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Effects of the Covid-19 pandemic on ART initiation and access to HIV viral load monitoring in adults living with HIV in West Africa: a regression discontinuity analysis

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Authors' contributions

JBF, DB, AJ, and FB conceived the study. TT and KM prepared the data extracts. JBF led the analysis of the data and produced manuscript outputs, with analysis contributions by DB, AJ, TT and KM. JBF, DB and AJ drafted and finalized the manuscript. AP, AM, EM, HC, OE, IO, DE, TT, KM and AJ were involved in the collection and harmonization of data. JBF, TT, KM, AP, AM, EM, HC, OE, IO, DE, FB, DB, AJ reviewed the manuscript, provided critical inputs and approved the final manuscript.

Abstract

Objectives: Efforts to control the COVID-19 pandemic have potentially compromised the availability and/or quality of HIV services. We aimed to assess the pandemic's impact on ART initiation and HIV viral load (VL) monitoring in three West African countries.

Methods: We used routinely collected data from five clinics contributing to the IeDEA collaboration in Burkina Faso, Côte d'Ivoire and Nigeria. We included ART-naïve adults living with HIV (ALWH) initiating ART from 01/01/2018. We conducted regression discontinuity analysis to estimate changes in the number of ART initiations and VL measures per week, before and during the pandemic period in each country.

Results: In clinics in Burkina Faso and Côte d'Ivoire, ART initiations per week remained constant throughout the studied periods (-0.24 points (p) of ART initiations/week 95%CI -5.5, 5.9, -0.9 p 95%CI -8.5,8.6, respectively), whereas in Nigeria's clinic, they decreased significantly (-6.3 p, 95% CI -10.8, -1.7) after the beginning of the pandemic. The volume of VL tests performed decreased significantly in all three countries (-17.0 p 95%CI -25.3, -8.6 in

Burkina Faso, -118.4 p 95%CI -171.1, -65.8 in Côte d'Ivoire and -169.1p 95%CI-282.6, -55.6 in Nigeria).

Conclusions: Access to ART was maintained for newly diagnosed ALWH despite pandemic-related physical/social distancing measures. However, VL monitoring was severely disrupted and did not return to pre-pandemic levels approximately one year after the beginning of the pandemic. While HIV services in West Africa appear rather resilient, the impact of disruptions in VL monitoring on virological and clinical outcomes should continue to be monitored.

Keywords: HIV care; ART initiation; Viral Load monitoring; Covid-19; West Africa; Regression Discontinuity Design.

Introduction

The COVID-19 pandemic has had far-reaching effects on societies, including their health systems and populations. Measures or restrictions implemented to mitigate transmission and reduce the impact of COVID-19 on health systems may have unintentionally led to an increase in illness and death from other causes, i.e. HIV/AIDS, tuberculosis, and malaria (1–3). More specifically, the international community feared the pandemic could thwart ongoing efforts globally to prevent HIV infections and ensure access to treatment and care (4). Early studies modelling the potential impact of disruptions in health services in resource-limited settings,

taking into account a range of parameters, suggested that in settings with a substantial burden of HIV, tuberculosis, and malaria, mortality from these diseases could increase by 10%, 20%, and 36% respectively over a period of 5 years as a result of the COVID-19 pandemic (5,6). Furthermore, early empirical evidence from the Global Fund highlighted the pandemic's impact on prevention and screening services (e.g., voluntary male circumcision, the prevention of mother-to-child transmission, HIV self-testing), documenting decreases in access compared to the previous year. HIV testing in particular fell by 22% between 2019 and 2020, resulting in declines in treatment initiation indicators (1,7).

West Africa is home to 5 million people living with HIV (PLWH), two-thirds of whom reside in five of the 16 countries in the region (8). The UNAIDS 90-90-90 targets had not yet been achieved prior to the pandemic in spite of improvements in timely screening, linkage to care, and sustained access to antiretroviral therapy in the region (8). While there is evidence that many clinics either closed or reduced their services during the pandemic (9), a large multi-regional survey conducted within the International epidemiologic Database to Evaluate AIDS (IeDEA) consortium found that HIV programs in high prevalence and low-income settings introduced or expanded measures to ensure ART adherence and engagement in care (10). Nevertheless, as local program representatives have raised concerns regarding the pandemic's impact on access to HIV VL monitoring in particular, the assessment of patient-level data is needed to understand the pandemic period's impact on the provision of HIV care in the region.

We aim to analyze and document the impact of the COVID-19 pandemic on the number of ART initiations and VL tests conducted before and during the pandemic in adults living with HIV (ALWH) initiating care in urban clinics in Burkina Faso, Côte d'Ivoire, and Nigeria.

Methods

Study design and population

The IeDEA West Africa (IeDEA-WA) collaboration gathers, harmonizes and aggregates routinely collected epidemiological and clinical data from seven HIV programs in Benin, Burkina Faso, Côte d'Ivoire, Nigeria and Togo. The IeDEA-WA database comprises nearly 50,000 ALWH (16 ≥ years old) who have ever started ART. The collaboration's overarching aim is to identify individual and structural barriers associated with the continuum of HIV care throughout West Africa (http://iedea-wa.org). Moreover, the IeDEA consortium conducts periodic assessments of its participating sites to better understand HIV-related health services delivery. In 2020, specific questions regarding the COVID-19 pandemic were added to the site assessment survey to better comprehend how the pandemic period had affected the availability, accessibility, acceptability and the quality of HIV services (10). For this analysis, data from the last version of the IeDEA-WA Merger (Version 8 – 04/13/2022) were used. Due to missing values and inconsistencies in data from two sites, we have restricted this analysis to five participating sites in three countries: Burkina Faso (Hôpital De Jour - Bobo Dioulasso), Côte d'Ivoire (Centre de Prise en charge de Recherche et de Formation, Centre Intégré de Recherches Biocliniques d'Abidjan, Centre National de Transfusion Sanguine – Abidjan) and Nigeria (The Nigerian Institute of Medical Research – Lagos). We included ART-naïve ALWH with a first visit date after 01/01/2018 and followed them until date of database closure (06/14/2021 in Burkina Faso, 05/12/2021 in Côte d'Ivoire and 04/14/2022 in Nigeria).

In Burkina Faso, HIV services have been expanded, both decentralized to lower-level health facilities and integrated into primary care. In 2018, 70% of PLWH knew their HIV status and 88% of them were on ART (11).

Similarly, in Côte d'Ivoire, achieving the UNAIDS 90-90-90 targets has been prioritized. The national HIV program that includes prevention, testing, and treatment services has been integrated into the broader health system since 2003. Notably, the Ministry of Health has centralized VL monitoring at the national laboratory. In 2018, 63% of PLWH knew their HIV status; 87% of them were on ART; and 75% of those on treatment had suppressed viral loads (11).

In Nigeria, HIV prevalence was estimated at 1.4% nationally in 2018, representing 1.9 million PLWH and the highest HIV burden in the region (11). While significant progress has been made in expanding access to HIV services, PLWH's access to HIV care and treatment services continues to be hindered by various factors, including geographical disparities, limited resources, and societal challenges. Efforts have been made to address these barriers and improve access to HIV services with significant success. In 2018, 67% of PLWH knew their HIV status, 80% were on ART and, of those on ART, 80% were virally-suppressed (12).

Demographics, ART initiation and HIV VL

Sex and age were documented at enrolment date and the latter categorized in four categories: 18-24, 25-34, 35-39 and 40+ years old. We defined enrolment in care as date of first visit in the center, date of database closure as the last visit date documented in the merger and the date of the start of the pandemic as date of first distancing measures put in place in the country (13). ART

initiation was defined as first date of ART treatment documented in the database and HIV VL monitoring as each documented test performed at laboratory level.

Statistical analyses

We described demographic data at enrolment and summarized characteristics before and after the pandemic. We defined the beginning of the "pandemic period" as 3/27/2020 in Burkina Faso, 4/9/2020 in Côte d'Ivoire and 3/30/2020 in Nigeria, reflecting when physical/social distancing measures were enforced nationally (14). We plotted crude summaries of the two outcomes by year and country. We performed a regression discontinuity analysis to estimate changes in the number of ART initiations and VL tests performed before and after the beginning of the pandemic, stratifying by country; using a regression discontinuity design (15,16). For this, we used local polynomial regression models within data-driven Imbens-Kalyanaraman (IK) bandwidth intervals, derived using a rectangular (uniform) kernel to estimate risk differences just before and just after pandemic as follows :$E[Yi|Zi] = \beta 0 + \beta 1 Zi + \beta 2 \times 1[Zi \geq 0] + \beta 3 Zi \times 1[Zi \geq 0]$ where Yi is the probability of observing the outcome of interest, Zi is the number of days between ART initiations' date and date of start of pandemic (negative for ART initiation before), and $1[Zi \geq 0]$ indicates initiation on or after the date reflecting the beginning of the pandemic. Calculated using the subset of observations within IK bandwidth intervals, the effect of interest is the difference in local linear predictions at the threshold (ie, as the threshold is approached from above vs below). We used the Rdrobust function to implement conventional local-polynomial RD effect point estimators and confidence intervals to assess differences in crude point (p) changes per week in testing in the pre– and post–pandemic periods. To present the

effect of the pandemic on the two outcomes of interest, we plotted binned sample means, tracing out the underlying regression function. All statistical analyses were performed using STATA 16.1 (StataCorp, College Station, TX, USA).

Ethics statement

The IeDEA-WA Collaboration was granted approval from the Ethics committee "Comite de Protection des Personnes Sud-Ouest et Outre-mer III" in Bordeaux, France (IRB00012788) to collect, merge and analyze deidentified data from involved HIV clinics in West Africa. Moreover, each participating site obtained approvals from their National Ethics committees (Côte d'Ivoire: IRB00009111; Burkina Faso: IRB00004738; Nigeria (NIMR): IRB00003224). Written informed consent requirements were deferred to the local Institutional Review Boards. The analysis only used de-identified data collected from routine clinical care.

Results

A total of 3,734 ALWH initiated ART between the 01/01/2018 and the database closures; 832 (22.3%) in Burkina Faso, 1562 (41.8%) in Côte d'Ivoire and 1340 (35.9%) in Nigeria. ALWH initiating ART were of similar in terms of age before and during the pandemic period in clinics in Burkina Faso and Côte d'Ivoire while in the clinic in Nigeria, they were older before compared to during pandemic period (median age 39 years [IQR 30-46] versus 51 years [IQR

46-57] respectively, p<0.001). No differences in terms of sex at ART initiation were found in clinics in Burkina Faso, however in the Nigerian clinic, fewer were men (37.0% versus 42.4% respectively, p=0.05) and, in Côte d'Ivoire's clinics, fewer were women (57.4% versus 66.4%, p=0.002) during pandemic compared to before (Table 1).

Changes in ART initiations and VL monitoring

In Figures 1 and 2, we describe the numbers of ART initiations and VL tests performed, by year and by country. In Burkina Faso, the number of ART initiations remained relatively stable over the years, with a decrease observed at the beginning of the pandemic period (April 2020). Similarly, in Côte d'Ivoire, the number of ART initiations showed a consistent pattern, with a slight decline during the pandemic (May-July 2020 and April 2021). In Nigeria, there was a notable increase in number of ART initiations in the beginning of 2021, above pre-pandemic levels.

Regarding VL monitoring, in Burkina Faso, the number of VL tests performed declined drastically after the beginning of the pandemic and remained below the pre-pandemic levels. In Côte d'Ivoire, the number of VL tests remained stable with a slight decrease at the beginning of the pandemic and a drastic decline in April, 2021. In Nigeria, the number of VL tests declined during the pandemic, with a dip observed at the beginning of the pandemic, but eventually returning to pre-pandemic levels in 2021.

We plotted the results of the regression discontinuity for the number of ART initiations (Figure 3) and the number of VL tests performed (Figure 4) for each country. In Burkina Faso and Côte d'Ivoire, the number of ART initiations per week did not significantly change throughout the pandemic period, with a change of -0.24 p and -0.9 p, respectively (95%CI -5.5, 5.9 and -8.5, 8.6, respectively). In contrast, at the clinic in Nigeria, we found the number of ART initiations to have significantly decreased (-6.3 p [95%CI -10.8, -1 .7]), although the number appears to gradually increase over the course of the pandemic period (Figure 3). In contrast, in all three countries, the number of VL tests decreased significantly during the pandemic compared to the pre-pandemic period, representing -17.0 p (95%CI -25.3, -8.6) in Burkina Faso, -118.4 p (95%CI -171.1, -65.8) in Côte d'Ivoire, and -169.1 p (95%CI -282.6, -55.6) in Nigeria.

Discussion

Despite strict physical and social distancing measures and reported reduced availability of HIV services, we found evidence to support that access to ART was maintained for ALWH in clinics in Côte d'Ivoire and Burkina Faso but was somewhat disrupted in the clinic in Nigeria. In contrast, VL monitoring was found to be severely compromised in all settings during the pandemic period. Furthermore, VL monitoring did not return to pre-pandemic levels one year after start of the COVID-19 pandemic. Examining actual changes in individual patient-level data, we have provided a more comprehensive understanding of the pandemic's impact on HIV care in prominent centers for HIV care in Burkina Faso, Côte d'Ivoire, and Nigeria. Our study confirms

predicted impacts on HIV services while highlighting country-specific challenges and the importance of tailored strategies during crises like the COVID-19 pandemic.

Our analysis of the site assessment (Supplementary table) also revealed significant reported disruptions in HIV services during the COVID-19 pandemic. Indeed, HIV testing/diagnostic services, enrolments of new patients and HIV VL monitoring were suspended or limited in the three countries. Stockouts of supplies for VL testing were also reported. As already described in the overall analysis of the IeDEA site assessment, HIV testing and diagnostic services were suspended or reduced in a considerable number of countries within the consortium (10), indicating a potential decline in early HIV diagnosis. This disruption in testing services is of great concern as it can impede ART initiation, threatening ALHIV's prognosis. Furthermore, the suspension of HIV VL collection and longer turnaround times for results may have implications for treatment monitoring and timely adjustment of ART regimens, potentially leading to suboptimal treatment outcomes. Additionally, it is important to note that our study focused on ART initiations, providing insight into the uptake of treatment among individuals diagnosed with HIV. However, it does not directly reflect access to HIV testing during the pandemic. Further investigation is warranted to examine the extent to which testing activities were affected and whether there were any disparities in HIV testing rates across different age groups. Understanding the dynamics between HIV testing and ART initiations can provide a more comprehensive picture of the impact of the pandemic on the HIV care continuum and guide targeted interventions to address gaps in testing and treatment access. In other regions, significant reductions in HIV testing activities have been described and highlighted as a consequence of the COVID-19 pandemic (17,18).

While no significant differences in the average number of ART initiations per week by period were found in the clinics in Burkina Faso and Côte d'Ivoire, the clinic in Nigeria did experience a significant decrease in the number ART initiations during the pandemic period compared to the pre-pandemic period, albeit with a gradual recovery over time. The maintenance of levels of ART initiations in Burkina Faso and Côte d'Ivoire are consistent with a recent President's Emergency Plan for AIDS Relief (PEPFAR) report, which confirms the effectiveness of HIV programs in mitigating the impact of the COVID-19 pandemic (19). Furthermore, in Côte d'Ivoire, investigators in one of the three clinics reported that community ART pick-up points had been set-up to ensure continued access to ART in the context of social distancing measures (Supplementary table), pointing to healthcare providers' adaptability and resourcefulness. The decrease in ART initiations in the clinic in Nigeria may reflect disruptions in access to the clinic or other barriers encountered by ALWH during the pandemic (e.g., fear of infection). Another possible explanation of this finding may be fewer diagnosed HIV infections in 2021, which have been reported in Nigeria, therefore may explain the observed difference in the average number of ART initiations (4). There is evidence that key strategies including community-based HIV care may have help to maintain access to ART during the pandemic through despite restricted access to clinics (20). Nonetheless, the significant decrease in ART initiations in the clinic in Nigeria during the pandemic, coupled with the higher proportion of females initiating ART, reflects the findings of previous studies that highlight the low access to HIV testing services among men in Nigeria (19,21,22). These findings emphasize the need for targeted interventions to ensure continued access to HIV testing and ART initiation, particularly in settings with significant disruptions in healthcare services, including proactive measures to reach those who may have not been tested as a result of these service disruptions.

All clinics experienced a significant reduction in the volume of HIV VL testing during the pandemic. This decline in testing raises concerns about the effectiveness of treatment monitoring among ALWH and its impact on clinical outcomes and long-term prognosis (23,24). HIV VL monitoring is a crucial component of HIV care, enabling healthcare providers to assess treatment response, detect virologic failure, and optimize treatment regimens (25). Furthermore, all three countries follow WHO guidance calling for HIV VL testing at 6-months after ART initiation and viral suppression at 1-year (26). The observed reductions in HIV VL testing highlight the need to strengthen laboratory services, ensuring consistent availability of testing supplies, and addressing logistical challenges to maintain reliable and timely testing services. The survey conducted by the IeDEA consortium also found similar disruptions, including the suspension of VL monitoring, longer turnaround times for results, stock-outs of essential supplies, and laboratories not accepting HIV VL samples (10). These documented operational challenges likely underlie our findings. Furthermore, these findings are consistent with reports from other African settings that have highlighted the impact of the pandemic on HIV VL monitoring and subsequent management of treatment failure (27,28). While it is possible that the pandemic period affected ART adherence in spite of evidence of maintained access to ART, interruptions in VL monitoring hamper an in-depth assessment of the proportion of those in care who have achieved/maintained virological suppression.

Further research is needed and will be conducted in a multi-regional analysis across low- and middle-income countries (LMICs) within the IeDEA consortium. This will provide a broader perspective on the challenges faced in different settings. A comprehensive understanding of the medium to long-term consequences of the pandemic on HIV care requires examining a larger

sample of countries and considering additional outcomes. This research will provide insights into the evolving landscape of HIV services, enabling targeted interventions.

Strengths and limitations

Our study provides complementary evidence regarding the impact of the COVID-19 pandemic on ART initiations and VL monitoring in prominent urban clinics in three West African countries, highlighting similarities but also intra-regional differences. While mathematical models had predicted a potential impact on HIV services at the beginning of the pandemic, our analysis goes beyond assumptions and examines the actual changes observed. It uses routine programmatic data, providing insights into the "real-world" implementation of HIV services both before and during the pandemic. This approach has contributed to the generalizability of our findings.

Nevertheless, our findings should be interpreted with some caution. First, this analysis relied on routine programmatic data which, while valuable for assessing real-world trends, may be subject to incomplete or missing data, variations in data collection practices across different healthcare facilities, and reporting biases. As our collaboration relies on data from a limited number of clinical centers in each country, we acknowledge that risk of information bias. For example, PLWH may initiate care (ART) at one clinic and then be followed-up at another. Unfortunately, the transfer of PLWH between clinical centers is not captured, potentially resulting in information bias. These transfers are not uncommon in PLWH on ART but are less likely among those starting ART. It is unclear whether this phenomenon (patient transfer) was more or less

likely during the pandemic compared to the pre-pandemic period. Second, as only limited demographic characteristics were available, our ability to capture individual-level variations or factors influencing ART initiations and HIV VL monitoring was limited. Also, our findings are based on data from urban clinics and may not be fully representative of dynamics in clinics nationally, particularly those in primary or secondary care in rural settings. The characteristics and challenges of HIV services in rural or remote areas could differ significantly, and therefore, caution should be exercised when generalizing the results nationally.

As the experiences of these clinical settings during the COVID-19 pandemic and their responses varied, it is crucial to recognize that the impact on HIV services and the effectiveness of programmatic adaptations may differ across the West African region. Furthermore, the timing of the database closure varied across the countries, which may have influenced the completeness and comparability of the data. While our study has primarily focused on average changes in volume before and during the pandemic, contributing valuable, albeit macro-level, insights regarding the COVID-19 pandemic's impact on HIV services, it does not consider the perspectives of ALWH, which could provide additional insights into the challenges faced during the pandemic.

Conclusions

HIV clinics in two out of three countries in West Africa demonstrated resilience as they successfully maintained access to ART for ALWH despite the challenges imposed by the pandemic. However, the pandemic and associated measures had a significant effect on HIV VL

monitoring across all three countries, and did not return to pre-pandemic levels one year after the beginning of pandemic. It is critical to closely monitor the HIV care continuum in the post-pandemic era to ensure that the documented disruptions in services do not have enduring effects on ALWH's virological and clinical outcomes.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Figure 1. Evolution of ART initiations, by year and country

Figure 2. Evolution of VL monitoring, by year and country

Figure 3: Plots of Regression Discontinuity Analysis for Art initiations by country

Figure 4: Plots of Regression Discontinuity Analysis for VL monitoring by country

Table 1. Summary of AEs in the Early-Switch and Late-Switch Dolutegravir/Lamivudine Groups Through Week 196 (Safety Populations)

AEs, n (%)	Early-switch dolutegravir/lamivudine (N=369)			Late-switch dolutegravir/lamivudine (N=298)
	Day 1-Week 48	Day 1-Week 144	Day 1-Week 196	Weeks 148-196
Any AE	295 (80)	336 (91)	347 (94)	239 (80)
AEs in ≥10% of participants[a]				
COVID-19	—	33 (9)	77 (21)	55 (18)
Nasopharyngitis	43 (12)	63 (17)	71 (19)	16 (5)
Diarrhea	30 (8)	50 (14)	54 (15)	12 (4)
Upper respiratory tract infection	31 (8)	50 (14)	52 (14)	7 (2)
Syphilis	24 (7)	39 (11)	49 (13)	14 (5)
Back pain	21 (6)	43 (12)	47 (13)	11 (4)
Arthralgia	12 (3)	31 (8)	46 (12)	15 (5)
Anxiety	17 (5)	35 (9)	44 (12)	7 (2)
Headache	24 (7)	35 (9)	41 (11)	17 (6)
AEs leading to withdrawal	13 (4)	23 (6)	25 (7)	9 (3)
Grade 2-5 AEs	193 (52)	279 (76)	295 (80)	165 (55)
Drug-related grade 2-5 AEs	17 (5)	21 (6)	23 (6)	11 (4)

Serious AEs	21 (6)	57 (15)	65 (18)	15 (5)
Fatal AEs[b]	1 (<1)	3 (<1)	4 (1)	0

AE, adverse event.

[a]Based on AEs reported in ≥10% of early-switch participants from Day 1-Week 196. [b]Fatal AEs were gunshot wound (homicide; Day 1-Week 48), substance abuse (Weeks 48-144), ischemic hepatitis (Weeks 48-144), and acute myocardial infarction (Weeks 144-196); none were considered related to study treatment.

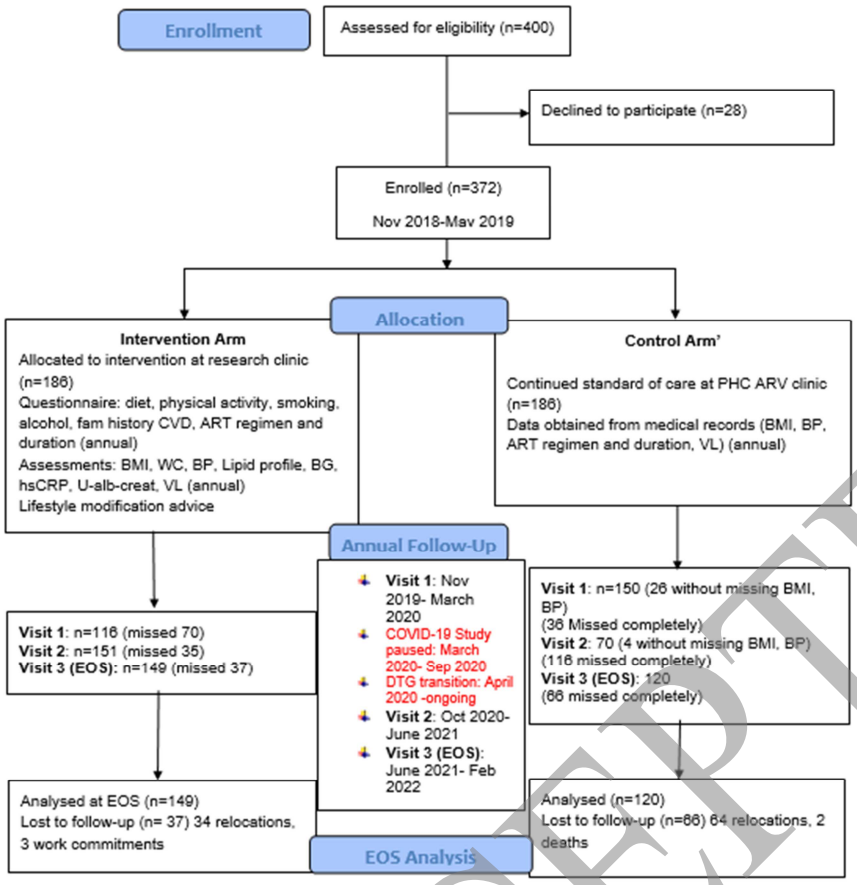

Figure 1. CONSORT diagram

Source: Author created using Microsoft word Consort 2010 template

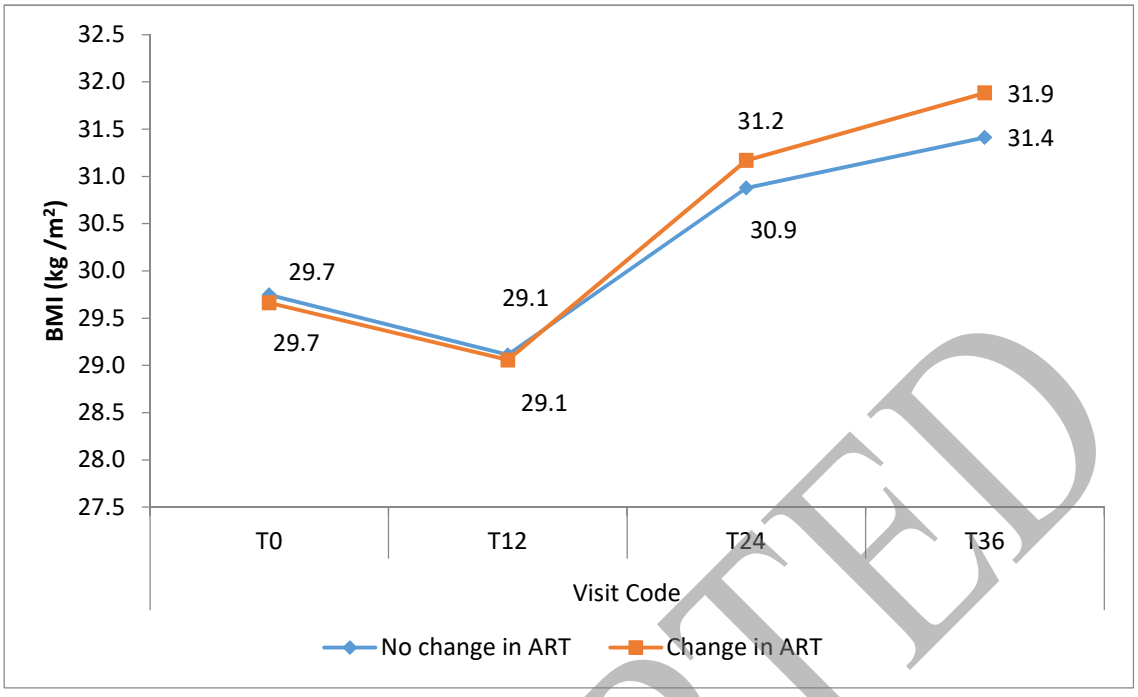

Figure 2: Incidence of Obesity in the Intervention Arm by Change in ART status

Figure 3: Plots of Regression Discontinuity Analysis for Art initiations by country

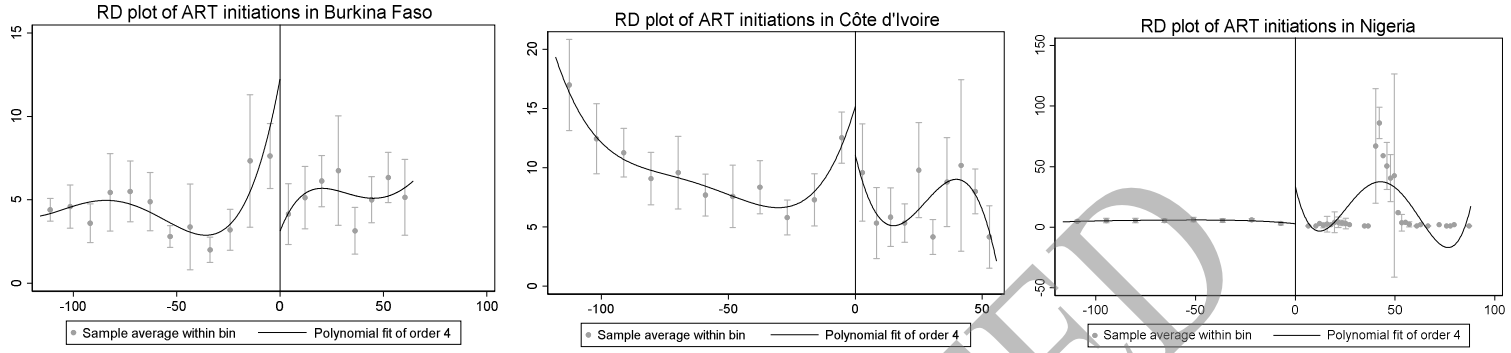

Figure 4: Plots of Regression Discontinuity Analysis for VL monitoring by country