Viral suppression among pregnant adolescents and women living with HIV in rural KwaZulu-Natal, South Africa: a cross sectional study to assess progress towards UNAIDS indicators and Implications for HIV Epidemic Control

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Abstract
Background: South Africa has made significant progress in scaling up antiretroviral therapy (ART) to achieve the aspirational goal of HIV epidemic control. The aim of this study was to determine the prevalence of HIV, assess progress towards each of the Joint United Nations Programme on HIV/AIDS (UNAIDS) indicators and determine factors associated with achieving viral suppression among pregnant adolescents and women living with HIV in rural KwaZulu-Natal, South Africa.

Methods: Pregnant adolescents and women, 12 years and older seeking antenatal care at six primary health care clinics were enrolled in a cross-sectional study. Following written informed consent, structured questionnaires were administered, and finger-prick blood samples were collected for HIV antibody testing and viral load measurement. Viral suppression was defined as HIV viral load of < 400 copies per mL.

Results: Between Dec 2016 and March 2017, among the 546 enrolled participants, data for 545 were analysed. The overall HIV prevalence was 40.2% [95% Confidence Interval (CI) 36.1–44.3]. Age-stratified prevalence increased from 22.1% (95% CI, 15.9–30.0) in the 14–19 year age group to 63.9% (95% CI, 55.1–71.9) among women ≥ 30 years (Χ² trend P < 0.0001). Of the HIV positive participants, 84.5% (95% CI, 79.0–88.8) knew their HIV positive status, 98.3% (95% CI 95.1–99.4) who knew their status were on ART, and of those on ART, 95.9% (95% CI 91.8–98.0) were virally suppressed. Among all HIV-positives 90.8% (95% CI, 86.3–94.0) had achieved viral suppression, whilst those in the 14–19 year age group were least likely to be virally suppressed at 82.8% (95% CI 65.5–92.4) compared to those in the
Background

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set ambitious HIV testing and treatment targets to “Fast-Track” the response to help end the AIDS epidemic [1]. These targets specified that 90% of all people living with HIV (PLHIV) should know their status; 90% of all people diagnosed with HIV should receive sustained antiretroviral therapy (ART) and 90% of all people receiving ART should achieve HIV viral suppression with a goal of reducing AIDS-related morbidity and mortality and the number new HIV infections [2]. Country-level commitment and resources to meet these indicators had been prioritized as the strategy was expected to provide both therapeutic and preventive benefits [1], with the potential to prevent onward transmission of HIV [3] and at a population level to reduce annual HIV incidence to less than 1% [1, 4]. Despite the efforts to meet these targets, the unequal distribution of ART, AIDS related mortality and the slow reduction in HIV incidence, many high HIV burden countries missed achieving these targets [5, 6]. The Global AIDS Strategy of 2021–2026 is yet another bold approach that has prioritized sexual reproductive health and rights for adolescents and women living with HIV, urging countries to overcome barriers preventing progress and raised the targets to 95–95–95 to be met by 2025 towards the control of HIV epidemic by the year 2030 [7].

In South Africa, the substantial scale-up of ART has resulted in reduced numbers of HIV-related deaths [8], nevertheless nationally, HIV prevalence and incidence remains persistently high [9] and prevalence among pregnant women was reported to be 30.7% [10] with the province of KwaZulu-Natal the worst affected with a HIV prevalence of 41.1% compared to the Western Cape with a prevalence of 15.9% [10]. In a region where heterosexual sex is the major route of HIV transmission, women of reproductive age are severely affected though far short of the target towards achieving epidemic control. Importantly, pregnant adolescents were less likely to know their HIV status and to achieve viral suppression, underscoring the public health implications of sustained risk of HIV transmission. Thus, greater effort and strong social support are essential to improve HIV knowledge of status and care continuum towards the goal to achieving HIV epidemic control.

Conclusions: The proportion of HIV positive pregnant women achieving viral suppression was encouraging though far short of the target towards achieving epidemic control. Importantly, adolescent pregnant women were less likely to know their HIV status and to achieve viral suppression, underscoring the public health implications of sustained risk of HIV transmission. Thus, greater effort and strong social support are essential to improve HIV knowledge of status and care continuum towards the goal to achieving HIV epidemic control.

Plain language summary: To “fast-track” the response to achieve HIV epidemic control and end the AIDS epidemic, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set ambitious HIV testing and treatment targets for people living with HIV. Meeting these targets through scaling up testing for HIV, initiating and sustaining antiretroviral therapy (ART) to maintain viral suppression provides both therapeutic and preventive benefits with the potential to reduce HIV transmission. Viral suppression among pregnant adolescents and women living with HIV is crucial for the prevention of mother-to-child transmission of HIV including onward transmission to sexual partners. As a public health approach, in South Africa all pregnant women are offered routine HIV testing and immediate initiation of lifelong ART irrespective of CD4 cell count. It is, therefore, important to ascertain progress towards reaching the targets. The proportion of HIV positive pregnant adolescents and women achieving viral suppression was encouraging though far short of the target towards achieving epidemic control. Importantly, pregnant adolescents were less likely to know their HIV status and to achieve viral suppression, underscoring the public health implications of sustained risk of HIV transmission. Thus, greater effort and strong social support are essential to improve HIV knowledge of status and care continuum towards the goal to achieving HIV epidemic control.

Keywords: Pregnant adolescents and women, HIV, HIV testing, ART, Viral suppression
viral suppression among pregnant women living with HIV in rural KwaZulu-Natal, South Africa.

**Methods**

**Study design, setting and population**

This cross-sectional study was undertaken across six public sector primary health care (PHC) clinics in the rural uMgungundlovu district in KwaZulu-Natal, between December 2016 to March 2017. Whilst this community has access to basic utility services such as water, sanitation, and electricity, the area is poor and is characterized by high rates of poverty, unemployment, and HIV [3]. The PHC clinics deliver basic health care services at no cost including HIV testing services with pre- and post-test counseling with linkage to care and ART initiation.

To strengthen HIV testing services, policies and procedures were implemented to align with international guidelines and recommendations such that the services were responsive to community needs and supportive of the South Africa National Strategic Plan for HIV, STIs and TB (NSP) [20, 21] and geared to the broader goal of the National Development Plan, Vision 2030 [22] and to the UNAIDS 90–90–90 indicators [23]. HIV testing services evolved to include HIV self-testing [24] and index testing [25] to strengthen routine offering of safe and ethical services for adolescents [14, 15] including for all family members and clients of people living with HIV (PLHIV); thus the policies aimed to enable “fast-tracking” towards achieving the goals aligned to the indicators [26]. The sample for this study was drawn from 1700 first visit attendees, the numbers who attend clinics on average per year, resulting in a coverage of almost 30% of seropositive samples, given the high HIV prevalence observed among pregnant women [27, 28].

**Study procedures**

Study information was provided to PHC clinic staff, who supported the study and guided study staff to designated clinic areas to facilitate access to and recruitment of study participants. Pregnant adolescents and women, 12 years and older attending PHC clinics for the current pregnancy were invited for study participation. Age-eligible participants were provided with study information. For those willing to participate, we obtained written informed consent in English or isiZulu for those 18 years and older. For those younger than 18 years we obtained assent and facilitated parental consent through the provision of study information and information on the South African legal framework that enables young children to access sexual reproductive health services autonomously from age 12. Furthermore, the community in the district acknowledges the high HIV burden and the CAPRISA Research Support Group facilitates research engagement for young people [27, 29]. Following consenting procedures, fingerprints were obtained with a mobile biometric scanner for identifying and preventing re-enrollment of study participants. Enrolled participants were assigned a unique study number and a corresponding barcode that linked the questionnaire data, finger prick blood samples, laboratory results and biometric fingerprints.

The standardized questionnaires were designed to obtain sociodemographic, behavioral, and clinical information including self-reported knowledge of HIV status, recency of HIV testing, linkage to PMTCT and uptake of ART. Questionnaires were pre-programed onto handheld personal digital assistant (PDA) tablets (MoberniR Researcher, Durban, South Africa) and administered by study staff. The appropriate selection options (i.e., single response, multiple response, open ended questions, drop down lists, etc.) were included to ensure that data were captured as accurately as possible. Skip patterns were incorporated to ensure that only required questions were completed whilst questions that were compulsory compelled interviewer to complete before proceeding. To maintain confidentiality, participants personal information was not included on the questionnaire. To safeguard the study data, the data were delivered through a wireless cellular connection and once transmitted the data were deleted from the PDA. Study staff were allocated user rights through secure passwords to enable administering of questionnaires.

All participants provided finger-prick blood samples into BD Microtainer® (Becton Dickinson, South Africa) blood collection tubes for laboratory measurements. HIV antibody testing was performed in a central laboratory using the fourth generation HIV enzyme BioMerieux Vironostika Uniform II Antigen/Antibody Microelisa system (BioMérieux, Marcy l’Etoile, France). Reactive samples were confirmed as positive with the HIV 1/2 Combi Roche Elecys (Roche Diagnostics, Penzberg, Germany). Any indeterminate results were resolved with ADVIA Centaur HIV Antigen/Antibody Combo (CHIV) Assay (Siemens, Tarry Town, NY, USA). HIV viral load was measured using the Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 v2.0 assay (CAP/CTM HIV-1 V2.0, Roche Diagnostics, Penzberg, Germany) with a dynamic range of 20–10 million copies per mL. Participants received their HIV antibody test and viral load results through clinic staff. HSV-2 antibodies were determined by the detection of human IgG class antibodies using the HerpeSelect1 HSV-2 enzyme-linked immunosorbent assay (Focus Diagnostics, Cypress, CA, USA) test [30].
Statistical analysis
Statistical analyses were performed using SAS (SAS Institute, Cary, North Carolina) version 9.4.

Data were summarized using descriptive summary measures, expressed as proportions for categorical variables and central measures of tendency for medians with interquartile range (IQR) for continuous variables. To determine the progress towards each of the 90–90–90 indicators, the study sample was age-stratified into 14–19, 20–24, 25–29 and ≥ 30 years age groups. The Wilson score test assessed the age-specific HIV prevalence, the 90–90–90 targets by study characteristics and the corresponding 95% Confidence Interval (CI). The Cochran–Armitage Chi-square ($X^2$) test was used to assess for linear trends in HIV prevalence. Based on self-reported data, one sample test of proportion using Wilson score test assessed the proportions and 95% CI for participants who achieved the “first 90”, “second 90” and the “third 90”. HIV viral suppression was defined as viral load < 400 copies per mL, as the potential risk for HIV viral transmission had been shown to be absent at HIV viral load < 400 copies per mL [31, 32]. All variables were tested for multicollinearity using Spearman’s rank correlation and variables that correlated were excluded from the model. Independent variables included in each of the multivariable models were age, education level, marital status, and the number of lifetime sexual partners. In evaluating each association, we fitted multivariable modified Poisson regression models to calculate prevalence risk ratio (PRR) and 95% CI. Statistical significance was assessed at 5% level for all analyses. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [33].

Results
Description of study population
A total of 610 pregnant clinic attendees were approached and invited to participate in the study. Of these, 64 (10.5%) were excluded. The reasons for exclusion were refusal (n=27, 42.2%), not returning for enrolment after routine clinic procedures (n=26, 40.6%), illness (n=2, 3.1%), being late for work (n=5, 7.8%), being mentally incapable of undergoing consent (n=1, 1.6%), not completing study procedures (n=1, 1.6%), lack of parental consent (n=1, 1.6%), and reason unknown (n=1, 1.6%). Five hundred and forty-six women provided written informed consent and / or assent and were enrolled. Of these, 545 had finger prick blood samples collected and were included in HIV prevalence measurement, whilst 539 had complete questionnaire data and included in the behavioural measurements (Additional file 1: Fig. S1).

Table 1 shows the baseline characteristics of study participants (denominators may vary due to missing data and has been indicated accordingly). The median age was 24 years (IQR: 20–28). Just over half, 53.6% (n=289/539) had completed high school, whilst 46.0% (n=245/532) reported a total household income of ≤ 5000 South African Rand (ZAR) per month (ZAR15 ~ US$1) and 9.6% (n=52/532) reported being married. About three quarters, 69.0% (n=372/539) reported that their biological mother was alive, whilst less than half, 44.5% (n=240/539) reported that their biological father was alive. Sexual debut had occurred at ≤ 16 years of age in 11.6% (n=63/545), at 17–18 years in 19.6% (n=107/545) and at > 18 years in 61.5% (n=335/545) and 64.2% (n=346/539) reported having two or more lifetime sex partners. Just under half, 48.2% (n=260/537) reported the current pregnancy to be the first; 37.2% (n=194/522) reported that their partner was circumcised; 29.5% (n=159/539) reported ever having symptoms of sexually transmitted infections (STI) and 61.8% (n=337/545) were positive for HSV-2 antibodies.

Prevalence of HIV
Table 2 shows the overall HIV prevalence of 40.2% [95% CI, 36.1–44.3], (n=219/545). HIV prevalence increased by age and was 22.1% (95% CI, 15.9–30.0), (n=29/131) in the 14–19 years age group, 29.9% (95% CI, 23.7–36.9), (n=55/184) in the 20–24 years age group, 52.8% (95% CI, 43.4–61.9), (n=57/108) in the 25–29 years age group and 63.9% (95% CI, 55.1–71.9), (n=78/122) in the ≥ 30 year age group ($X^2$ trend $P<0.001$). Whilst HIV prevalence was similar across most variables, prevalence was higher among women with two or more lifetime sex partners (50.6%, n=175/346)) and in those who refused to answer or responded with “don’t know” (67.7%, n=21/31) compared to having one partner (13.0%, n=21/162); women who had an HIV test done > 12 months ago (88.5%, n=69/78) compared to ≤ 12 months (31.6%, n=144/456); women with two or more pregnancies (51.6%, n=143/277) compared to current pregnancy only (28.2%, n=73/260); women whose partner was not circumcised (51.2%, n=128/250) and don’t know of partners circumcision status (47.4%, n=37/78) compared to knowing that partner was circumcised (21.6%, n=42/194) and women who were HSV-2 antibody positive (57.3%, n=193/337) compared to those testing negative (12.5%, n=26/208), (all $P<0.001$).

Progress towards UNAIDS HIV treatment indicators and overall viral suppression
Table 3 provides the progress towards the UNAIDS indicators. Of the 219 women who tested positive for HIV, questionnaire data were available for 213. Overall, for the
“first 90”, 84.5% (95% CI, 79.0–88.8) (n = 180/213) were aware of their HIV positive status and for the “second 90”, 98.3% (95% CI, 95.1–99.4) (n = 173/176) had initiated ART and for the “third 90”, 95.9% (95% CI, 91.8–98.0) (n = 165/172) had achieved viral suppression. Among women in the ≥ 30 year age group, all three indicators had been achieved. However, among adolescents 14–19 years, the “first 90” was achieved in 69.2% (95% CI, 50.0–83.5), and increased among women 20–24 years (75.9% (95% CI, 63.1–85.4) and those 25–29 years (87.5% (95% CI, 76.4–93.8). The “second 90” of ART initiation among adolescents 14–19 years was 88.9% (95% CI 67.2–96.9) and was 100% among the 20–24 and 25–29 age groups. For the “third 90”, viral suppressions among those who had initiated ART exceeded 90% (Table 3). Among all HIV positive women (n = 219), viral suppression was achieved in 90.8% (95% CI 86.3–94.0) (198/218), (data excludes one participant with no viral load measurement). The overall viral suppression was lowest among adolescents aged 14–19 years (n = 24/29) at 82.8% (95% CI 65.5–92.4) and in women aged 20–24 years (n = 49/55) at 89.1% (95% CI 78.2–94.9). However, viral suppression increased to 94.7% (95% CI 85.6–98.2) among women aged 25–29 years (n = 54/57) and to 92.2% (95% CI 84.0–96.4) among women ≥ 30 years (n = 71/77) (Table 3).
### Table 2  HIV prevalence by baseline characteristics of pregnant adolescents and women in a rural KwaZulu-Natal, South Africa

| Characteristics                        | HIV prevalence* | n/N     | % (95% CI) |
|----------------------------------------|-----------------|---------|------------|
| Overall                                | 219/545         | 40.2    | (36.1–44.3) |
| Socio-demographic characteristics      |                 |         |            |
| Age group in years                     |                 |         |            |
| 14–19                                  | 29/131          | 22.1    | (15.9–30.0) |
| 20–24                                  | 55/184          | 29.9    | (23.7–36.9) |
| 25–29                                  | 57/108          | 52.8    | (43.4–61.9) |
| ≥ 30                                   | 78/122          | 63.9    | (55.1–71.9) |
| Education levels                       |                 |         |            |
| Completed high school                  | 110/289         | 38.1    | (32.7–43.8) |
| Incomplete high school                | 107/250         | 42.8    | (36.8–49.0) |
| Household income per month             |                 |         |            |
| ≤ ZAR 5000                             | 96/245          | 39.2    | (33.3–45.4) |
| > ZAR 5000                             | 48/110          | 43.6    | (34.7–53.0) |
| Don’t know                             | 71/178          | 39.9    | (33.0–47.2) |
| Marital status                         |                 |         |            |
| Married                                | 26/52           | 50.0    | (36.9–63.1) |
| Unmarried                              | 191/487         | 39.2    | (35.0–43.6) |
| Family characteristics                 |                 |         |            |
| Biological mother alive                |                 |         |            |
| Yes                                    | 133/372         | 35.8    | (31.1–40.7) |
| No                                     | 82/163          | 50.3    | (42.7–57.9) |
| Don’t know                             | 2/4             | 50.0    | (15.0–85.0) |
| Biological father alive                |                 |         |            |
| Yes                                    | 81/240          | 33.8    | (28.1–39.9) |
| No                                     | 133/290         | 45.9    | (40.2–51.6) |
| Don’t know                             | 3/9             | 33.3    | (12.1–64.6) |
| Behavioral characteristics             |                 |         |            |
| Age at first sex                       |                 |         |            |
| At ≤ 16 years                          | 12/63           | 19.0    | (11.2–30.4) |
| At 17–18 years                         | 30/107          | 28.0    | (20.4–37.2) |
| At > 18 years                          | 168/335         | 50.1    | (44.8–55.5) |
| Refused                                | 9/40            | 22.5    | (12.3–37.5) |
| Total number of lifetime sex partners  |                 |         |            |
| 1 partner                              | 21/162          | 13.0    | (8.6–19.0)  |
| 2 or more partners                     | 175/346         | 50.6    | (45.3–55.8) |
| Don’t know/Refused                     | 21/31           | 67.7    | (50.1–81.4) |
| Total number of current sex partners   |                 |         |            |
| 1 partner                              | 207/520         | 39.8    | (35.7–44.2) |
| 2 or more partners                     | 1/4             | 25.0    | (45.6–70.0) |
| Refused                                | 9/15            | 60.0    | (35.8–80.2) |
| Alcohol use                            |                 |         |            |
| No                                     | 136/339         | 40.1    | (35.0–45.4) |
| Yes                                    | 81/200          | 40.5    | (33.9–47.4) |
| Drug use (n,%)                         |                 |         |            |
| No                                     | 187/463         | 40.4    | (36.0–44.9) |
| Yes                                    | 23/59           | 39.0    | (27.6–51.7) |
| HIV Testing history                    |                 |         |            |
| Last HIV test done                     |                 |         |            |
Factors associated with achieving UNAIDS indicators and overall HIV viral suppression

Table 4 shows the PRR for factors associated with achieving UNAIDS indicators and overall HIV viral suppression. Women 25 years and older compared to women 14–24 years of age [PRR = 1.22 (95% CI, 1.05–1.42)]; married women compared to unmarried women [PRR = 1.15 (95% CI, 1.06–1.25)] and women with incomplete high school education compared to women who had completed high school education [PRR = 1.16 (95% CI, 1.04–1.30)] were all more likely to achieve the “first 90” indicator. We found no discernable factors associated with achieving the “second 90” indicator of ART initiation, whilst married women compared to those unmarried were more likely to achieve the “third 90” indicator of HIV viral suppression [PRR = 1.11 (95% CI, 1.05–1.18)] (Table 4).

Discussion

Viral suppression among all pregnant adolescents and women living with HIV attending public sector PHC clinics in rural KwaZulu Natal was 90.8%. This finding is important as it reflects South Africa’s commitment and efforts in scaling up of ART towards reaching the UNAIDS target of 90% of viral suppression towards attaining HIV epidemic control [1, 7]. Despite facing many challenges, the South African HIV treatment program has reached more than 5 of the 7.5 million adults (aged 15 years and older) who are receiving ART especially in a country that has the largest global burden of HIV. However, there remains an urgency that the remaining 2.5 million PLHIV initiate ART and simultaneously those on ART are sustained in care. In parallel it is critically important to monitor whether the increasing ART coverage has the desired effect of reducing HIV incidence towards the target of 1.00 per 1000 person-years [4]. Whilst our study focused on pregnant adolescents and women achieving viral suppression, we expect coverage of ART to be similar even in the general population.

Linked to HIV viral suppression, it is crucial to achieve the “first 90” which requires knowledge of HIV status, and failure to reach this target across key age groups is a major barrier to HIV diagnosis and care continuum. The lower proportion of adolescents and women below the age of 30 years in knowing their HIV positive status ranging from 69.2 to 87.5% is concerning, despite the offer of HIV testing services to all pregnant women accessing the PHC clinics. Therefore, every opportunity must be made to facilitate HIV testing to improve knowledge of HIV status. Although universal HIV testing for pregnant women is available through PHC clinics, the delivery of programs through facilities may create a gap.
Table 3  Proportion of enrolled pregnant adolescents and women achieving each of the UNAIDS 90–90–90 targets and overall HIV viral suppression in rural KwaZulu-Natal, South Africa

| Characteristics                                                                 | HIV testing and linkage to care cascade                                                                 | Overall HIV viral suppression at viral load < 400 copies per mL among all HIV positive participants |
|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
|                                                                                 | “First 90”                                                                                              | “Second 90”                                                                                          |
|                                                                                 | Knowledge of HIV status                                                                               | HIV positive and on ART                                                                              |
|                                                                                 |                                                                                                       | HIV viral suppression at viral load < 400 copies per mL among participants aware of HIV status and reporting to be on ART |
|                                                                                 | n/N % (95% CI)                                                                                          | n/N % (95% CI)                                                                                       | n/N % (95% CI)                                                                                     |
| Overall                                                                         | 180/213 84.5 (79.0–88.8)                                                                              | 173/176 98.3 (95.1–99.4)                                                                            | 198/218 90.8 (86.3–94.0)                                                                          |
| Socio-demographic characteristics                                               |                                                                                                       |                                                                                                   |                                                                                                   |
| Age group in years                                                              |                                                                                                       |                                                                                                   |                                                                                                   |
| 14–19                                                                           | 18/26 69.2 (50.0–83.5)                                                                                 | 16/18 88.9 (67.2–96.9)                                                                             | 16/16 100 (80.6–100)                                                                             |
| 20–24                                                                           | 41/54 75.9 (63.1–85.4)                                                                                 | 37/37 100 (90.6–100)                                                                               | 35/37 94.6 (82.3–98.5)                                                                            |
| 25–29                                                                           | 49/56 87.5 (76.3–93.8)                                                                                 | 49/49 100 (92.7–100)                                                                               | 47/49 95.9 (86.3–98.9)                                                                            |
| ≥30                                                                             | 72/77 93.5 (85.7–97.2)                                                                                 | 71/72 98.6 (92.5–99.8)                                                                             | 67/70 95.7 (88.1–98.5)                                                                            |
| Education levels                                                                |                                                                                                       |                                                                                                   |                                                                                                   |
| Completed high school                                                           | 86/109 78.9 (70.3–85.5)                                                                               | 98/110 89.6 (90.0–98.8)                                                                            | 98/110 89.6 (90.0–98.8)                                                                          |
| Incomplete high school                                                          | 94/104 90.3 (83.2–94.7)                                                                               | 98/106 95.5 (88.9–98.2)                                                                             | 98/106 92.5 (87.4–97.5)                                                                          |
| Household income per month                                                       |                                                                                                       |                                                                                                   |                                                                                                   |
| ≤ ZAR 5000                                                                      | 85/96 88.5 (80.6–93.5)                                                                                 | 82/83 98.8 (93.5–99.8)                                                                             | 78/81 96.3 (89.7–98.7)                                                                            |
| > ZAR 5000                                                                      | 37/46 80.4 (66.8–89.3)                                                                                 | 36/36 100 (90.4–100)                                                                               | 34/36 94.4 (81.9–95.5)                                                                            |
| Don’t know                                                                       | 57/69 82.6 (72.0–89.8)                                                                                 | 54/56 96.4 (87.9–99.0)                                                                             | 52/54 96.3 (87.5–99.0)                                                                            |
| Marital status                                                                   |                                                                                                       |                                                                                                   |                                                                                                   |
| Married                                                                         | 26/26 100 (87.1–100)                                                                                   | 26/26 100 (87.1–100)                                                                               | 25/25 100 (86.7–100)                                                                             |
| Unmarried                                                                        | 154/187 82.4 (76.3–87.1)                                                                               | 147/150 98.0 (94.3–99.3)                                                                            | 171/191 89.5 (84.4–93.1)                                                                          |
| Family characteristics                                                           |                                                                                                       |                                                                                                   |                                                                                                   |
| Biological mother alive                                                         |                                                                                                       |                                                                                                   |                                                                                                   |
| Yes                                                                              | 110/129 85.3 (78.1–90.4)                                                                               | 104/107 97.2 (92.1–99.0)                                                                            | 97/103 94.2 (87.9–97.3)                                                                            |
| No                                                                               | 68/82 82.9 (73.4–89.5)                                                                                 | 67/67 100 (94.6–100)                                                                               | 66/67 98.5 (92.0–99.7)                                                                            |
| Don’t know                                                                       | 2/2 100 (34.2–100)                                                                                     | 2/2 100 (34.2–100)                                                                                 | 2/2 100 (34.2–100)                                                                               |
| Biological father alive                                                          |                                                                                                       |                                                                                                   |                                                                                                   |
| Yes                                                                              | 67/80 83.8 (74.2–90.3)                                                                                 | 62/64 96.9 (89.3–99.1)                                                                             | 58/61 95.1 (86.5–98.3)                                                                            |
| No                                                                               | 110/130 84.6 (77.4–89.8)                                                                               | 108/109 99.1 (90.5–99.8)                                                                            | 104/108 96.3 (90.9–98.6)                                                                          |
| Don’t know                                                                       | 3/3 100 (43.9–100)                                                                                     | 3/3 100 (43.9–100)                                                                                 | 3/3 100 (43.9–100)                                                                               |
| Behavioral characteristics                                                       |                                                                                                       |                                                                                                   |                                                                                                   |
| Age at first sex                                                                 |                                                                                                       |                                                                                                   |                                                                                                   |
| At ≤ 16 years                                                                    | 9/11 81.8 (52.3–94.9)                                                                                  | 8/9 88.9 (56.5–98.0)                                                                               | 8/8 100 (67.6–100)                                                                               |
| At 17–18 years                                                                   | 21/29 72.4 (54.3–83.3)                                                                                 | 19/20 95.0 (76.4–99.1)                                                                             | 18/19 96.4 (91.9–98.5)                                                                            |
| At > 18 years                                                                    | 144/167 86.2 (80.2–90.6)                                                                               | 140/141 99.3 (96.1–99.9)                                                                            | 134/139 96.4 (91.9–98.5)                                                                          |
| Refused                                                                          | 6/6 100 (61–100)                                                                                       | 6/6 100 (61–100)                                                                                   | 5/5 83.3 (43.6–97.0)                                                                             |
| Total number of lifetime sex partners                                             |                                                                                                       |                                                                                                   |                                                                                                   |
| 1 partner                                                                        | 17/20 85.0 (64.0–94.8)                                                                                 | 17/17 100 (81.6–100)                                                                               | 14/17 82.4 (59.0–93.8)                                                                            |
| 2 or more partners                                                               | 144/172 83.7 (77.5–88.5)                                                                               | 138/140 98.6 (94.9–99.6)                                                                            | 135/138 97.8 (93.8–99.3)                                                                          |
| Don’t know/Refused                                                               | 19/21 90.5 (71.1–97.3)                                                                                 | 18/19 94.7 (75.4–99.1)                                                                             | 16/17 94.1 (73.0–99.0)                                                                            |
| Total number of current sex partners                                              |                                                                                                       |                                                                                                   |                                                                                                   |
| 1 partner                                                                        | 171/203 82.2 (78.6–88.6)                                                                               | 165/167 98.8 (95.7–99.7)                                                                            | 157/164 95.7 (91.5–97.9)                                                                          |
| 2 or more partners                                                               | 1/1 100 (20.7–100)                                                                                     | 1/1 100 (20.7–100)                                                                                 | 1/1 100 (20.7–100)                                                                               |
| Refused                                                                          | 8/9 88.9 (56.6–98.0)                                                                                    | 7/8 87.5 (52.9–97.8)                                                                               | 7/7 100 (64.6–100)                                                                               |
| Alcohol use                                                                      |                                                                                                       |                                                                                                   |                                                                                                   |
as services may not reach all age groups. Whilst decen-
tralization of services provides easier access to services,
new modalities of HIV testing including self-testing [24]
may have not reached saturation in some communities.
Furthermore, many individuals in these communities
face structural and individual level barriers that decrease
access to both information about services and to the ser-
vices themselves, and may also include fear of stigma and
discrimination, all of which pose major obstacles to HIV
testing [34–36]. Many individuals may also be unaware
of the benefits and services to which they are entitled to
and often lack skills required to engage with authorities
around services. Thus, missed opportunities continue to
prevail that impede the benefits of knowledge of HIV sta-
tus and progress to achieving the “first 90” target.

Towards achieving the “second 90” target, our data
show remarkable progress on the uptake of ART among
those who were aware of their HIV positive status, how-
ever, young adolescents in the 14–19 year age group were
least likely to achieve this target (88.9%). Whilst there are
concerns that women initiating early ART during preg-
nancy are more likely to become disengaged over time
compared to women starting ART because of advanced
HIV disease [37], our study showed that in women who
had initiated ART, viral suppression was achieved, show-
ing that women were retained in programs through the

### Table 3 (continued)

| Characteristics | HIV testing and linkage to care cascade | Overall HIV viral suppression at viral load < 400 copies per mL among all HIV positive participants |
|-----------------|----------------------------------------|-------------------------------------------------|
|                 | “First 90” | “Second 90” | “Third 90” |
| Knowledge of HIV status | HIV positive and on ART | HIV viral suppression at viral load < 400 copies per mL among all HIV positive participants |
| n/N | % (95% CI) | n/N | % (95% CI) | n/N | % (95% CI) | n/N | % (95% CI) |
| No | 112/134 | 83.6 (76.4–88.9) | 109/111 | 98.2 (93.7–99.5) | 101/108 | 93.5 (87.2–96.8) | 120/135 | 88.9 (82.5–93.1) |
| Yes | 68/79 | 86.1 (76.8–92.0) | 64/65 | 98.5 (91.8–99.7) | 64/64 | 100 (94.3–100) | 76/81 | 93.8 (86.4–97.3) |
| Drug use | | | | | | | | |
| No | 156/184 | 84.8 (79.4–89.7) | 152/154 | 98.7 (95.4–99.6) | 144/151 | 95.4 (90.7–97.7) | 169/186 | 90.9 (85.9–94.2) |
| Yes | 17/22 | 77.3 (56.6–89.9) | 15/16 | 93.8 (71.7–98.9) | 15/15 | 100 (79.6–100) | 20/23 | 87.0 (67.9–95.5) |
| HIV Testing history | | | | | | | | |
| Last HIV test done | | | | | | | | |
| > 12 months | 64/69 | 92.8 (84.1–96.9) | 64/64 | 100 (94.4–100) | 60/63 | 95.2 (86.9–98.4) | 62/68 | 91.2 (82.1–95.9) |
| ≤ 12 months | 116/144 | 80.6 (73.3–86.2) | 109/112 | 97.3 (92.4–99.1) | 105/109 | 96.3 (90.9–98.5) | 130/144 | 90.3 (84.3–94.1) |
| Clinical characteristics | | | | | | | | |
| Pregnancies | | | | | | | | |
| Current only | 52/71 | 73.2 (61.9–82.1) | 48/50 | 96.0 (86.5–98.9) | 46/48 | 95.8 (86.0–98.8) | 64/73 | 87.7 (78.2–93.4) |
| 2 or more | 127/141 | 90.1 (84.0–94.0) | 124/125 | 99.2 (95.6–99.9) | 118/123 | 95.9 (90.8–98.3) | 131/142 | 92.3 (86.7–95.6) |
| The first time that you had sex, was your partner circumcised | | | | | | | | |
| No | 113/125 | 90.4 (84.0–94.4) | 109/110 | 99.1 (95.0–99.8) | 102/108 | 94.4 (88.4–97.4) | 114/127 | 89.8 (83.3–93.9) |
| Yes | 30/41 | 73.2 (58.1–84.3) | 30/30 | 100 (88.6–100) | 30/30 | 100 (88.6–100) | 41/42 | 97.6 (87.7–99.6) |
| Don’t know | 28/37 | 75.7 (59.9–86.6) | 26/27 | 96.3 (81.7–99.3) | 25/26 | 96.2 (81.1–99.3) | 33/37 | 89.2 (75.3–95.7) |
| Ever had any STI symptoms | | | | | | | | |
| Yes | 66/78 | 84.6 (75.0–91.0) | 62/64 | 96.9 (89.3–99.1) | 60/62 | 96.8 (89.0–99.1) | 70/78 | 89.7 (81.0–94.7) |
| No | 114/135 | 84.4 (77.4–89.6) | 111/112 | 99.1 (95.1–99.8) | 105/110 | 95.5 (89.8–98.0) | 126/138 | 91.3 (85.4–95.0) |
| HSV-2 antibodies | | | | | | | | |
| Positive | 160/189 | 84.7 (78.8–89.1) | 154/156 | 98.7 (95.4–99.6) | 148/153 | 96.7 (92.6–98.6) | 176/192 | 91.7 (86.9–94.8) |
| Negative | 20/24 | 83.3 (64.1–93.3) | 19/20 | 95.0 (76.4–99.1) | 17/19 | 89.5 (68.6–97.1) | 22/26 | 84.6 (66.5–93.8) |

Missing data were excluded from percentage calculation.
Refused and don’t know data were included in percentage calculation.

IQR = Interquartile range; ZAR = South African Rand (ZAR15 ~ US$1); ART = Antiretroviral therapy; STI = sexually transmitted infections;
Ever had any STI symptoms = any symptoms of abnormal vaginal discharge, burning or pain when passing urine, or presence of any genital ulcers/warts;
HSV-2 = Herpes simplex virus type 2;
supportive environment of health services and family. Adolescent friendly interventions, tailored towards addressing adolescent general and reproductive health needs are therefore a priority to improve HIV testing and linkage to care services [14, 15]. Over the years, suboptimal response to HIV services has been shown and continues to pose a threat in adolescents—a double threat in pregnant adolescents—as they pose high risk of HIV transmission to the unborn baby because of late presentation to health facilities.

The “third 90” target of achieving viral suppression is a critical component towards the goal to epidemic control. It is noteworthy that as per UNAIDS targets, 95.9% of adolescents and women in the study who had knowledge of their HIV status and had initiated ART were virally suppressed, whilst overall 90.8% of all pregnant women living with HIV had achieved viral suppression. The high rates of viral suppression among women on ART, though self-reported, suggest that the health systems have established processes and procedure to ensure HIV care continuum and expelling the notion of the potential to be disengaged. Viral suppression is critical for the PMTCT of HIV, improving mothers’ health outcomes and simultaneously preventing transmission to sex partners [11]. Nevertheless, supporting women during and post-pregnancy to sustain adherence to ART is crucial to maintaining viral suppression in the long term.

Younger women were less likely to have knowledge of their HIV status, directly affecting ART initiation and to achieve viral suppression. Several surveys have demonstrated the challenges in reaching out to key groups of younger individuals [38]; and district and national level population-based studies have shown variable and suboptimal achievements towards the UNAIDS set targets even at viral load suppression threshold at < 1000 copies per mL [9, 16, 35, 36]. However, our findings show that these targets could be achieved among select populations of pregnant women who do better than women from the general population despite the expansion of HIV related services [21, 37]. Thus, our findings and those of the community-based studies emphasize the need for a targeted approach to reach key groups of individuals, specifically those in the younger age groups. Whilst viral suppression was close to 90%, the gap to reaching 90% was also in the age groups that has the highest HIV incidence rates [39]. This trend among young women are similar to the findings from the national antenatal survey which showed the gap in the awareness of HIV positive status and linkage to treatment among HIV positive pregnant women are in the 15 to 24 year age group [40].

Table 4 Baseline characteristics associated with achieving each of the UNAIDS 90–90–90 targets and overall HIV viral suppression among enrolled pregnant adolescents and women in a rural KwaZulu-Natal, South Africa

| Characteristics            | HIV testing and linkage to care cascade | Overall HIV viral suppression at viral load < 400 copies per mL among all HIV positive participants |
|----------------------------|----------------------------------------|---------------------------------------------------------------------------------------------|
|                            | “First 90”                              | “Second 90”                                                                                   |
| Knowledge of HIV status    |                                        |                                                                                              |
| On ART                     |                                        |                                                                                              |
|                            | PRR (95% CI)  P value                  | PRR (95% CI)  P value  |
| Age group in years         |                                        |                                                                                              |
| 14–24                      | Ref                                    | Ref                                                                                         |
| ≥ 25                       | 1.22 (1.05–1.42)  0.01**               | 1.04 (0.97–1.11)  0.30                                                                 |
| Marital Status             |                                        |                                                                                              |
| Unmarried                  |                                        |                                                                                              |
| Married                    | Ref                                    | Ref                                                                                         |
|                            | 1.15 (1.06–1.25)  <0.01**              | 1.01 (0.99–1.03)  0.25                                                                 |
| Education levels           |                                        |                                                                                              |
| Completed high school      |                                        |                                                                                              |
| Incomplete high school     | Ref                                    | Ref                                                                                         |
|                            | 1.16 (1.04–1.30)  0.01**               | 1.00 (0.96–1.04)  0.83                                                                 |
| Total number of lifetime sex partners |                |                                                                                              |
| 1 partner                  |                                        |                                                                                              |
| 2 or more partners         | 1.12 (0.91–1.37)  0.28                 | 1.03 (0.99–1.07)  0.16                                                                 |

ART = Antiretroviral therapy, PRR = Prevalence Risk Ratio, CI = Confidence Interval, Ref = Reference category

** Significant at P value < 0.05

Variables not included in the adjusted model because of collinearity were employment status, ever tested for HIV, ever had sex, age at first sex, lifetime number of sex partners, current number of sex partners.
Whilst we found no distinct factors associated with viral suppression, married women were more likely to be virally suppressed, highlighting a supportive environment that married women might be in and disclosure of HIV positive status to partners may play an important role in facilitating adherence to ART [41]. Though women 25 years and older, married and those with incomplete high school education were more likely to know their HIV status and linked to HIV care continuum. A major concern is the unacceptably high HIV prevalence of 40.2% among pregnant women [27] reflecting the substantial long-term care and treatment needs for a relatively young population in this community. More importantly, in the age group 14–19 years, HIV prevalence of 22.1% emphasizes that young girls continue to be highly vulnerable to HIV and infections in this age group provides a reliable approximation of incident HIV infection [16]. Given that HIV viral load is highest during this early stage of infection and the gap in achieving the UNAIDS targets in this age group has the potential to sustain the cycle of HIV transmission [42, 43]. These findings remain deeply concerning as many of these young girls were still in school underscoring the need for expanding effective pregnancy prevention options to protect young girls from early pregnancy and HIV. The evaluation of the impact of school-based interventions on sexual risk behaviours and sexually transmitted infections among young adolescents found that for 14,426 secondary school learners who participated across nine RCTs in Zimbabwe, South Africa, Tanzania, Zambia, Liberia, Swaziland, and Uganda, declines were observed in the number of pregnancies and improvements in HIV/AIDS related knowledge, normative beliefs, knowledge and self-efficacy in condom use, positive attitudes to HIV testing, with a moderate decline in sexual debut and intimate partner violence but no long-term change on condom use, or curable STIs, HSV-2 and HIV infections [44]. With the high rate of attrition, it is possible that risk taking behaviours may increase among learners leaving school prematurely and enhancing risk for HIV acquisition, thus explaining the link between incomplete high school school and low knowledge of HIV status. The key strength of this study was our eligibility criteria of enrolling pregnant women as young as 12 years and together with our age-stratified data allowed us to identify key groups that contribute to achieving HIV viral suppression. However, the study presents some limitations. The study sample of pregnant women from a rural setting living under constrained structural and socio-economic conditions with potentially differential exposure to HIV related services reflects the characteristics of pregnant women accessing services in poor communities and limits the generalizability of our findings to this setting. Additional limitations of this study included the substantial proportion of participants refusing to respond to sensitive behavioral questions limiting the association of these factors to accessing HIV related services to facilitate viral suppression. Since this study was cross-sectional in design no causal link could be established between achieving HIV viral suppression and characteristics of pregnant women.

Conclusions
This study showed that adolescent pregnant women aged 14–19 years were less likely to achieve viral suppression, underscoring the public health implications of sustained risk of HIV transmission through MTCT and to sexual partners. Thus, greater effort and strong social support are essential to improve HIV knowledge of status and care continuum. The overall HIV viral suppression of 90.8% among all HIV positive pregnant women is encouraging, though still far short of the targets to be achieved by 2025. Thus, HIV knowledge of status and care continuum must remain a collective important public health priority to attain viral suppression, reduce transmission risk and achieve the aspirational goal of HIV epidemic control.

Abbreviations
ANC: Antenatal clinic; ART: Antiretroviral therapy; BREC: Biomedical Research Ethics Committee; CI: Confidence interval; DOH: Department of Health; IQR: Interquartile Range; KZN: KwaZulu-Natal; NSP: South Africa National Strategic Plan for HIV, STIs and TB; MTCT: Mother to child transmission; PDA: Personal digital assistant; PHC: Primary health care; PLHIV: People living with HIV; PMTCT: Prevention of mother-to-child transmission; PRR: Prevalence ratio; STI: Sexually Transmitted Infections; UNAIDS: The Joint United Nations Programme on HIV/AIDS; WHO: World Health Organization; ZAR: South African Rand.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12978-022-01419-5.

Acknowledgements
The authors sincerely thank all the women for their time and commitment to study participation. To all the traditional and municipal leadership for their support with the study. To all the Provincial Department of Health and uMgungundlovu District office, the local primary health care clinics for facilitating access to and clinical management of participants. To all the study staff, laboratory, and primary health care clinic staff for study related procedures.

Author contributions
ABMK, LRM and HP-K conceptualised the study and secured funding for the study. NPN contributed to overall field supervision of study related procedures, data collection and prepared the first draft of the manuscript. ABMK and NPN were responsible for project administration and writing of the manuscript. NPN and AS were responsible for data curation and contributed to data cleaning and analysis. AS and NY-Z were responsible for the data quality checks, statistical analysis, finalisation and confirmation of the tables and figures. ABMK and LRM contributed to designing analysis, scientific...
integrity, and final review of the manuscript. ABM/K, NPN and CB contributed to interpretation of the data, writing and finalisation of the manuscript. All authors contributed to the critical review and approval of the final version of the manuscript. All authors read and approved the final manuscript.

Funding
The study was made possible through The Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD), Office of the Director and National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health: R01HD083343 (Multi-PI: Kharsany and Kohler). Further funding support was provided to N. Ntombela from the University Capacity Development Programme from the College of Health Sciences by the University of KwaZulu-Natal. REF: 207525096. N. Ntombela, A. Soogun and A&M. Kharsany received support from the South African Department of Science and Innovation and the National Research Foundation’s Centre of Excellence in HIV Prevention (Grant number 96354). The design of the study, data collection, analyses are not influenced by the funders. Findings and conclusions presented in this manuscript are those of the author(s) and do not necessarily represent the official position of the funding agencies.

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

Declarations

Ethics approval and consent to participate
The study was reviewed and approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (reference number BF001/16), KwaZulu-Natal Provincial Department of Health (DOH) (Ref:HRKM90/16, KZ_2016RPI4_S28) and the University of Pennsylvania (REF: # 825071). Written informed consent was obtained for those 18 years and older and individual assent with parental consent for those younger than 18 years in English or isiZulu.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 27 January 2022 Accepted: 18 April 2022
Published online: 12 May 2022

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