest risk.” To distinguish this from the objective of the study mentioned in the same paragraph, the authors would rather state that; “The findings from the analysis will be used to guide HIV programs to target population groups at the highest risk.” or otherwise as they see fit.

We have rephrased the sentence to reflect as follows:
“The findings from the analysis can be used to guide HIV programs to target the PLHIV on ART with the highest likelihood of having a non-suppressed VL.

9. Study design, setting and population; can the authors list the 16 states in Nigeria that were supported by the United States Agency for International Development (USAID) that were considered for the analysis? It is also essential that the authors mention the age of the clients, e.g. 0-above 60 years, under this section in line 73.

We have mentioned the name of the 16 states in the “Study design, setting, and population” section and we have stipulated the age categories in the section as well, reflecting as:
“The study was a cross-sectional analysis of clients who were enrolled on ART at 580 facilities across 16 States (Adamawa, Akwa Ibom, Bauchi, Bayelsa, Borno, Cross River, Edo, Jigawa, Kano, Kebbi, Kwara, Lagos, Niger, Sokoto, Yobe, Zamfara) in Nigeria that were supported by the United States Agency for International Development (USAID)…. The age of clients ranged between 0 and 101 with a median of 37 and a mean of 37.2.”

10. Line 97; “with a lasat drug pickup date between January 1st, 2017, and December 31st, 2021”. I think the authors meant to write last instead of lasat.

The manuscript now reflects “last”.

11. Lines 98-100 “for downstream analysis to isolate a cohort that was active during the latest VL suppression policy rolled out in Nigeria, whereby every client on treatment for 6

months is due for a VL test, and VL tests should be repeated every 12 months" I suggest the authors use "which is" instead of "whereby" as they describe the policy. Whereby makes it come off as part of what they did and not the policy description itself.

We have replaced "whereby" with "which is".

12. Line 104, …. number is captured instead. Shouldn't the tense be past? (was instead of is)

We have replaced "is" with "was".

13. Line 218; "Akwa Ibom state has the highest proportion of clients in the record (36.8%)" The tense in the results section has to be past. Please correct this throughout the document. Use the appropriate tense for each section. Plus, since the outcome is Viral non-suppression, for consistency, the authors need to interpret the proportions of nonsuppression and not suppression throughout the results section. The relative measures were correctly interpreted in this regard.

We have corrected to use past tense throughout the manuscript.

14. Lines 244-256 need to be in the methods section. If there are any results that the authors want to state, let them do so without necessarily repeating the methodology in this paragraph. Stick to the results in this section.

We have removed any text that repeats the methodology and we have only presented results in the results section.

15. The authors must interpret the RRs as PRs based on the study design.

We have firstly conducted a modified Poisson regression which rendered rate ratios that were interpreted as prevalence ratios throughout the manuscript.

16. Line 297 "who started treatment before 2020 and have been on treatment for less than one year". Authors should stick to the past tense whenever giving or stating any results. The present tense is for sentences that discuss the results. Let them do this in the entire document.

We have attentively corrected the phrasing throughout the manuscript to be in the past tense.

17. Line 310 "The increased risk of viral non-suppression among ART clients". Crosssectional designs can't measure risk. The authors need to change this language with regard to my earlier comment on the appropriate measure of association. This should be rectified throughout.

We have refrained from using the term "risk", instead we have used the term "likelihood" throughout the manuscript, especially when referring to the results from this study.

18. In Line 320, the authors talk about how stigmatization can possibly be circumvented. They, however, don't tell us earlier how stigma is part of the problem. Could they please make a brief statement on this in the earlier lines for consistency?

Statements were made on previous lines to clarify and provide consistency as follows:

“This could be due to smaller clinics being located within smaller communities, as a result, patients may avoid stigmatisation within their community by not pick-up treatment as routinely as patients that attend clinics that are outside of their communities [22]. Such clients that would miss their drug pickup appointments more frequently to avoid stigma, are reasonably expected to have non-suppressed viral loads. A possible circumvention of the stigmatisation within communities would be to offer clients that live within communities a referral to HIV care facilities that are located outside of their communities.”

19. Lines 325-329 are inconsistent. “Clients that received care at privately owned facilities have a lower risk of a non-suppressed VL seeing that there are fewer clients represented in the private sector. However, clients receiving care at privately owned facilities were non-suppressed in higher proportion than those receiving care at public facilities…..”
The authors need to rectify this.

We have rectified the statement as follows:
“Clients that received care at privately owned facilities had lower risk of a non-suppressed VL when adjusting for the other variables included in the model.”

20. Line 341-343; authors need to explicitly point out some of the recommended strategies that can be emphasised as great attention, like Intensified adherence counselling and others.

We have mentioned interventions such as enhanced/intensive adherence counselling, improved follow-up programs or more frequent follow-ups as interventions to improve adherence and retention in care.

21. Line 349, authors should change ‘this advocates” to include a noun (someone or group or an organization) that should advocate. Findings only indicate or highlight the need for advocacy, but they don’t advocate.

We have rephrased as follows, replacing “this advocates” with “these findings motivate for…”:
Nevertheless, these findings motivate for support of newly enrolled clients to develop treatment-adherence habits.

22. Lines 371-381, authors may need to consider recommending attitudinal change interventions for such communities. Community refills alone may not suffice if a person still has no good social support to use the ART.

We have mentioned the implementation of enhanced adherence counselling, regular visits from case managers alongside community refills.

23. The authors indicate the limitation of the study design very well in lines 382-391, but they inconsistently use “risk in their write-up. This study design cannot measure risk; it is only giving us a snapshot for a particular period (period prevalence).

We agree with the reviewer, and we have replaced the term “risk” with “likelihood” throughout the manuscript.

24. Lines 403-408, what then does this do to the validity of the results? The authors need to acknowledge that the factors reflected in this study maybe not be exhaustive.

We have stated that the factors reflected in this study may not be exhaustive.

Reviewer: 3
Ms. Lauren Bailey , US Agency for International Development
Comments to the Author:
The main issues regarding MMD that I outlined in my initial review have all been addressed in the revised version. MMD has essentially been eliminated from the paper (except for a listing of months of ART dispensed in Table 2, do you want to keep that in the Table?); and while it is unfortunate to not include ART dispensing intervals in the analysis, it is necessary due to the fact that virologically non-suppressed individuals are not technically eligible for 3MMD or greater. It might be worth noting in the methods and/or discussion, however, why dispensing intervals were not included.

We chose to retain MMD in the descriptive Table 2 because other researchers may find value in this variable being included.

WE have included a statement in the Statistical analysis section as follows:
“The multi-month dispensing variable (MMD) was excluded from the regression models because the variable is not independent of the VL outcome. That is, eligibility criteria for MMD requires that clients are virally suppressed.”

VERSION 3 – REVIEW

REVIEWER	Nabukeera , Sarah Makerere University
REVIEW RETURNED	09-Mar-2023

GENERAL COMMENTS	To the best of my knowledge, the manuscript is ready to be published and I commend the authors for heeding to all the recommendations made during my reviews.