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Clinic and care: Associations with adolescent ART adherence in a prospective cohort in South Africa

Clinic, care and adolescent ART adherence

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Abstract

Objective. Adolescent anti-retroviral treatment (ART) adherence remains critically low. We lack research testing protective factors across both clinic and care environments.

Design: A prospective cohort of adolescents living with HIV (sample n=969, 55% female, baseline mean age 13.6) in the Eastern Cape Province in South Africa were interviewed at baseline and 18-month follow-up (2014-15, 2015-16). We traced all adolescents ever initiated on treatment in 52 government health facilities (90% uptake, 93% 18-month retention, 1.2% mortality).

Methods: Clinical records were collected; standardised questionnaires were administered by trained data collectors in adolescents’ language of choice. Probit within-between regressions and average adjusted probability calculations were used to examine associations of caregiving and clinic factors with adherence, controlling for household structure, socio-economic and HIV factors.

Results: Past-week ART adherence was 66% (baseline), 65% (follow-up), validated against viral load in sub-sample. Within-individual changes in three factors were associated with improved adherence: 1) no physical and emotional violence (12.1 percentage points increase in adjusted probability of adherence, p<.001), 2) improvement in perceived healthcare confidentiality (7.1 percentage points, p<.04) and 3) shorter travel time to the clinic (13.7 percentage points, p<.02). In combination, improvement in violence prevention, travel time, and confidentiality were associated with 81% probability of ART adherence, compared to 47% with a worsening in all three.

Conclusions: Adolescents living with HIV need to be safe at home and feel safe from stigma in an accessible clinic. This will require active collaboration between health and child protection systems, and utilisation of effective violence prevention interventions.

Key Words: Adolescence, Adherence, ART, Violence, Confidentiality, Decentralisation
Introduction

Adolescents have the lowest ART adherence rate among all age groups\(^1\), leading to elevated morbidity, viral resistance, onwards infection\(^2, 3\), and mortality\(^4\). Retention in HIV care is further challenged in the context of COVID-19\(^5\).

Eighty-five percent of adolescents living with HIV live in sub-Saharan Africa. Systematic reviews have found limited evidence for effective interventions to increase adolescent ART adherence\(^6, 7\). Evidence shows that healthcare factors are important\(^8\), and interventions to date have primarily focused on health systems: supporting young people to take their medication and increasing the availability, affordability and acceptability of HIV care\(^9, 10\).

Social relationships in healthcare settings and relationships in the community have also been identified as key for adolescents\(^11\). Confidentiality and trust may be both indicators of and predictors of quality of care and healthcare outcomes\(^12\). New evidence in the region also shows positive impacts of interventions including peer supporters, support groups, and counselling\(^9, 13\).

But we may be missing an additional social pathway. Developmental psychology shows that adolescent behaviour is closely linked to family and home relationships\(^14\). In particular, caregiving or parenting – which refers to any biological or non-biological primary caregiver – has lasting effects including and beyond health-seeking behaviours\(^15\). Nurturing and supportive caregiving increases adolescent capacity to manage risks\(^16\), while violent caregiving increases risk behaviours and mental health distress\(^17\). In qualitative research, adolescents living with HIV have identified both healthcare and family influences on their medication-taking\(^18-21\). The importance of caregiving has been heightened during the COVID-19 epidemic, with revolving lockdowns, closures of schools and community-based services, and restricted peer-mixing\(^22\).

Despite this, we lack longitudinal studies that test whether caregiving is linked with adolescent adherence in sub-Saharan Africa. There are strong indications from cross-sectional studies: in Uganda, family and caregiver social support were associated with higher adolescent ART adherence, but support from peers and teachers were not\(^23\). Caregiver violence was associated with lower adherence in cross-sectional studies in South Africa, Malawi, and Zambia\(^24-26\).

It is essential to examine both healthcare provision and family care factors in longitudinal research to identify further ways to support adherence. We conducted a community-based prospective cohort of adolescents living with HIV (aged 10-19 at baseline) from 2014-2017 in 180 communities of South Africa’s Eastern Cape. We use baseline and 18-month follow-up data from 969 adolescents to examine associations of clinic and care factors with past-week ART adherence, accounting for household structure, socioeconomic and HIV-related factors, shown in prior research to affect adherence\(^27-29\).
Methods

The study took place in the Eastern Cape province of South Africa, characterized by high morbidity, low human development, and poor infrastructure. We conducted standardised interviews and extracted clinical records for 1,046 adolescents living with HIV at baseline (2014-15), with 979 re-interviewed at 18-month follow-up (2016-17). 969 had complete data on key variables. The study included both adolescents engaged in clinical care and those who were lost to follow-up in clinical care, and thus, it is the region’s first large-scale community-traced cohort of this group.

In a health district including rural, urban, and peri-urban settlements, we identified all 52 community health centres, primary clinics, and hospitals that provided ART to adolescents. In each facility, all patient files (paper and electronic) were reviewed to identify all those who had ever initiated ART and were aged 10-19 years. Throughout 180 communities, adolescents were interviewed at a location of their choice. At 18 months after baseline, all adolescents who had consented to be re-approached were asked for consent for follow-up. Reflecting high mobility, 18% of participants have moved households between study waves, and by follow-up participants lived in six provinces: Eastern Cape, Gauteng, KwaZulu-Natal, Free State, Western Cape, and North-West.

Ethical approvals were given by the University of Cape Town (CSSR 2013/4), Oxford University (CUREC2/12-21), provincial Departments of Health and Education, and healthcare facilities. All adolescents and their primary caregivers gave written informed consent at both time points in their language of choice (Xhosa or English), read aloud in cases of low literacy. The study did not provide financial incentives, but adolescents did receive a snack, a certificate of participation, and a small gift pack including soap and pencils. These were recommended by our adolescent advisory group [30] and provided regardless of interview completion.

Clinical records were extracted in healthcare facilities (see Supplementary Materials Box S1), and trained local researchers supported participants in completing tablet-based questionnaires lasting 60-90 minutes. Adolescents chose their language of participation. Questionnaires were co-designed with an adolescent advisory group; the South African National Departments of Health, Social Development, Basic Education and National AIDS Council; UNICEF; PEPFAR-USAID, and local NGOs. Pre-piloting was conducted locally with 25 adolescents living with HIV.

To avoid stigma or unintended disclosure of HIV status, the research focus was presented as general adolescent social and health needs, and 456 neighbouring adolescents were also interviewed (not included in these analyses). Confidentiality was maintained except in cases of risk of harm. For rape, abuse, suicidality, or untreated severe illness (e.g., symptomatic TB), researchers made immediate health and social service referrals with follow-up support (n=157 referrals over three years for 104 adolescents).
Procedures

Full questionnaires are available at http://www.youngcarers.org.za/youthpulse. All variables in these analyses were measured and defined in the same way at baseline and follow-up.

Outcome

ART adherence was measured using adapted items from the Patient Medication Adherence Questionnaire and measures developed in Botswana [31, 32]. ART adherence was defined as past seven days adherence >95% (including weekdays and weekend), based on currently taking ART and not having missed any doses in the past seven days [33]. We validated self-reported adherence against viral loads available in clinical records, using the viral load measurement closest to the interview date. 8% of adolescents’ clinical records did not include any viral load measurements, and about 60% of adolescents with an available viral load had a measurement from the two years before or after the questionnaire date [34]. Thus, our validation focused on adolescents whose clinical records included viral load measurements within this period, excluding measurements in a 30-day range around ART initiation (n=650 adolescents at baseline and n=598 at follow-up).

Explanatory variables

Clinic factors: Medication stock-outs were measured as past-year inability to access ART due to clinic stock-outs. Confidentiality was measured as feeling that their information would be kept safe and confidential at the clinic most or all of the time in the past year. Wait time in the clinic above 1 hour and travel to the clinic above 1 hour were measured as past-year experiences in respect to the main clinic the adolescent attends [27-29].

Caregiving factors: Past-year physical or emotional abuse victimisation by caregivers or other adults were measured using UNICEF Measures for National-level Monitoring of Orphans and Vulnerable Children [35] (12 items) and defined as having experienced at least one type of violence, such as being hit with a hard item. Past-week witnessing domestic violence between adults in the home (physical or verbal) also used these UNICEF measures [35] (2 items). Good parent/caregiver monitoring and supervision (9 items, for example, having rules for when adolescents come home) and positive caregiving (6 items, for example, positive reinforcement) were measured over the past 2 months, using subscales of the Alabama Parenting Questionnaire [36], and defined as not having experienced any poor monitoring and supervision, and as always experiencing positive caregiving. Good communication between primary caregivers and adolescents was measured over the past 2 months using adapted Child-Parent Communication Apprehension Scale for use with young adults, asking about ease and openness of communication and defined as agreeing or strongly agreeing to all items (5 items) [37]. All caregiving and clinic factors were dichotomised to facilitate interpretability.
Control variables

Household structure factors included orphanhood (maternal or paternal) measured using items adapted from the 2011 South African census [38]; number of changes of caregiver experienced; household size, and relationship of primary caregiver to child, i.e., biological parent or not. Socioeconomic factors included adolescent age, sex, urban/rural location, and living in formal or informal housing, using census-based items [39]. Household poverty was measured as access to eight highest socially-perceived necessities for children in the nationally representative South African Social Attitudes Survey (e.g., enough food) [40]. HIV-related factors were measured using clinical records, checked against self-report where possible, and included mode of HIV infection (vertical/horizontal) and recent HIV infection (<2 years before baseline).

Statistical analyses

First, we validated self-reported ART adherence against undetectable viral load (<50 copies/mL) from clinical records using multivariable logistic regression, controlling for age, sex, rural/urban, orphanhood, informal housing, mode of infection, and health status. Second, we examined frequencies of adherence, hypothesised explanatory and control variables. Third, we compared participants who were followed up and included in this analysis, and those who were not, to check for potential differences using t-tests for continuous variables and chi-squared tests for dichotomous variables.

Fourth, we examined associations of clinic and care factors with past-week adherence. We used a within-between regression model, also known as a hybrid model, which allows us to look at within-person variation as well as compute average adjusted probabilities of the outcome [41-43]. For each explanatory variable, we used a person’s average value and time-specific deviation from this average (see equation (1)).

\[
P(\text{Adherence}_{it} = 1 | x_{it}) = \Phi(\beta_0 + \beta_1(x_{it}) + \beta_2(x_{it} - \bar{x}_i) + \nu_{i0} + \varepsilon_{it})
\]

where \( \Phi \) is the cumulative normal distribution, adherence is the time-varying dependent variable, \( \beta_0 \) represents the overall intercept, \( x_{it} \), is a time-varying explanatory variable for person \( i \) at time \( t \), \( \bar{x}_i \) is the average of the explanatory variable for person \( i \) across both time points, \( \beta_1 \) represents the average between-person effect and \( \beta_2 \) represents the average within-person effect, \( \nu_{i0} \) a random person-level intercept, assumed to be normally distributed, and \( \varepsilon_{it} \) the residuals.

This provides a “between-person” coefficient (estimated by \( \bar{x}_i \)), the difference between individuals, and a “within-person” coefficient (estimated by \( x_{it} - \bar{x}_i \)), which examines the changes within individual’s levels of the explanatory variable over time. With two time points, the within-person estimate is equivalent to a first difference model [44]. The within-person estimate is the focus of our analyses as it allows to account for all time-invariant confounders [44]. Participant sex, ART initiation and mode of infection were modelled as time-invariant, while all other control variables were modelled as time-variant.
Analyses were conducted in Stata 14.2 (code available at https://osf.io/znse9/). We used a probit model (xtprobit command) with robust clustered standard errors at the individual level. To aid interpretation of the relationships between the explanatory variables and adherence, we estimated average adjusted probabilities [45] of the clinic and caregiving factors that were statistically significant in the multi-variable regression (p<0.05), using margins and lincom commands [46].

Results

Adherence rates and viral load

Self-reported ART adherence was low, with 66% of adolescents at baseline and 65% at follow-up reporting adherence in the past week. Only 45% reported past-week adherence at both time points. Self-reported adherence was associated with undetectable viral load (<50 copies/ml) at both time points, controlling for age, sex, rural/urban, orphanhood, informal housing, mode of infection, and health status (see Table 1, baseline OR 1.46, 95% CI 1.02-2.08, p=0.037, n=650; follow-up OR 1.45 95% CI 1.01-2.07, p=0.045, n=598).

Sample characteristics

Descriptive data are summarised in Table 2. The sample was 55% female with mean age 13.6 years (SD=2.9) at baseline. Around two-thirds of adolescents were orphaned (maternal, paternal, or double), and less than half lived with a biological parent. At both baseline and follow-up, around one third of adolescents reported good caregiver supervision and good communication. 11% reported past-week physical or verbal violence between adults in the home. 30% (baseline) and 38% (follow-up) reported experiencing physical or emotional abuse. 11% (baseline) and 5% (follow-up) reported travel time to clinic >1 hour, and about half of the sample at baseline and follow-up reported wait time at the clinic >1 hour. 5% at each time-point reported medication stock-outs, and 24% (at baseline) and 36% (at follow-up) did not feel that their information would mostly be kept confidential at the clinic.

67 (6%) adolescents recruited at baseline were lost to follow-up, including 12 who died between timepoints. 10 (1%) had incomplete data. We compare 969 participants included (complete cases) and 77 participants not included (Table S1). There were no differences on most baseline characteristics, but participants lost to follow up were more likely to be non-adherent, older, horizontally infected, and live with a biological parent.

Associations of caregiving and healthcare factors with adherence

Key results of the within-between probit regression are presented in Table 3 (single-variable regression results in Table S2 and full output of multi-variable regression in Table S3).

To aid the interpretation of the regression coefficients’ magnitude, Table 4 demonstrates adjusted probabilities of adherence at each value of the within-person explanatory variables.
that were statistically significant in the regression analysis, and the differences between the probabilities of adherence at the different values of these explanatory variables.

Within-person variation in two clinic factors was associated with adherence. Improvement in confidentiality in the clinic setting was associated with a greater likelihood of adolescents becoming adherent (7.1 percentage points, p=0.0325). Travel time to the clinic reducing to under one hour was also associated with higher likelihood of becoming adherent (13.7 percentage points difference, p=0.0143).

Within-person variation in one caregiving factor was associated with adherence. Ending exposure to violence was associated with a greater likelihood of adolescents becoming adherent (12.1 percentage points difference, p=0.0001).

Predicted probability of adherence for those experiencing a reduction in violence and travel time as well as improved confidentiality was estimated, based on the regression model, to be 81%, compared to 47% for those experiencing a deterioration on these three factors, thus a 34 percentage points difference (95% CI 21%;46%, p<0.001).

**Discussion**

The high rates of adolescent non-adherence in this study reflect similar trends in national and regional data, and are well below UNAIDS targets [47]. It is essential that we understand and mitigate barriers to ART adherence for young people. These are the first known findings from a longitudinal study identifying associations of both care and clinic factors to adolescent adherence, advancing the evidence by using a prospective cohort and including variables across different settings of the adolescents’ lives.

The study finds three factors were associated with better adherence. Non-exposure to violence was associated with better adherence. Associations of violence with ART adherence were as strong or stronger than healthcare factors. This is particularly relevant in the context of South Africa, which has high rates of violence against children [48]. There is also evidence that social protection such as cash transfers or other forms of economic strengthening can help to reduce family violence [49], and existing cash transfer policies within South Africa may be an essential component of violence reduction. Other effective interventions to reduce child abuse do exist, but are not yet scaled to population levels in any high HIV-prevalence country [50]. Evidence-based non-commercialised parenting/caregiving programmes have been tested in randomised trials in South Africa, South Sudan, and Burundi. They show reduced violence, and improved parenting, reduced parental substance use, and mental health distress that are strong predictors of violence [51-53], with similar engagement and outcomes amongst HIV/AIDS-affected and non-affected families [54, 55]. Parenting/caregiver programmes have also been shown to be cost-effective [56] with delivery costs of around $20 per family.
HIV and child protection services are rarely explicitly linked. Overcoming this may require increased collaboration between these systems, and across health and social development agencies. There are existing entry points. Health facilities and peer supporters could ask brief screening questions to identify violence exposure, such as those included in the WHO-recommended HEADSS and HEADSS+ questions [57, 58] – although caregiver presence may present challenges in reporting. Anecdotally, HIV peer supporter services already report high levels of violence disclosure. Governments, UNICEF, PEPFAR-USAID and the International Rescue Committee deliver parenting/caregiving programmes in the region, and these could provide platforms for reaching more adolescents living with HIV. Community-based services [9, 59, 60] may provide excellent opportunities to co-deliver effective violence prevention, screening, and support. In the COVID-19 pandemic, violence prevention and adherence support services are being adapted to remote and digital delivery modes [61, 62], and this may provide opportunities for combining with HIV services.

Reductions in travel time to clinics and improvements in perceived confidentiality within clinics were also associated with improved adolescent adherence. This suggests potential positive implications for Sub-Saharan Africa’s decentralisation from hospital-based ART provision to primary care, which often reduces patient travel burden. Systematic reviews suggest – from limited data – that decentralisation may support adolescent retention in care [63] [34]. WHO Global Standards for Quality Healthcare Services for Adolescents have identified insufficient respect for adolescent confidentiality and privacy as a major barrier for service access [64]. Confidentiality is important in building trust between adolescents living with HIV and their healthcare providers, and this has new implications as we grapple with providing remote support in the COVID context.

This study has limitations. First, we need to be cautious in determining causality. A strength of the within-person estimates is that they account for unmeasured stable person-level characteristics, such as adolescent early childhood experiences, since we examine changes within the same individuals [65, 66]. However, this estimate assumes no unobserved time-varying confounders (for instance, a policy change that affects both violence and adherence) [41]. We control for wave of data collection to help account for period effects. The within-person estimate relies on the adolescents who experienced changes in their exposures and in their adherence, reducing statistical power to detect associations. We assume that our outcome does not affect the explanatory variables, but we should also consider risks of reverse causality. It is possible that non-adherence could increase the travel time to HIV services if an adolescent was subsequently up-referred to a more specialised and distant facility – however the reverse could also be true of down-referral to improve accessibility. Our findings suggest that caregiver violence is associated with adolescent ART-non-adherence. We also considered the reverse possibility that adolescent ART non-adherence could contribute to caregiver violence, but epidemiological evidence suggests that adolescent behaviour is not a primary contributor to the social and structural factors driving family violence [67]. Notably, two thirds of adolescents living with HIV who participated in recent qualitative research in Zambia felt that family violence was negatively impacting their adherence, clinic attendance, or virologic results [68].
Second, we use self-reported adherence as the outcome, due to very limited clinical recording of treatment outcomes. We validated adherence against viral load measures but the low rates of viral load testing in this context meant that only up to 650 measures could be compared. Third, adolescents who reported non-adherence at baseline were more likely to be lost to follow-up. Fourth, our measure of violence focused on victimisation by adults at home or school (for example at a boarding school or orphanage) but in this sample almost all children lived in households. Fifth, we were not able to measure treatment stockouts for adolescents who were disengaged from HIV care. We did not include clinic in which adolescents received care as a factor in the models as inter-facility mobility and attendance of multiple healthcare facilities concurrently were common in this cohort: 31% had clinical records from at least two facilities within the study area.

The study also has several important strengths. It provides evidence from a sample of adolescents initiated on ART through government services in over 50 clinics in the South African Eastern Cape province. Affected by the legacy of apartheid, the Eastern Cape has high rates of poverty, unemployment, with over a quarter of the province’s households food insecure. Eastern Cape also has poor healthcare infrastructure and high rates of HIV prevalence (at 15.3% in 2017). Therefore, findings from this study setting may be generalizable to other countries in Sub-Saharan Africa as well as other resource-constrained settings.

Our study uses standardised questionnaires and repeated measures, with clinical record data. It traces and interviews adolescents as a community sample, allowing inclusion of adolescents who have disengaged from care or move between healthcare settings. It is the only known longitudinal study to provide evidence of associations between caregiving factors and adherence amongst adolescents living with HIV in Sub-Saharan Africa, and it is also unique in allowing the simultaneous examination of clinic and care factors, while controlling for HIV, social and economic factors. Further research on the multiple drivers of adolescent adherence is needed to build on these results and inform more effective services. It will also be essential to build longer-term evidence to improve lifetime adherence. Our future research includes a third wave of data collection, and using linked National Health Laboratory Service data as these adolescents become adults.

The HIV epidemic has taught us a hard lesson: that our capacity to prevent and treat a fatal virus is intertwined with the complexity of life experiences. For this highly vulnerable group of adolescents living with HIV, we need to respond both within and beyond the clinic system. Ensuring access to effective violence prevention and response services is an essential component for adolescent survival and success.

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Author contributions:

E.T and LC designed and oversaw the data collection. Y.S. and L.C. led the statistical analysis and data interpretation with contributions from E.T., S.Z., W.E.R., A. A., and M.O. All authors contributed to the writing of the manuscript and approved its final version.

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Table 1. Multivariable logistic regressions testing associations between self-reported ART adherence and undetectable viral load

<table>
<thead>
<tr>
<th>Explanatory variable</th>
<th>Baseline viral load (n=650)</th>
<th>Follow-up viral load (n=598)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AOR</td>
<td>Lower 95% CI</td>
</tr>
<tr>
<td>Self-reported adherence</td>
<td>1.457</td>
<td>1.024</td>
</tr>
<tr>
<td>Age</td>
<td>0.928</td>
<td>0.867</td>
</tr>
<tr>
<td>Sex (girl)</td>
<td>1.117</td>
<td>0.801</td>
</tr>
<tr>
<td>Rural area</td>
<td>0.948</td>
<td>0.654</td>
</tr>
<tr>
<td>Orphan</td>
<td>0.661</td>
<td>0.464</td>
</tr>
<tr>
<td>Informal housing</td>
<td>0.707</td>
<td>0.471</td>
</tr>
<tr>
<td>Horizontal infection</td>
<td>0.877</td>
<td>0.534</td>
</tr>
<tr>
<td>Poor health</td>
<td>0.459</td>
<td>0.230</td>
</tr>
</tbody>
</table>

AOR - adjusted odds ratio, 95% CI – 95% confidence interval

Table 2. Descriptive characteristics of the analytic sample (n=969)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline n (%)</th>
<th>Follow-up n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART adherence</td>
<td>642 (66)</td>
<td>628 (65)</td>
</tr>
<tr>
<td>Healthcare factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No medication stock-outs</td>
<td>918 (95)</td>
<td>920 (95)</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>740 (76)</td>
<td>625 (64)</td>
</tr>
<tr>
<td>Variables</td>
<td>Baseline n (%)</td>
<td>Follow-up n (%)</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Travel to the clinic below 1 hour</td>
<td>859 (89)</td>
<td>923 (95)</td>
</tr>
<tr>
<td>Wait time in the clinic below 1 hour</td>
<td>503 (52)</td>
<td>450 (46)</td>
</tr>
<tr>
<td><strong>Caregiving factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good monitoring and supervision</td>
<td>332 (34)</td>
<td>364 (38)</td>
</tr>
<tr>
<td>Good caregiver-teen communication</td>
<td>258 (27)</td>
<td>331 (34)</td>
</tr>
<tr>
<td>No emotional or physical violence in the past year</td>
<td>680 (70)</td>
<td>601 (62)</td>
</tr>
<tr>
<td>Not witnessing arguments or fights between adults in the home in the past week</td>
<td>859 (89)</td>
<td>861 (89)</td>
</tr>
<tr>
<td><strong>Household structure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orphan</td>
<td>578 (60)</td>
<td>592 (61)</td>
</tr>
<tr>
<td>Number of caregivers with whom the teen has ever lived</td>
<td>1.89 (1.04)</td>
<td>2.07 (1.25)</td>
</tr>
<tr>
<td>Biological parent is primary caregiver</td>
<td>423 (44)</td>
<td>395 (41)</td>
</tr>
<tr>
<td>Household size</td>
<td>6.78 (2.94)</td>
<td>6.21 (3.87)</td>
</tr>
<tr>
<td><strong>Socio-economic factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (girl)</td>
<td>532 (55)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.58 (2.87)</td>
<td>15.10 (2.87)</td>
</tr>
<tr>
<td>Rural area</td>
<td>258 (27)</td>
<td>238 (25)</td>
</tr>
<tr>
<td>Informal housing</td>
<td>180 (19)</td>
<td>141 (15)</td>
</tr>
<tr>
<td>Can afford 8 basic necessities</td>
<td>310 (32)</td>
<td>215 (22)</td>
</tr>
<tr>
<td><strong>HIV factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode of infection (horizontal)</td>
<td></td>
<td>201 (21)</td>
</tr>
<tr>
<td>Recent ART initiation (under 2 years prior to baseline)</td>
<td></td>
<td>256 (26)</td>
</tr>
</tbody>
</table>

Table 3. Multivariable probit regressions testing associations of adolescent clinic and care experiences and their adherence (n=969 people, 1,928 observations)
<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>Lower 95% CI</th>
<th>Higher 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No medication stock outs-</td>
<td>0.335</td>
<td>-0.116</td>
<td>0.786</td>
<td>0.146</td>
</tr>
<tr>
<td>Perceived confidentiality at the clinic</td>
<td>0.240*</td>
<td>0.042</td>
<td>0.438</td>
<td>0.018</td>
</tr>
<tr>
<td>Travel to the clinic below 1 hour</td>
<td>0.451*</td>
<td>0.105</td>
<td>0.796</td>
<td>0.011</td>
</tr>
<tr>
<td>Wait time in the clinic below 1 hour</td>
<td>-0.170</td>
<td>-0.352</td>
<td>0.012</td>
<td>0.068</td>
</tr>
</tbody>
</table>

*Family care factors – within-person variation*

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>Lower 95% CI</th>
<th>Higher 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good monitoring and supervision</td>
<td>-0.082</td>
<td>-0.287</td>
<td>0.124</td>
<td>0.438</td>
</tr>
<tr>
<td>Good caregiver-teen communication</td>
<td>-0.003</td>
<td>-0.196</td>
<td>0.189</td>
<td>0.972</td>
</tr>
<tr>
<td>No emotional or physical violence victimisation</td>
<td>0.378 ***</td>
<td>0.183</td>
<td>0.574</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Not witnessing any arguments or fights between adults at home</td>
<td>0.191</td>
<td>-0.083</td>
<td>0.464</td>
<td>0.171</td>
</tr>
</tbody>
</table>

*Control factors are orphanhood, caregiver being a biological parent, household size, number of previous caregivers, adolescent age, rural residence, informal housing, poverty, study wave, participant sex, mode of HIV infection, and recent ART initiation. 95% CI - confidence interval. All coefficients are presented in supplementary table 3S.*
Table 4. Adjusted average predicted probabilities of adherence at various levels of the key explanatory variables, based on regressions reported in Table 3.

<table>
<thead>
<tr>
<th>Explanatory variables</th>
<th>Adjusted probability of adherence</th>
<th>Lower 95% CI</th>
<th>Higher 95% CI</th>
<th>Difference of adjusted probabilities of adherence</th>
<th>Lower 95% CI</th>
<th>Higher 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceived confidentiality at the clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decrease in confidentiality</td>
<td>0.621</td>
<td>0.580</td>
<td>0.661</td>
<td>ref</td>
<td>0.006</td>
<td>0.137</td>
<td>0.0325</td>
</tr>
<tr>
<td>Increase in confidentiality</td>
<td>0.692</td>
<td>0.654</td>
<td>0.730</td>
<td>0.071</td>
<td>0.137</td>
<td>0.0325</td>
<td></td>
</tr>
</tbody>
</table>

| Travel to the clinic below 1 hour | | | | | | | |
| Increase in travel time | 0.586 | 0.523 | 0.649 | ref | | | |
| Decrease in travel time | 0.723 | 0.668 | 0.777 | 0.137 | 0.027 | 0.2460 | 0.0143 |

| No emotional or physical violence victimisation | | | | | | | |
| Increase in violence | 0.595 | 0.555 | 0.635 | ref | | | |
| Decrease in violence | 0.716 | 0.680 | 0.752 | 0.121 | 0.058 | 0.183 | 0.001 |

*Average adjusted probabilities are reported at the observed values of other variables in the model (average marginal effects). 95%CI - confidence interval*