Check for updates

BRIEF REPORT

Children and adolescents on anti-retroviral therapy in Bulawayo, Zimbabwe: How many are virally suppressed by month six? [version 1; peer review: 2 approved, 1 approved with reservations]

Silungile Moyo[1], Ronald Thulani Ncube[2], Hemant Deepak Shewade [ID] [3,4], Solwayo Ngwenya [ID] [1], Wedu Ndebele[1], Kudakwashe Collin Takarinda[3,5], Janet Dzangare[5], Tafadzwa Priscilla Goverwa-Sibanda[6], Tsitsi Apollo[5]

[1]Mpilo Central Hospital, Bulawayo, Zimbabwe
[2]The Union Zimbabwe Office, Harare, Zimbabwe
[3]International Union Against Tuberculosis and Lung Disease (The Union), Paris, France
[4]The Union South East Asia Office, New Delhi, India
[5]AIDS and TB Directorate, Ministry of Health and Child Care, Harare, Zimbabwe
[6]AIDS Health Care Foundation, Harare, Zimbabwe

Abstract

Background: Zimbabwe is one of the countries in sub-Saharan Africa disproportionately affected by human immunodeficiency virus. In the "treat all" era, we assessed the gaps in routine viral load (VL) monitoring at six months for children (0-9 years) and adolescents (10-19 years) newly initiated on anti-retroviral therapy (ART) from January 2017 to September 2018 at a large tertiary hospital in Bulawayo.
Methods: In this cohort study using secondary data, we considered first VL done within six to nine months of starting therapy as 'undergoing VL test at six months'. We classified repeat VL≥1000 copies/ml despite enhanced adherence counselling as virally unsuppressed.
Results: Of 295 patients initiated on ART, 196 (66%) were children and 99 (34%) adolescents. A total 244 (83%) underwent VL test at six months, with 161 (54%) virally suppressed, 52 (18%) unsuppressed and 82 (28%) with unknown status (due to losses in the cascade). Switch to second line was seen in 35% (18/52). When compared to children, adolescents were less likely to undergo a VL test at six months (73% versus 88%, p=0.002) and more likely to have an unknown VL status (40% versus 22%, p=0.001).
Conclusion: At six months of ART, viral suppression was low and losses in the cascade high.

Keywords
Children living with HIV, Adolescent living with HIV, EAC, Mpilo, Operational research, SORT IT

Open Peer Review

Reviewer Status ✓ ✓ ?

	Invited Reviewers		
	1	**2**	**3**
version 1 16 Mar 2020	✓ report	✓ report	? report

1   **Obinna Ikechukwu Ekwunife** [ID] , Nnamdi Azikiwe University, Awka, Nigeria

2   **Brian van Wyk** [ID] , University of the Western Cape, Cape Town, South Africa

3   **Catherine Kegakilwe Koofhethile** [ID] , Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana
Harvard T.H. Chan School of Public Health, Boston, USA

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding authors: Silungile Moyo (silungile@yahoo.com), Hemant Deepak Shewade (hemantjipmer@gmail.com)

Author roles: Moyo S: Conceptualization, Data Curation, Formal Analysis, Methodology, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Ncube RT**: Conceptualization, Formal Analysis, Methodology, Software, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Shewade HD**: Conceptualization, Formal Analysis, Methodology, Software, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Ngwenya S**: Conceptualization, Methodology, Writing – Review & Editing; **Ndebele W**: Conceptualization, Methodology, Writing – Review & Editing; **Takarinda KC**: Data Curation, Writing – Review & Editing; **Dzangare J**: Data Curation, Writing – Review & Editing; **Goverwa-Sibanda TP**: Data Curation, Writing – Review & Editing; **Apollo T**: Conceptualization, Methodology, Project Administration, Supervision, Writing – Review & Editing

How to cite this article: Moyo S, Ncube RT, Shewade HD *et al.* **Children and adolescents on anti-retroviral therapy in Bulawayo, Zimbabwe: How many are virally suppressed by month six? [version 1; peer review: 2 approved, 1 approved with reservations]** F1000Research 2020, **9**:191 https://doi.org/10.12688/f1000research.22744.1

First published: 16 Mar 2020, **9**:191 https://doi.org/10.12688/f1000research.22744.1

Introduction

In 2014, the Joint United Nations Programme HIV/AIDS (UNAIDS) announced ambitious new global 90-90-90 fast-track HIV targets for 2020[1]. These targets were further supported by the 2016 "treat-all" WHO recommendations[2]. With the expansion of anti-retroviral treatment (ART) coverage, investments in the global response are shifting towards sustained viral suppression for improved survival and epidemic control. This is in the context of scaling up viral load (VL) monitoring to ensure 90% of people in care are virally suppressed (VL<1000 copies per ml)[3]. Globally in 2018, only 918 000 (54%) children aged 0–14 years living with HIV received ART[4]. HIV is among the top 10 leading causes of death among adolescents, a period where sustained adherence is particularly challenging, the only age group where deaths from HIV has not decreased[5].

Zimbabwe is disproportionately affected by HIV. In 2017, 1.4 million people were living with HIV, with 5.8% being children 0–14 years[6]. An estimated 15% on ART have high VL[7]. The national ART guidelines recommend routine VL monitoring at six and 12 months, and then annually if stable on ART[8]. The extent to which routine VL monitoring is being implemented specifically for children and adolescents in the "treat-all" era has not been explored in Zimbabwe. We therefore assessed the gaps in routine VL monitoring at six months for children (0–9 years) and adolescents (10–19 years) initiated on ART at a large tertiary hospital in Bulawayo, Zimbabwe.

Methods

Study design
We conducted a cohort study involving secondary data.

Setting
Mpilo Opportunistic Infections (OI) Clinic is within Mpilo Central Hospital in Bulawayo (the second largest city in Zimbabwe). It is a tertiary facility, managing complicated referrals, including patients on second and third line treatment. VL testing is offered as per national guidelines at the hospital HIV laboratory, adjacent to the clinic. Patient data are routinely entered in the electronic point of care database, ART register and patient care booklet[8].

First line ART regimen for children <3 years is ABC+3TC+LPV/R or AZT+3TC+LPV/r. Children 3–9 years and adolescents <35kg receive AZT+3TC+NVP or ABC+3TC+EFV, while adolescents >35kg receive TDF+3TC+NVP or EFV[8]. Those with VL ≥1000 copies/ml at six-months are offered enhanced adherence counseling (EAC), and a second VL test after three months. A repeat VL ≥1000 copies/ml (despite EAC) is classified as virally unsuppressed, and eligible for second line ART[8].

Study population
We included all children (0–9 years) and adolescents (10–19 years) newly initiated on first line ART at Mpilo OI Clinic between January 2017 and September 2018.

Data extraction and analysis
We extracted anonymized patient data from electronic patient and laboratory databases, analyzed using STATA (version12.1 STATA Corp., College Station, TX, USA). If data were missing in electronic databases, we referred to paper-based registers and booklets. We defined low CD4 count as follows: CD4 count ≤350 cells/mm^3 for children and adolescents >5 years, and CD4% <25% of total lymphocytes for children <5years[8]. We defined 'undergoing VL testing at six months' as those with first VL tests done within six to nine months of starting ART. Comparisons were made between children and adolescents using chi squared test.

Ethics
We received ethics approval from Medical Research Council of Zimbabwe (MRCZ E/248), The Union Ethics Advisory Group, Paris, France (EAG 52/19) and the Mpilo Hospital Ethics Board. As the study involved review of secondary data, the ethics committee(s) waived the need for written informed consent.
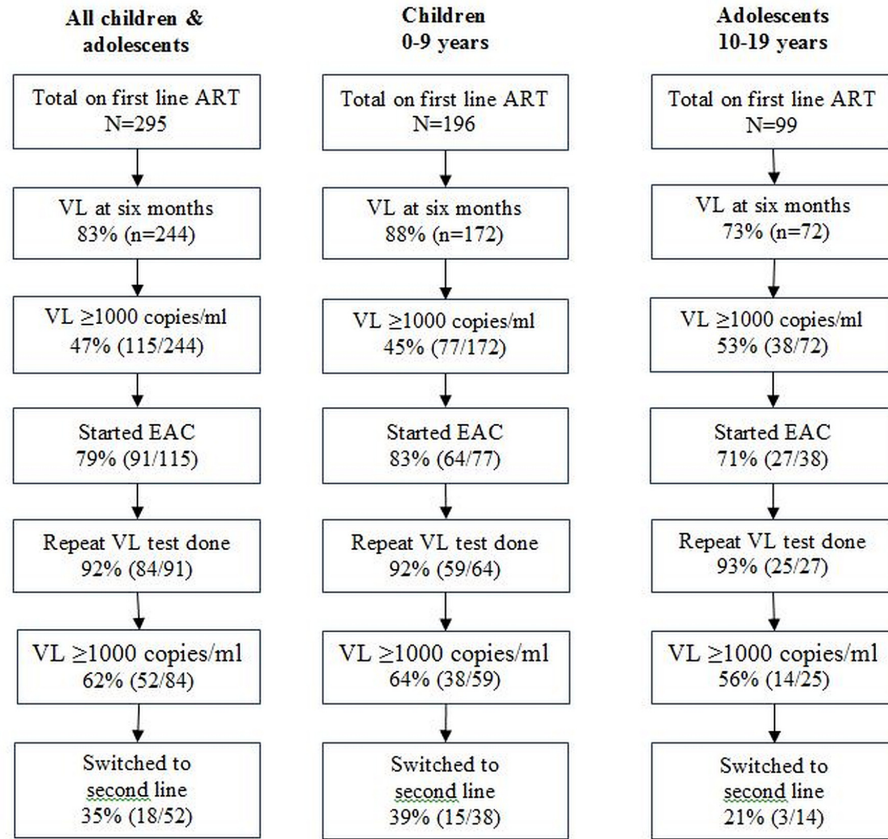
Results

Of 295 patients initiated on ART during the study period, 196 (66%) were children and 99 (34%) adolescents. A total 141 (48%) were boys, 209 (71%) were WHO stage I or II, and 119 (40%) had severe anemia. Baseline CD4 count was available for 188, among whom 94 (50%) had low CD4 cell count.

Of 295, a total of 244 (83%) underwent VL test at six months, which was significantly lower among adolescents when compared to children (73% versus 88%, p=0.002) (Figure 1). Of 295, 52 (18%) were virally unsuppressed, 161 (54%) virally suppressed and 82 (28%) unknown (unknown due to loss to follow up after ART initiation). Unsuppressed VL was not different among children and adolescents, though unknown VL suppression status, was higher among adolescents (40% versus 22%, p=0.001) (Table 1). Switch to second line was among 18 out of 52 eligible (35%), with no significant difference between adolescents and children (21% versus 39%, p=0.376) (Figure 1).

Discussion

This is one of the first studies from Zimbabwe attempting to assess the extent to which routine VL monitoring at six months is being implemented, specifically for children and adolescents in the "treat-all" era.

Overall, one in five of those initiated on ART were virally unsuppressed at six months. The true estimate could be higher considering viral suppression was unknown for one-third of children. High unsuppressed VL and the observed attrition along the care cascade, undermines the last '90' of the UNAIDS 90-90-90 targets in this special sub-population[1]. In this study, adolescents were more likely to be lost in the cascade compared to children, calling for focussed interventions for this sub-group. This is inspite of a comprehensive adolescent ART

All children & adolescents	Children 0-9 years	Adolescents 10-19 years
Total on first line ART N=295	Total on first line ART N=196	Total on first line ART N=99
VL at six months 83% (n=244)	VL at six months 88% (n=172)	VL at six months 73% (n=72)
VL ≥1000 copies/ml 47% (115/244)	VL ≥1000 copies/ml 45% (77/172)	VL ≥1000 copies/ml 53% (38/72)
Started EAC 79% (91/115)	Started EAC 83% (64/77)	Started EAC 71% (27/38)
Repeat VL test done 92% (84/91)	Repeat VL test done 92% (59/64)	Repeat VL test done 93% (25/27)
VL ≥1000 copies/ml 62% (52/84)	VL ≥1000 copies/ml 64% (38/59)	VL ≥1000 copies/ml 56% (14/25)
Switched to second line 35% (18/52)	Switched to second line 39% (15/38)	Switched to second line 21% (3/14)

Figure 1. Viral load monitoring cascade for children and adolescents with HIV newly initiated on ART during January 2017 to 30 September 2019 at Mpilo Central Hospital, Bulawayo, Zimbabwe. HIV=human immunodeficiency virus; ART=antiretroviral therapy; VL=viral load; EAC= enhanced adherence counselling.

Table 1. Viral suppression at six months among children and adolescents with HIV newly initiated on ART during January 2017 to 30 September 2019 at Mpilo Central Hospital, Bulawayo, Zimbabwe.

	Overall (0–19 years)		Children (0–9 years)		Adolescents (10–19 years)	
	N	(%)	N	(%)	N	(%)
Total	295	(100)	196	(100)	99	(100)
Virally unsuppressed*	52	(18)	38	(19)	14	(14)
Virally suppressed**	161	(54)	116	(59)	45	(46)
Unknown***	82	(28)	42	(22)	40	(40)

Col%

HIV=human immunodeficiency virus; ART=antiretroviral therapy.

*repeat VL≥1000 copies per ml despite enhanced adherence counseling; **VL<1000 at six months or after repeat VL testing (post enhanced adherence counseling); ***not fitting into any of the above two categories, represents children or adolescents that were lost at any point in the cascade.

program at the clinic, and suggests a reversal of gains made earlier in the progarm[9].

Compared to findings in Harare, where two-thirds of those virally unsuppressed were switched to second line ART, only one-third were switched in our study[10]. Adherence to national ART guidelines should be an important priority focus in routine clinical mentorship[11].

Four in five underwent VL test by six months and EAC in our study, consistent with findings in Harare[10]. However, we found high proportion with VL≥1000 copies/ml at first and repeat testing. In Swaziland, children and adolescents were more likely to have high VLs and the least likely to achieve viral suppression. This calls for ART treatment support to address adherence problems of children and adolescents[12].

The study had some limitations. Missing last visit dates prevented computation of proportion undergoing VL test among those retained at six-months. Missing baseline characteristics precluded analysis of factors associated with not undergoing a VL test and unsuppressed VL.

In conclusion, our study points to gaps in VL monitoring among children and adolescents in Bulawayo. Future studies are needed to understand reasons for attrition along the care cascade to better target interventions.

Data availability

Underlying data

Figshare: Dataset for Moyo S *et al.* study: https://doi.org/10.6084/m9.figshare.c.4884726.v1[13]

File 'silungiledata' contains all de-identified variables extracted for this study, alongside a codebook explaining all fields and field values.

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

Acknowledgements

We acknowledge Anna Fambira for her support in data extraction.

Disclaimer

The views represented here are those of the authors and do not represent the institutions they are affiliated to.

References

1. UNAIDS: **90-90-90: A transformative agenda to leave no one behind.** Geneva, Switzerland, 2014.
   Reference Source

2. World Health Organization: **Consolidated guidelines on the use of Antiretroviral drugs for treating and preventing HIV infection; 2016 recommendations for a public health approach.** 2nd ed. Geneva, Switzerland. 2016.
   Reference Source

3. Piot P, Quinn TC: **Response to the AIDS pandemic--a global health model.** *N Engl J Med.* 2013; **368**(23): 2210–2218.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

4. UNAIDS: **Fact Sheet - Global AIDS Update 2019.** Geneva, Switzerland.
   Reference Source

5. Kim SH, Gerver SM, Fidler S, *et al.*: **Adherence to antiretroviral therapy in adolescents living with HIV: Systematic review and meta-analysis.** *AIDS.* 2014; **28**(13): 1945–1956.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

6. Zimbabwe Ministry of Health and Child Care: **Zimbabwe National and Sub-National HIV estimates report 2017.** Harare, Zimbabwe. 2018.
   Reference Source

7. Ministry of Health and Child Care: **Zimbabwe Population-based HIV Impact Assessment Report.** Harare, Zimbabwe. 2016.
   Reference Source

8. Ministry of Health and Child Care: **Guidelines for Antiretroviral Therapy for the Prevention and Treatment of Guidelines for Antiretroviral Therapy for the Prevention and Treatment of HIV in Zimbabwe.** Harare, Zimbabwe. 2016.
   Reference Source

9. Shroufi A, Gunguwo H, Dixon M, *et al.*: **HIV-infected adolescents in southern Africa can achieve good treatment outcomes: results from a retrospective cohort study.** *AIDS.* 2013; **27**(12): 1971–1978.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

10. Bvochora T, Satyanarayana S, Takarinda CK, *et al.*: **Enhanced adherence counselling and viral load suppression in HIV seropositive patients with an initial high viral load in Harare, Zimbabwe: Operational issues.** *PLoS One.* 2019; **14**(2): e0211326.
    PubMed Abstract | **Publisher Full Text** | **Free Full Text**

11. World Health Organization: **WHO recommendations for clinical mentoring to support scale-up of HIV care, antiretroviral therapy and prevention in resource-constrained settings.** Geneva, Switzerland. 2005.
    Reference Source

12. Jobanputra K, Parker LA, Azih C, *et al.*: **Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland.** *PLoS One.* 2015; **10**(2): e0116144.
    PubMed Abstract | **Publisher Full Text** | **Free Full Text**

13. Shewade, HD: **Codebook for dataset Moyo S et al study.** *figshare.* Online resource. 2020.
    http://www.doi.org/10.6084/m9.figshare.11948475.v1

Open Peer Review

Current Peer Review Status: ✓ ✓ ?

Version 1

Reviewer Report 26 May 2020

https://doi.org/10.5256/f1000research.25113.r61603

? **Catherine Kegakilwe Koofhethile** iD

1 Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana
2 Harvard T.H. Chan School of Public Health, Boston, MA, USA

I think that this manuscript is addressing a very important gap in knowledge that is relevant for the current 'treat all' recommendations.

They accessed the gaps in routine viral load monitoring at six months for children and adolescents who initiated antiretroviral therapy in a hospital in Zimbabwe. Their sample number is good enough for this analysis. The manuscript is very well written, it is very clear and concise. The study was based on analysis of secondary data which was approved by IRB.

I only have one comment that need clarification- the authors keep comparing their analysis with a study done in Harare and it is not clear whether this study that they are comparing to was conducted on adult population or the same population as they describe in their analysis. This needs to be clarified. In addition, they need to explain what could be accounting for the differences found.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
No source data required

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Immunology, HIV,

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 28 April 2020

https://doi.org/10.5256/f1000research.25113.r61601

Brian van Wyk iD
School of Public Health, University of the Western Cape, Cape Town, South Africa

The study reports on viral load monitoring at 6 months for of children and adolescents who were initiated on HIV treatment in a tertiary hospital in Bulawayo. The study is important because of the HIV epidemic in Zimbabwe, and the need to reach the third 90 of UNAIDS 90-90-90 targets.

The methodology is sound and clearly reported on. Appropriate statistical analysis is done, and these are aligned with the objectives of the study.

Few other sociodemographic and clinical factors were collected and analysed; which is a limitation to the study. This should be indicated.

In the discussion, enhanced adherence counseling is mentioned as being implemented in the hospital. However, little information on this is provided in the background. Also, it would be useful if the analysis could report on how many of the current cohort received enhanced adherence counseling.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: HIV/AIDS; Health Systems; Adolescent Health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 29 Apr 2020
Hemant Deepak Shewade, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

Thank you very much for your constructive comments.

Reviewer
Few other sociodemographic and clinical factors were collected and analysed; which is a limitation to the study.
Authors
We have included this and mentioned it as a limitation in the last but one paragraph of the discussion section. We hope this is fine.

Reviewer
In the discussion, enhanced adherence counseling is mentioned as being implemented in the hospital. However, little information on this is provided in the background. Also, it would be useful if the analysis could report on how many of the current cohort received enhanced adherence counseling.
Authors
We have information regarding when enhaned adherence conselling is provided in the settings section. We hope this is fine. We have provided information regarding how many recevied enhanced adherence counselling in this cohort. Please see figure 1.

We hope our response is satisfactory and the current version does not require any edits. Hence, we are not submitting a revised manuscript.

Competing Interests: None

Reviewer Report 08 April 2020

https://doi.org/10.5256/f1000research.25113.r61604

✔ **Obinna Ikechukwu Ekwunife** 🆔

Department of Clinical Pharmacy and Pharmacy Management, Nnamdi Azikiwe University, Awka, Nigeria

This short report aimed to assess the gaps in routine VL monitoring at six months for children (0-9 years) and adolescents (10-19 years) newly initiated on anti-retroviral therapy from Jan 2017 to Sep 2018.

This study is essential as such data is needed to assess how programs are fairing with regards to the UNAIDS 90-90-90 target.

The study was succinctly reported. All the essentials results based on their study objective were addressed. The study should be accepted.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacoeconomics, evidence-based public health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 29 Apr 2020

Hemant Deepak Shewade, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France

Thank you for the constructive comments

Competing Interests: None

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias

- You can publish traditional articles, null/negative results, case reports, data notes and more

- The peer review process is transparent and collaborative

- Your article is indexed in PubMed after passing peer review

- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research