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Trends in continuity of treatment among children and adolescents living with HIV in 14 districts in South Africa from 2018-2023: A retrospective program analysis

Bridget Mugisa[1,#,*], Kathleen Kehoe[1,#], Tabisa Silere-Maqetseba[2], Hlamalani Mabasa[1], Rachel Golin[3], Joel Chehab[1], Alexandra Vrazo[4], Meena Srivastava[3]

[1] Bilateral Health Office, United States Agency for International Development, Pretoria, South Africa

[2] National Department of Health, Pretoria, South Africa

[3] Office of HIV/AIDS, United States Agency for International Development (USAID), Washington, United States of America

[4] Global Health Training, Advisory, and Support Contract (GH-TASC), Credence Management Solutions LLC, supporting the Office of HIV/AIDS, United States Agency for International Development (USAID), Washington, United States of America

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ABSTRACT

Objectives: UNAIDS estimates 152,984 children under 15 years living with HIV (C/ALHIV) by 2022 in South Africa. Monitoring the continuity of antiretroviral treatment remains challenging without electronic health records. We explored treatment cohort growth and interruption trends in 14-USAID-PEPFAR-supported districts.
Methods: We reviewed data from 2018 to 2023. We triangulated this data with NAOMI HIV estimates. We used Tableau version 2023.2 for analysis to understand heterogeneity in outcomes.
Results: HIV incidence halved from 4.3 per 1000 in 2017 to 2.5 per 1000 in 2022. HIV testing doubled: 188,371 in FY19Q1 to 399,708 in FY23Q4 while testing positivity declined from 3.3% to 0.7%. Linkage to treatment increased from 67% to 102%, viral suppression increased from 79% to 84%. C/ALHIV treatment cohort started at 82,897 in FY19Q1 and increased to 105,107 in FY20Q2. Subsequently, the cohort decreased to 79,288 in FY23Q4 despite 42,498 initiations and 62,256 returns.
Conclusions: The C/ALHIV treatment and viral suppression increased substantially commensurate with expected trends. Subsequent cohort decline was aligned to vertical transmission reduction, HIV incidence decline, and expected aging. We highlight the inadequacy of the information systems to quantify losses. We underscore a need for resources to enhance program monitoring and interventions to address this gap.

Introduction

Global estimates indicate that 1.5 million (1.2 million-2.1 million) children and young adolescents aged 0-14 years were living with HIV in 2022 according to the Joint United Nations Program on AIDS (UNAIDS) [1]. UNAIDS estimates that globally, there has been a 58% decline in new HIV infections among children and young adolescents, from 310,000 in 2010 to 130,000 in 2022 [1]. As children and adolescents aged 0-19 years (C/ALHIV) initiate antiretroviral therapy (ART) early in life, some during infancy, ensuring continuity of antiretroviral treatment for life is crucial but remains difficult, as C/ALHIV are dependent on a caregiver or treatment supporter for continuous care. For large-scale pediatric HIV programs, programmatic monitoring of continuity of treatment for C/ALHIV is complex, particularly in the absence of fully integrated and synchronized electronic health record systems. Continuity of antiretroviral treatment is particularly important for children and adolescents in this sub-population because it is a determinant of viral suppression and good health outcomes throughout the life course. The World Health Organization emphasizes the need to enhance monitoring of the transitions of C/ALHIV from birth to childhood and adolescence, as treatment needs change with time [2,3]. The lack of pertinent data to support better programming has contributed to consistently poor progress on case identification and virologic suppression among children and adolescents compared to adults.

South Africa has the largest pediatric HIV epidemic globally with an estimated 152,984 children living with HIV (CLHIV) <15 years in 2023

* Corresponding author: (B. Mugisa); Tel.: + 27 636 967 910.
E-mail address: bmugisa@usaid.gov (B. Mugisa).
# Bridget Mugisa and Kathleen Kehoe contributed equally.

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according to the NAOMI district-level HIV estimates [4]. The 2023 South Africa National HIV Prevalence, Incidence, Behavior, and Communication Survey (SABSSM VI) showed an overall reduction in HIV prevalence from 2.8% in 2017 to 2.4% in 2022 among children <15 years of age. SABSSM VI also showed that HIV prevalence among adolescent females aged 15-19 years was almost two-fold higher than males (5.7% vs 3.1%) in 2022 [5]. Although great strides have been made with the HIV response, children remain disproportionately affected and left behind. According to national programmatic data, 82% of CLHIV under 15 years were of known HIV status, compared to 96% for adult females and 94% for adult males. 73% of CLHIV under 15 years were on treatment, compared to 81% for adult females and 73% for adult males, in 2022 [4].

Both national program data and PEPFAR program reports show frequent and cyclical treatment interruption among children and adolescents on antiretroviral treatment in 2023 [6,7]. These findings, similar to other studies such as Pennar et al in 2019, revealed patterns of interruption and re-engagement in care in high-burden HIV settings [8]. In addition, the transition from pediatric to adolescent and adult HIV care clinics results in lower retention especially for adolescents who acquired HIV through perinatal transmission according to studies such as Zanoni et al in 2020 [9].

Closing the antiretroviral treatment gap among C/ALHIV requires stringent monitoring of continuity of treatment. Little is known about the continuity of treatment throughout the life course of C/ALHIV in the absence of cohort monitoring systems using electronic medical records. We aimed to explore trends in treatment interruption and growth for C/ALHIV using available routine data in 14 districts supported under the United States President's Emergency Plan for AIDS Relief (PEPFAR), through the United States Agency for Agency for International Development (USAID) in South Africa.

Methods

Study type, population, and setting

We conducted a retrospective program analysis of data reported during the 5-year period from 2018 to 2023. We included aggregated data for C/ALHIV aged 0-19 years from 14 districts located in four provinces, that were consistently reporting and continuously supported by USAID over the 5-year period. The data are presented for the United States (US) Government fiscal years (FY), which span from October through September of the following calendar year. Data are reported in quarters comprising October to December (Q1), January to March (Q2) April to June (Q3), and July to September (Q4). Data from October 01, 2018, to September 30, 2023, were included. PEPFAR-USAID reporting systems were changed in June 2020 (FY20Q3) to ensure consistent and uniform definitions and generation of all reports through the National Department of Health information systems, rather than through PEPFAR-USAID implementing partner reporting systems.

Data sources

We used district-level HIV estimates that are developed annually from the NAOMI model, a small-area estimation model that synthesizes population-based surveys, surveillance, and program data [4]. We used the number of new HIV infections and population estimates to determine HIV incidence overall and for 0-14-, and 15-19-year age bands. We abstracted routine aggregated program data reported by USAID South Africa district support partners in PEPFAR's Data for Accountability, Transparency and Impact Monitoring (DATIM), according to PEPFAR Monitoring, Evaluation and Reporting Guidelines [10]. A select set of HIV indicators were abstracted from the national electronic reporting system, known as the Three Interlinked Electronic Registers (TIER.Net), which collates data from primary healthcare facilities to the district, provincial, and national levels, and subsequently are recorded in DATIM [11]. These indicators were disaggregated by age in 5-year age bands up to 19 years of age. No individual patient data were included.

Data variables

Indicators for children and adolescents included the number who: (i) received testing services, (ii) tested HIV positive, (iii) linked to treatment, (iv) newly initiated ART, (v) currently on ART without a reported interruption in 28+ days, (vi) experienced treatment interruptions 28+ days from the last clinical or medication pick-up appointment date, disaggregated by: timing on ART at time of interruption, mortality, transfer-out or refusal/stopped treatment, (vii) returned to treatment after experiencing a treatment interruption, (viii) had a documented viral load test, and (ix) had a documented suppressed viral load result. These indicators were defined as service quality indicators and were abstracted based on data availability.

Data analysis

Using the estimates from the NAOMI model, we calculated the HIV incidence by dividing the number of new HIV infections by the total population and compared the 2017 to 2022 values. We did this for the lower and upper bounds to calculate the 95% confidence intervals. Using the programme data, we reported key indicators across the clinical cascade and calculated key metrics to monitor program fluctuations as detailed in Table 1. These included: HIV testing positivity, proxy linkage to ART, proxy viral load testing coverage, adjusted viral load suppression rate, treatment growth, total treatment interruptions, and treatment interruptions for children <3 months on ART. Viral load suppression was defined as plasma HIV RNA <1000 copies/ml. The denominators used to determine treatment interruptions were calculated to represent a proxy cohort, given that the program data are recorded quarterly in aggregate and not for treatment cohorts. We analyzed and visualized data using Tableau version 2023.2 [12].

Table 1
Calculations for key metrics visualized and described in the results using programmatic data.

Metric	Calculation
HIV testing positivity (%)	Number of persons tested positive for HIV/Number of persons tested for HIV
Proxy linkage to antiretroviral treatment (%)	Number of persons initiated on HIV treatment/Number of persons tested positive for HIV
Proxy viral load testing coverage (%)	Number of persons with a viral load test/Number of persons on ART 6 months prior
Adjusted viral suppression rate (%)	Number of persons with suppressed viral load/Number of persons with a viral load test
Antiretroviral treatment (ART) growth (%)	[Number of persons on ART in the current quarter – Number of persons on ART in the previous quarter]/Number of persons on ART in the previous quarter
Proportion of persons interrupting antiretroviral treatment (%)	Number of persons interrupting ART in the current quarter / [Number of persons on ART in the previous quarter + Number of persons initiating ART in the current quarter]
Number of treatment interruptions for persons on antiretroviral treatment for <3 months	Number of persons on ART for <3 months reported as interrupting ART in the current quarter / [$\frac{1}{2}$ of persons initiating ART in the previous quarter + $\frac{1}{4}$ persons initiating ART in the current quarter]

ART, antiretroviral therapy.

Table 2
Quarterly key indicators for children and adolescents aged 0-19 years in 14 USAID-supported districts in South Africa.

	Age range	FY 2019 Quarter 1 (October-December 2019)	Quarterly sum or average (<19 years)	FY2023 Quarter 4 (July-September 2023)	Quarterly sum or average (<19 years)
HIV incidence (new HIV infections per 1000 persons)	0-14 years	0.04[a] (95% CI: 0.03-0.05)	N/A	0.03[b] (95% CI: 0.02-0.04)	N/A
	15-19 years	7.89[a] (95% CI: 5.92-10.22)		4.90[b] (95% CI: 3.41-6.83)	
Number of persons receiving an HIV test	0-14 years	85,548	188,371	186,538	399,708
	15-19 years	102,823		213,170	
Number of persons diagnosed as HIV-positive	0-14 years	2750	6230	770	2664
	15-19 years	3480		1894	
HIV testing positivity yield (%)	0-14 years	3.2%	3.3%	0.4%	0.7%
	15-19 years	3.4%		0.9%	
Number of persons initiated in antiretroviral treatment	0-14 years	1695	4179	948	2735
	15-19 years	2484		1787	
Proxy linkage to antiretroviral treatment (%)	0-14 years	61.6%	67%	123.1%	102%
	15-19 years	71.3%		94.4%	
Number of persons continuing antiretroviral treatment	0-14 years	51,464	82,897	38,839	79,288
	15-19 years	31,433		40,449	
Number of persons receiving a viral load test	0-14 years	39,699	63,620	32,374	64,932
	15-19 years	23,921		32,558	
Proxy viral load testing coverage (%)	0-14 years	126%	90%	81%	82%
	15-19 years	66%		82%	
Number of persons with viral load <1000 copies/ml	0-14 years	31,591	50,153	26,430	54,226
	15-19 years	18,562		27,796	
Adjusted viral suppression rate (%)	0-14 years	80%	79%	82%	84%
	15-19 years	78%		85%	

[a] 2017.
[b] 2022.

Results

HIV incidence, case finding, and treatment initiation

During this period, HIV incidence among those aged <19 years halved from 4.25 (95% confidence interval [CI]: 3.18-5.55]) in 2017 to 2.47 (95% CI: 1.73-3.450) infections per 1000 persons in 2022 (Table 2). Adolescents aged 15-19 years had a 37.9% reduction in HIV incidence (7.89 compared to 4.90 new HIV infections per 1000 persons), children <15 years had a 25% reduction in HIV incidence (0.04 compared to 0.03 new HIV infections per 1000 persons) between 2017 and 2022 (Table 2). Quarterly testing increased among children and adolescents doubled from 188,371 in December 2018 (FY19Q1) to 399,708 in October 2023 (FY23Q4). While there was an increase in testing, the HIV testing positivity declined from 3.3% to 0.7%, and a reduction in the number of children and adolescents diagnosed with HIV from 6,230 in December 2018 (FY19Q1) to 2,664 in October 2023 (FY23Q4) (Table 2). There was a proportionate halving of the number of C/ALHIV newly initiated on antiretroviral treatment from 4,149 in December 2018 (FY19Q1) to 2,735 in October 2023 (FY23Q4). Overall, linkage to treatment for C/ALHIV improved from 67% in December 2018 (FY19Q1) to 102% in September 2023 (FY23Q4); with some positive C/ALHIV identified in the previous quarter initiated on treatment in FY23Q4 (Table 2).

The greatest declines were reported in September 2020 (FY20Q4) at 2,972 new initiations—coinciding with the strictest COVID-19 lockdown periods—compared to the 5,103 new initiations reported in March 2023 (FY22Q2). Proxy viral load testing coverage decreased from 90% in FY19Q1 to 82% in FY23Q4; with the adjusted viral suppression rate increasing from 79% to 84%. Overall, the number of C/ALHIV on treatment reduced from 82,897 to 79,288 during this period (Table 2).

Antiretroviral treatment cohort gains and losses

An in-depth analysis of patterns of treatment gains and losses, quarter on quarter, revealed that the number of C/ALHIV receiving treatment peaked at 105,107 in March 2020 (FY20Q1), representing a 57% growth over 2.5 years when compared to 66,790 in March 2018 (Figure 1). From December 2018 (FY19Q1) to March 2020 (FY20Q2), the treatment cohort growth of 33,677 was attributed more to new initiations (30,559) than returns to care (estimated as returns to care were not reported up to this point). After the March 2020 (FY20Q2) peak, there was a 24.5% reduction in those on ART to 79,288 in September 2023 (FY23Q4), despite 42,498 ART initiations and 62,256 returns in the same period (Figure 1).

Those interrupting treatment ranged from 3-8% of the treatment cohort each year during this period (Figure 1); C/ALHIV were reported as interrupting treatment if they missed their scheduled clinical or medication pick-up appointment for more than 28 days. The highest interruptions in treatment of 14.4% occurred in June 2020 (FY20Q3) in line with changes in reporting systems. The proportion of C/ALHIV interrupting treatment increased (range: 6-8%) during the COVID-19 pandemic lockdown (i.e., June 2020 [FY20Q3] to December 2020 [FY21Q1]) with improvements (range: 3-6%) after the restrictions were lifted (Figure 2). Treatment interruption within 3 months following treatment initiation ranged from 9-32% and was marked by seasonality, with double the proportion of C/ALHIV interrupting treatment during the holiday months (FYQ4 and FYQ1) compared to the non-holiday months (FYQ2 and FYQ3) (Figure 2). During this 5-year period, 1298 deaths among C/ALHIV on ART occurred, while 17,944 C/ALHIV on ART were recorded as having transferred (without method for verification) to other non-USAID-PEPFAR-supported facilities.

Lastly, return into care was lowest in the first two quarters of reporting (1151 in December 2019 [FY19Q1] and 1967 in March 2019 [FY19 Q2]), but more than doubled to 4772 in June 2020 (FY20 Q3), coinciding with standardization of reporting through the National Department of Health. Thereafter, return to care typically peaked in March annually, after the holiday period. Finally, there was no reporting or method to derive from the data set the number or proportion of children <15 years who turned 15 years of age and continued treatment during this period.

Discussion/interpretation

Our main findings demonstrate that the cumulative number of C/ALHIV continuing HIV treatment is commensurate with the expected cohort group in this sub-population, given the trends in treatment inter-

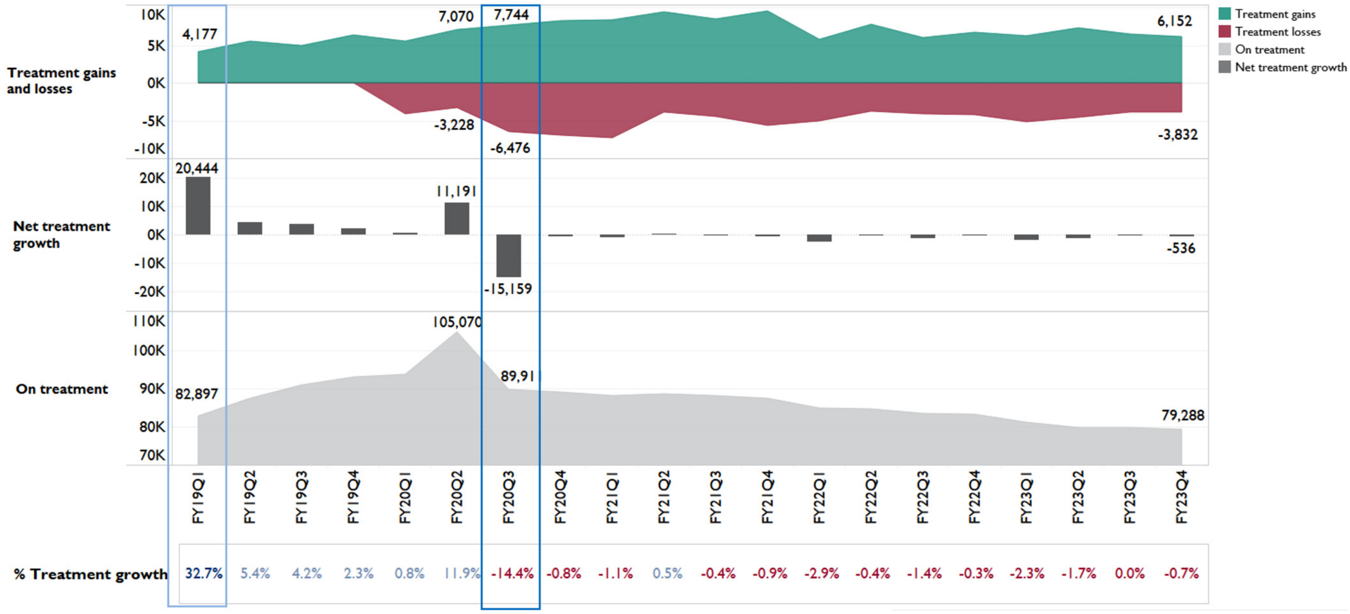

Figure 1. Quarterly trends of HIV treatment gains and losses, net treatment growth, and treatment continuity among children and adolescents aged 0-19 years in 14 United States Agency for International Development-supported districts in South Africa, 2018-2023. The light blue box represents the period in which the reporting definition for persons on treatment changed from 90 days to 28 days since the last visit. The dark blue box represents the change in reporting through the National Department of Health information systems, with consistent and uniform definitions, rather than through individual United States Agency for International Development implementing partner reporting systems.

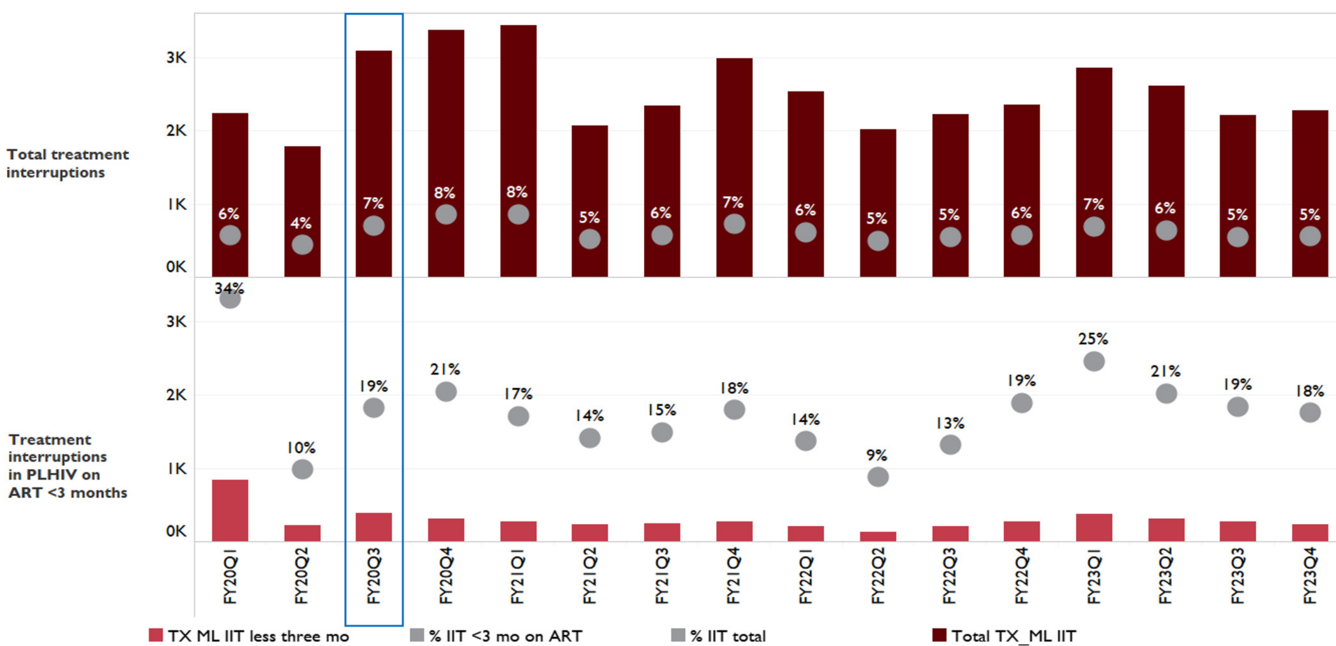

Figure 2. Quarterly trends in total interruptions and interruptions <3 months on HIV treatment among children aged 0-19 years in 14 United States Agency for International Development-supported districts in South Africa, 2019-2023. The dark blue box represents the change in reporting through the National Department of Health information systems, with consistent and uniform definitions, rather than through the United States Agency for International Development implementing partner reporting systems.

ruption and expected aging. This was evidenced by fewer cases being identified over time, despite an increase in testing for children and adolescents, suggesting that case identification gaps were being closed. This finding is similar to other studies such as Traub et al. [13] and Penazzato et al. [14] that demonstrated pediatric case identification trends [15]. Overall, there was a 4.4% reduction in the treatment cohort for C/ALHIV despite new initiations and returns to care. These findings correlate with the reduction in HIV incidence and estimated persons living with HIV for this sub-population over this period. This is further supported by South Africa's tremendous progress in the reduction of vertical transmission rates from 24.5% in 2000 to 2.32% in 2024 according to the NAOMI estimates [4].

The improvement in service quality indicators pointed to optimization of service delivery as the improvements in viral load testing and suppression, and linkage to treatment confirmed the closing of the gaps in treatment coverage for this population, similar to reports by UNICEF in 2020 [16]. Subsequently, there was a nexus between HIV estimates, treatment coverage, and viral suppression for this sub-population. Similarly, Zuma et al. [17] and Mukonda et al. [18] showed with their publications the estimation of population-level viral suppression. The spikes and dips in the treatment cohort were attributed to the standardization of reporting systems to ensure that all reporting was done using the National Department of Health district health information systems. As these systems utilize aggregate data, this analysis did not account for each individual longitudinally but rather used proxies to approximate those continuing treatments over time.

Our analyses indicate that treatment interruptions among C/ALHIV are cyclical and occur in a seasonal pattern, with additional impact from the COVID-19 pandemic [19]. Reviews of overall PEPFAR programmatic data in South Africa confirm a similar trend among the adult population on ART. Particularly, we observed that the treatment cohort for adolescents aged 15-19 years remained fairly stable throughout this review period, pointing to the possibility that these are adolescents who were perinatally infected prior to the Option B+ era. This finding is similar to other studies, such as Dollfuss et al in 2010, who prospectively followed children who acquired HIV perinatally into adolescence and found that they thrived despite being born in an era with limited therapeutic options [20–24].

Patterns of health-seeking behavior may be indicative of how social dynamics and socioeconomic status influence the continuity of long-term treatment for chronic conditions. Additionally, these social constraints were likely drivers of treatment interruptions specifically related to mobility as C/ALHIV are dependent on caregivers for continuous care. This finding is similar to Slogrove et al in 2018 and Dorward et al in 2020 which conducted a cohort analysis for adolescents with perinatally acquired HIV [25–27]. A look at mortality trends over the period of analysis did not reveal a correlation between an increase in deaths during the periods of increased treatment interruption, further supporting those social determinants. A comparison of these trends in treatment interruption, with the disruptions that occurred during the COVID-19 pandemic lockdown periods, revealed that the program losses never fully rebounded to previous levels across both the adult and pediatric treatment programs. This finding is also corroborated by other studies such as Davies et al. [22] and Bachanas et al. [28] that showed how treatment interruptions during COVID-19 lockdowns impacted mortality [29–31]. This lack of rebound was aggravated by system limitations due to lacking unique patient identifiers to ensure precise monitoring of cohorts. This inadequacy in monitoring systems is also demonstrated by Sohn et al. [32] in a study in 2018 that utilized observational data to inform policy change for monitoring children and youth.

Overall, these trends in the treatment cohort size over time and trends in the cohort declines raise concern for treatment interruption, but mostly emphasize the need for better cohort monitoring strategies that can distinguish *true treatment interruptions* (that warrant further investigation into causes and mitigating interventions) from *benign reasons for decline* (aging out and silent transfers to continued treatment elsewhere).

Limitations

The findings in this review have some limitations. First, the lack of a synchronized health information system with unique patient identifiers limited the precision with which this analysis could monitor the continuity of treatment for C/ALHIV throughout the life course as aggregate data and proxy indicators were used. To control for this limitation, we compared our findings with other districts that are not supported by USAID (data available on request), and this analysis revealed similar trends. Second, returns to care were only reported for four years of the 5-year period due to PEPFAR MER guidelines change starting in FY20 Q1, and as such, it is likely that treatment gains might be underestimated in our findings. Thirdly, we were limited by the data available in DATIM. For example, we may have underestimated the number of losses from the C/ALHIV treatment cohort, given that deaths may be underreported at facilities.

Conclusion

From 2018 to 2023, the number of C/ALHIV on treatment and viral suppression increased substantially; this increase coincides with the notable decrease in HIV incidence and is commensurate with the expected trends in continuity of treatment. The reductions noted in the pediatric and adolescent treatment cohorts are well aligned with the success of the vertical transmission prevention program and expected aging in this mature program. These findings highlight that the pediatric and adolescent HIV programs are closing the remaining gaps evidenced by the improvements in service quality indicators such as linkage to treatment and viral suppression. Although treatment interruptions occurred, these were seasonal and impacted by the COVID-19 pandemic and health-seeking behaviors. These findings point to the need to accelerate three key interventions to close the remaining gaps. First, augment support for health information systems to account for C/ALHIV on treatment throughout the life course while accounting for program losses due to actual treatment interruptions. Second, mitigate further vertical transmission to reduce HIV incidence. Lastly, utilize multi-pronged approaches to reduce treatment interruptions through more investment in social behavior change interventions for caregivers and young CLHIV as they age to adolescence while addressing socioeconomic determinants of health.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval

Ethics clearance was not needed for this review as no personal identifiable information was used. Client consent was not required as the authors neither interacted with the clients nor had access to identifiable data.

Author contributions

BM was the lead author responsible for conceptualization of the work and incorporation of all intellectual content including feedback from the other authors. K.K. led the acquisition of the data, reviewed data quality, verified with different data sources, performed the statistical analyses, and developed the data visualizations. B.M. and K.K. wrote the manuscript. M.S., R.G, J.C., H.L., A.V., and T.S.M. contributed to the conceptualization and provided intellectual input into shaping the manuscript. All authors provided valuable input to the interpretation of the data and critically reviewed the paper for important intellectual content. All authors reviewed and approved the final version of the manuscript.

Data sharing

Publicly available datasets were analyzed in this study, accessible at https://data.pepfar.gov/. Correspondence for the data should be addressed to the corresponding author.

Disclaimer

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2024.100435.

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