

Determinants of Viral Suppression Among Adolescents on Antiretroviral Therapy in Ehlanzeni District, South Africa: A Retrospective Cohort Analysis

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Research Article

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Abstract

Background

Achieving undetectable viral loads is crucial for the reduction of HIV transmissions, AIDS related illnesses and death. Adolescents living with HIV on antiretroviral therapy (ART) have worse treatment adherence and lower viral suppression rates compared to adults. We report on the clinical factors associated with viral suppression among adolescents 10–19 years living with HIV in the Ehlanzeni district, Mpumalanga in South Africa.

Methods

A retrospective cohort analysis was conducted with 9,543 adolescents living with HIV, aged 10–19 years, who were enrolled in 136 ART clinics in the Ehlanzeni district. Clinical and immunological data were obtained from electronic medical records (Tier.net). Adolescents were categorized as having achieved viral suppression if their latest viral load count was < 1000 ribonucleic acid (RNA) copies/mL. Using a backward stepwise approach, a multivariate logistic regression analysis was performed to identify factors independently associated with viral suppression.

Results

The mean age of the participants was 14.75 years (SD = 2.8), and 55.43% were female. Mean duration on ART was 72.26 (SD = 42.3) months. Of the 9,543 adolescents with viral load results recorded, 74% had achieved viral suppression. After adjusting for other covariates, the likelihood of achieving viral suppression remained significantly higher among adolescents who were: female (AOR = 1.21, 95% CI 1.05–1.38), had CD4 count > 200 (AOR = 2.29, 95% CI 1.89–2.79), and on ART for more than 6 months (AOR = 2.75, 95% CI 1.74–4.34). Furthermore, the likelihood of having viral suppression was lower among adolescents with CD4 count < 200 at baseline (AOR = 0.76, 95% CI 0.64–0.90), and who were switched to second line regimen (AOR = 0.42, 95% CI 0.35–0.49).

Conclusions

Viral suppression amongst adolescents at 74% is considerably lower than the WHO target of 90%. Of particular concern for intervention is the lower rates of viral suppression amongst male adolescents. Greater emphasis should be placed to enrol adolescents on ART earlier before CD4 counts are depleted (< 200) and keeping them engaged in care (beyond 6 months). Furthermore, improved viral load monitoring may prevent unnecessary switching to second line treatment, which are costly and is a risk factor for viral non suppression.

Introduction

In 2018, UNAIDS estimated that 1.6 million young people aged 10–24 years were living with HIV [1, 2]. Therefore, young people living with HIV (YPLHIV) constitute a growing and key sub-population of people living with HIV globally. The increase in HIV prevalence amongst adolescents (10–19 years) is the result of the generation of children infected with HIV perinatally who are surviving into adolescence because of improved access to antiretroviral therapy (ART), and increased HIV incidence as a result of risky (sexual) behaviour in this age group [3, 4]. Despite tremendous gains in the reduction of over-all AIDS-related deaths to the tune of 43%, AIDS-related deaths amongst adolescents in Eastern and Southern Africa have increased in the last decade [5]. This is mainly because adolescents struggle to initiate and remain engaged on antiretroviral treatment (ART) [6].

Monitoring the level of detectable viral load and achieving undetectable viral loads are crucial in the reduction of HIV transmission, earlier detection of treatment failure, and timely switching to second-line ART [7–10]. The aim of ART is to suppress the replication of the HIV thereby protecting people living with HIV from AIDS-related illnesses and death and preventing further transmission to sexual partner [3, 11]. Conversely, adolescents who have poor ART adherence are at greater risk of morbidity, mortality, treatment failure, the development of drug resistant forms of HIV, viral progression, opportunistic infections, and transmission to babies and sexual partners [8, 12–16].

Compared to adult populations living with HIV, adolescents living with HIV have a higher likelihood of suboptimal adherence, viral load progression, lost to follow up, morbidity and mortality [11, 17, 18]. This is because adolescence is accompanied by rapid physical, psychological and physiological changes, which influence health-related behaviour [19]. Therefore, understanding the treatment outcomes for adolescents is crucial as they become aware of their HIV status and have to navigate health care facilities and self-manage their medication adherence and retention in ART care [20]. Regrettably, there is limited information on viral outcomes of adolescents in sub-Saharan Africa where the biggest burden of deaths is experienced [17, 19].

The aim of this study is to investigate the predictors of viral load suppression among HIV-positive adolescents (10–19 years) receiving antiretroviral therapy (ART) in the Ehlanzeni district of South Africa before the introduction of the Right To Care (RTC) adolescent program. Improved reporting of virological outcomes from a wider range of settings is required to support efforts to improve HIV care and treatment for adolescents [19].

Setting

Ehlanzeni District municipality is in Mpumalanga province, located in the Northern Eastern part covering the whole Southern part of the Kruger National Park. The district is surrounded by Mozambique in the East and Swaziland in the South. The district comprises of four sub-districts namely: - Bushbuckridge, City of Mbombela, Nkomazi, and Thaba Chweu.

According to the 2017 South African National HIV prevalence, incidence, behaviour and communication survey, among people living with HIV in South Africa Mpumalanga province has the second highest HIV prevalence with an estimated prevalence rate of 17.3%, and the lowest in viral load suppression (82.9%) [21, 22]. Furthermore, the Ehlanzeni district compared to other districts has high rate of people living with HIV who know their HIV status (1st 90), 90.6%. On the contrary, ART coverage (2nd 90) remains low at 67.2%, and lowest rate of viral load suppression at 65.3% [21].

Methods

Study design and participants

A retrospective cohort analysis of adolescents living with HIV, aged 10–19 years, who were registered to receive ART from 136 clinics in the Ehlanzeni district between September 2002 and October 2019. We extracted individual patient data (sociodemographic variables), clinical data and treatment outcomes (viral loads results after 3 months of ART initiation) from electronic medical records (TIER.net) as part of a larger study assessing the effects of psychosocial support on adherence, treatment outcomes (viral suppression) and retention in care amongst adolescents on ART. Patients who have been on ART for less than 3 months were excluded from the analysis as they are not eligible for viral load test.

The primary outcome, viral suppression, was defined according to the South African National Department of Health as patients achieving a viral load < 1000 RNA copies/mL [23]. The predictor variables such as age, gender, method of entry into ART program at the health facility, pregnant on ART, age at ART initiation, duration on ART, initiated on Isoniazid Preventive Therapy (IPT), TB history, ART regimen, CD4 count at baseline and last ART visit, WHO stage at initiation, and same day ART initiation were employed in a bivariate and multivariate analysis to determine factors influencing viral suppression.

Analysis

Data were extracted from Tier.Net in Excel, and imported to STATA statistical software version 16.0 (STATA Corporation, College Station, Texas, USA) for analyses. Information on clinical stationery was reviewed against information on Tier.net. Patient clinical records identified as incomplete or not correctly captured on Tier.net was retrieved and subsequently updated on Tier.net.

Descriptive statistics were used to characterize the demographic and clinical variables (at baseline and/or specific time points after ART initiation). Comparisons between viral suppression and clinical parameters among adolescent living with HIV were achieved using chi-square tests for proportions (replaced by Fisher's exact test for sparse data), and bivariate logistics regression analysis to examine associations.

Furthermore, a multivariate logistic regression model was used to estimate factors associated with viral suppression adjusting for potential confounders using the following variables: age, gender, age at ART initiation, duration on ART, CD4 cell count at baseline and last visit, WHO stage at initiation, and initiated

on ART same day. The multivariate logistic regression model employed a backward stepwise analysis. In the backward selection model, we included all candidate variables in the model. At each step, the variable that is the least significant is removed. This process continued until no non-significant variables remained. The significance level was set at 95% at which variables can be removed from the model. Analyses were conducted among all patients with viral load test done after 3 months of ART initiation.

Ethical approval

Ethics clearance was obtained from the University of the Western Cape Biomedical Research Ethics committee (BM19/1/8) and informed consent to use the electronic medical dataset (Tier.net) was obtained from the National Health Research Ethics committee. We adhered to the 1964 declaration of Helsinki guidelines. According to the declaration, research that involves human subjects amongst others must keep with the following (1) strive to protect life, health, privacy, and the dignity of the research participants, (2) employ greater care to protect the participants from harm and (3) conduct the research because the importance of the research purpose, outweighs the risk that might be attributed to the study either at present or in the future (18th WMA General Assembly, Helsinki, 2001).

Data extraction excluded adolescent's unique identifiers such as name, surname, patient folder number and identity number.

Results

Table 1 shows the demographic characteristics of adolescents living with HIV enrolled in the ART program in 136 facilities in Ehlanzeni district South Africa. This study included 9,543 adolescents (aged 10 to 19 years) with mean age 14.75 years (SD=2.9); of whom 55.43% were female. In terms of gender comparison, females are more likely to have viral load below 1000 RNA copies/mL ($p=0.000$). Most (67.88%) of the adolescents attended the ART program in the clinic they were initiated as new patients as opposed to transferred in from another clinic. Amongst the female adolescents, 9.60% were reported pregnant at the time of enrolling into ART.

Demographic and clinical history

Table 1 shows the clinical history of adolescents enrolled in the ART programme in Ehlanzeni district South Africa. The mean age at which the adolescents started ART was 8.7 years (SD=4.8); and 84.03% were on ART for more than 24 months. Adolescents on ART for three to six months were less likely to attain viral suppression compared to adolescents on ART for more than six months ($p=0.000$).

Only 23.33% ($n=2,226$) were started on Isoniazid preventative therapy (IPT) after ART initiation. *Only 2.6% completed* TB preventive therapy. A very small proportion (0.1%) developed TB after initiation on TB preventive therapy. Adolescents who were started on IPT after ART initiation were more likely to attain viral suppression compared to those who did not ($p=0.038$).

Regarding history of TB, 0.88 % had TB and HIV comorbidly. Adolescents with a history of TB were less likely to have viral load <1000 RNA copies/mL ($p=0.002$).

Compared to adolescents with CD4 count >200 at last visit and at baseline, adolescents with CD4 count <200 at baseline and last visit were less likely to have viral load <1000 RNA copies/mL ($p=0.000$).

Slightly more than half (53.40%) of the adolescents were initiated on ART at WHO stage 1. Compared to adolescents with WHO stage 1, 2, and 3 at ART initiation, adolescents with WHO stage 4 were less likely to have viral load <1000 RNA copies/mL ($p=0.003$).

Most (64.65%) of the adolescents were initiated on ART on the same day of HIV diagnosis. However, there was no association between adolescent's time of ART initiation with viral load suppression ($p=0.726$).

Factors associated with suppression of viral load among adolescent living with HIV (N=9,543)

Table 2 shows the factors associated with viral suppression in a multivariate logistic regression model. After controlling for the effect of other covariates, the likelihood of attaining viral suppression remained significantly higher among female adolescents (AOR = 1.21, 95% CI 1.05–1.38), adolescents who had been on ART for seven months and more (AOR = 1.74, 95% CI 1.4–4.3), had most recent and baseline CD4 count of > 200 (AOR = 2.29, 95% CI 1.89-2.79) and (AOR = 0.76, 95% CI 0.64-0.90) respectively. Adolescents on second line treatment were less likely to attain viral suppression compared to their reference group (AOR = 0.42, 95% CI 0.35-0.49).

Discussion

In this study, we set out to investigate the predictors of viral load suppression among HIV-positive adolescents (10–19 years) receiving antiretroviral therapy (ART) in the Ehlanzeni district of South Africa before the introduction of the RTC adolescent program. The proportion of adolescents living with HIV with viral suppression was relatively high at 73.96%, but falls short of the global target of 90%. Furthermore, our study revealed that being female, on ART for more than 6 months, having CD4 count level >200 at baseline and last ART visit were protective factors against viral non suppression. On the other hand, being on second line treatment was an enhancing factor for viral non-suppression.

Evidence on the relationship between gender and viral load suppression is mixed. While one study showed that males were more likely to achieve viral load suppression compared to females [20], another study found that males are more likely to achieve viral non suppression [24]. However, we found that females were more likely to attain viral suppression compared to males. Adherence among males living with HIV is poor compared to females; males have poor treatment seeking behaviours [25], and as such to get males to test for HIV, link and retain them to ART care is quite a challenge [26]. The poor treatment outcome reported among males have been attributed to strong gender norms and practices specifically the perception of masculinity inherent within societies. In addition, lack of male friendly services inhibits males from seeking health care services [26–28].

The literature indicates that older age group or adults can achieve viral suppression because they possess self-efficacy and self-competency on ART adherence [9]. Interestingly, our study did not show any

significant difference between viral suppression among adolescents in the age group 10-14 years and 15-19 years. This is likely because if no support is provided, adolescents (10-19 years) are faced with psychosocial challenges, lack self-efficacy and self-esteem, and are unable to self-manage themselves with regard to medication adherence [29]. However, a retrospective study conducted among adolescents registered in the Cape Metropole ART clinic in South Africa found younger adolescents (10-14 years) were more likely to achieve viral suppression compared to older adolescents (15-19 years). It was reported that the older adolescents face adherence challenges as a result of transitioning from adolescence to adulthood in which they are expected to self manage themselves with regard to medication adherence [20].

We also found that shorter duration on ART was a risk factor for viral non-suppression. This is consistent with evidence that patients on ART for shorter period are more likely to experience virological failure [9]. The contrary is to be expected given that patients who have been on treatment longer have more experience in managing their treatment [9]. Similar findings were reported in a study, which reported that adolescents who had been on ART between 6 and 12 months were more likely to have viral non-suppression (viral load > 400 RNA copies/mL) compared with those who had been on treatment for longer [9].

Immunological treatment failure refers to a CD4 cell count of <100 cells/ μ L after 6 months of therapy [9]. According to the WHO guidelines, a decreasing CD4 cell count is considered a proxy marker for treatment failure when viral load monitoring is not available, and should trigger a switch in ART, particularly if the CD4 cell count is <200 cells/ μ L [9]. Although the relationship between viral non-suppression and immunological responses, is not always consistent [9], our study found that adolescents with CD4 cell count >200 cells/ μ L at baseline and at last ART visit were more likely to achieve virological suppression. However, the ability of CD4 counts to predict virologic failure is poor [11]. The use of CD4 count may, therefore, lead to unnecessary switching to second-line ART among patients with suppressed viral replication, or cause undue delays in switching among patients with real – but undetected – virological failure.

Studies have shown that delayed detection of treatment failure may increase drug toxicity, which in turn lead to the accumulation of drug resistance-associated mutations, hence may result in increased morbidity and mortality [30]. On the contrary, switching to second-line ART on a timely manner after virological failure along with adherence counselling is a protective factor against viral progression and mortality [10]. Our findings showed that adolescents on second line treatment were less likely to attain viral suppression. This is because second line regimens are more complex than first line regimens, are often twice daily regimens and have more adverse side effect than first line regimens. Furthermore, the misclassification of treatment failure could lead to the premature switch to and use of valuable second-line regimens, which are costly and may represent the last available regimen [30]. Our findings is consistent with another study that found among ART adherent patients, having a history of treatment failure is a risk factor for viral suppression [17].

Findings implications

Several implications arise from our findings. First, psychosocial support interventions designed to improve adherence should target adolescent (10-19 years) living with HIV. Adopting a combination of multiple approaches including psychosocial support intervention may be necessary to improve adherence. For instance, providing social support and focusing on psychosocial needs of adolescents to bolster their self-esteem and self-efficacy will in turn improve their self-management regarding medication adherence and subsequently improve their treatment outcomes.

Timely and accurate identification of virological failure is crucial to avoid misclassification of non-suppression leading to switching to a second line or third line which are costly and can lead to viral non suppression. It is recommended that second line regimens especially for adolescents are simplified and changed to once daily, and less toxic regimens.

Study limitations

This study has a number of limitations, which should be taken into account when interpreting the findings. Firstly, adolescents who are eligible for viral load assessment but failed to have it done because they were lost to follow-up, died or transferred out, were not included, which could have resulted in overestimating the rate of viral load suppression. Secondly, as is the case for all retrospective cohort studies, it is subject to other risk or confounding factors that may be present but were not measured. For example, household income status, head of household, type of social support and psychosocial well being.

Conclusion

Viral suppression amongst adolescents at 74% is considerably lower than the WHO target of 90%. Of particular concern for intervention is the lower rates of viral suppression amongst male adolescents. Greater emphasis should be placed to enrol adolescents on ART earlier before CD4 counts are depleted (<200) and keeping them engaged in care (beyond 6 months). Furthermore, improved viral load monitoring will help prevent unnecessary switching to second line treatment which are costly and is a risk factor for viral non suppression.

Appraisal of the study quality

Not applicable

Reporting

Not applicable

List Of Abbreviations

ART - Antiretroviral therapy

AOR - Adjusted Odds Ratio

HIV - Human Immunodeficiency-Virus

WHO - World Health Organization

TB - Tuberculosis

YPLHIV - Young People Living with HIV

Declarations

Ethics approval and consent to participate

Ethics clearance was obtained from the University of the Western Cape Biomedical Research Ethics committee and informed consent to use the electronic medical dataset (Tier.net) was obtained from the National Health Research Ethics committee. We adhered to the 1964 declaration of Helsinki guidelines. According to the declaration, research that involves human subjects amongst others must keep with the following (1) strive to protect life, health, privacy, and the dignity of the research participants, (2) employ greater care to protect the participants from harm and (3) conduct the research because the importance of the research purpose, outweighs the risk that might be attributed to the study either at present or in the future (18th WMA General Assembly, Helsinki, 2001).

Ethics approval number. BM19/1/8

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due it belonging to the South African National Department of Health, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests

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Authors' contributions

EFO and BVW designed the study. EFO analysed the data and developed the manuscript with editorial and content input from BVW, FCM, and GH. All authors read and approved the final manuscript

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Authors' information

The main author EO is currently working as senior monitoring and evaluation manager for Right to Care an NGO that provides treatment care and support for people living with HIV and AIDS in South Africa. This paper is part of his PhD programme that aim to make a case for a psychosocial support intervention specifically designed to improve adherence and retention amongst adolescents living with HIV and AIDS.

Footnotes

Not applicable.

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Tables

Table 1

Viral load suppression by demographic and clinical characteristics of adolescents 10–19 years living with HIV in Ehlanzeni district, South Africa (N = 9,543).

| | TOTAL | Viral load suppression | | p-value |
|--|------------------|--------------------------|--------------------------|--------------|
| | | Yes n (%) | No n (%) | |
| | 9,543 | 7,058 (73.96) | 2,485 (26.04) | |
| Current Age (in years) | | | | 0.000 |
| 10–14 | 4,537 (47.54) | 3,455 (76.15) | 1,082 (23.85) | |
| 15–19 | 5,006 (52.46) | 3,603 (71.97) | 1,403 (28.03) | |
| Gender | | | | 0.000 |
| Female | 5,290 (55.43) | 4,020 (75.99) | 1,270 (24.01) | |
| Male | 4,253 (44.57) | 3,038 (71.43) | 1,215 (28.57) | |
| Pregnant at ART start (N = 5,290) | | | | 0.157 |
| No | 4,782 (90.40) | 3,621 (75.72) | 1,161 (24.28) | |
| Yes | 508 (9.60) | 399 (78.54) | 109 (21.46) | |
| Age at ART start (in years) | | | | 0.000 |
| 0 to 9 | 5,512 (57.76) | 4,116 (74.67) | 1,396 (25.33) | |
| 10 to 14 | 2,583 (27.07) | 1,801 (69.73) | 782 (30.27) | |
| 15 to 19 | 1,448 (15.17) | 1,141 (78.80) | 307 (21.20) | |
| Duration on ART (in months) | | | | 0.000 |
| 3–6 months | 233 (2.44) | 146 (62.66) | 87 (37.34) | |
| 7 to 12 months | 446 (4.67) | 349 (78.25) | 97 (21.75) | |
| 13 to 18 months | 468 (4.90) | 349 (74.57) | 119 (25.43) | |
| 19 to 24 months | 377 (3.95) | 301 (79.84) | 76 (20.16) | |

| | TOTAL | Viral load suppression | | |
|--|-------------------|-------------------------------|-------------------|-------|
| 25 months and above | 8,019 (84.03) | 5,913 (73.74) | 2,106 (26.26) | |
| Initiated on Isoniazid Preventative Therapy (IPT) | | | | 0.038 |
| Yes | 2,226 (23.33) | 1,684 (75.65) | 542 (24.35) | |
| No | 7,317 (76.67) | 5,374 (73.45) | 1,943 (26.55) | |
| History of TB | | | | 0.002 |
| Yes | 81 (0.88%) | 48 (59.26%) | 33 (40.74%) | |
| No | 9,087 (99.12%) | 6,742 (74.19%) | 2,345 (25.81%) | |
| CD4 count at last ART visit | | | | |
| < 200 | 1,400 (16.20%) | 861 (61.50%) | 539 (38.50%) | 0.000 |
| > 200 | 7,241 (83.80%) | 5,501 (75.97%) | 1,740 (24.03%) | |
| CD4 count at baseline | | | | 0.010 |
| CD4 < 200 | 1,731 (28.34%) | 1,238 (71.52%) | 493 (28.48%) | |
| CD4 > 200 | 4,377 (71.66%) | 3,271 (74.35%) | 1,106 (25.27%) | |
| WHO Stage at initiation | | | | 0.001 |
| 1 | 4,202 (53.40%) | 3,180 (75.68%) | 1,022 (24.32%) | |
| 2 | 1,887 (23.98%) | 1,368 (72.50%) | 519 (27.50%) | |
| 3 | 1,530 (19.44%) | 1,090 (71.24%) | 440 (28.76%) | |
| 4 | 250 (3.18%) | 177 (70.80%) | 73 (29.20%) | |
| Initiated same day | | | | 0.726 |
| Yes | 940 (64.65%) | 701 (74.57%) | 239 (25.43%) | |

| | TOTAL | Viral load suppression | |
|----|-----------------|-------------------------------|-------------|
| No | 514 (35.35%) | 379 (73.74%) | 135 (26.26) |

Table 2

Multivariate logistic regression analysis of factors associated with viral non suppression among adolescents living with HIV in Ehlanzeni district South Africa (N = 9,543)

| | Crude OR | 95% CI | Adjusted OR | 95% CI |
|----------------------------|----------|-----------|-------------|-----------|
| Age | 1* | 0.73–0.88 | 1 | |
| 10–14 | | | | |
| 15–19 | 0.80 | | 0.90 | 0.77–1.06 |
| Gender | | | | |
| Male | 1* | 1.15–1.39 | 1* | |
| Female | 1.27 | | 1.21 | 1.05–1.38 |
| Method into ART | | | | |
| Transferred in | 1 | | | |
| New | 0.91 | 0.83–1.01 | | |
| Started IPT | | | | |
| No | 1* | | 1 | |
| Yes | 1.12 | 1.01–1.25 | 1.03 | 0.88–1.20 |
| History of TB | | | | |
| No | 1* | | 1 | |
| Yes | 0.51 | 0.32–0.79 | 0.67 | 0.35–1.25 |
| WHO stage | | | | |
| Stage 1 | 1* | | 1 | |
| Stage 2 | 0.85 | 0.75–0.95 | 0.91 | 0.77–1.07 |
| Stage 3 | 0.79 | 0.69–0.91 | 0.87 | 0.73–1.04 |
| Stage 4 | 0.78 | 0.59–1.03 | 0.91 | 0.62–1.32 |
| ART initiation on same day | | | | |
| No | 1 | | | |
| Yes | 1.05 | 0.82–1.34 | | |
| Duration on ART | | | | |

*p-value statistically significant at 5%

| | Crude OR | 95% CI | Adjusted OR | 95% CI |
|---|----------|-----------|-------------|-----------|
| 0–6 months | 1* | | 1* | |
| 7–12 months | 2.14 | 1.51–3.04 | 2.75 | 1.74–4.34 |
| 13–18 months | 1.75 | 1.24–2.45 | 1.64 | 1.06–2.55 |
| 19–24 months | 2.36 | 1.63–3.40 | 2.61 | 1.59–4.29 |
| 25 months+ | 1.67 | 1.28–2.19 | 2.33 | 1.58–3.46 |
| Age at art start | | | | |
| 0–9 years | 1* | | 1 | |
| 10 to 14 years | 0.78 | 0.70–0.87 | 0.85 | 0.72–1.01 |
| 15 to 19 years | 1.26 | 1.09–1.45 | 1.30 | 0.98–1.74 |
| Pregnant during ART start | | | | |
| No | 1 | | | |
| Yes | 1.18 | 0.94–1.47 | | |
| CD4 count at last visit | | | | |
| CD4 < 200 | 1* | | 1* | |
| CD4 > 200 | 1.97 | 1.75–2.23 | 2.29 | 1.89–2.79 |
| CD4 count at baseline | | | | |
| CD4 < 200 | 1* | | 1* | |
| CD4 > 200 | 1.18 | 1.04–1.33 | 0.76 | 0.64–0.90 |
| Second line | | | | |
| No | 1* | | 1* | |
| Yes | 0.39 | 0.35–0.44 | 0.42 | 0.35–0.49 |
| <i>*p-value statistically significant at 5%</i> | | | | |

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AdditionalTable3.docx](#)