



POLICY BRIEF

DIFFERENTIATED SERVICE
DELIVERY FOR ADOLESCENTS
LIVING WITH HIV IN ZIMBABWE
– THE ZVANDIRI CLUSTER
RANDOMIZED TRIAL

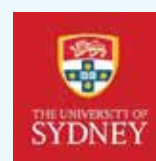
AUGUST 2019

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Collaborative Research Project



LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Differentiated Service Delivery for Adolescents Living with HIV in Zimbabwe – the Zvandiri cluster randomized trial

Introduction

Globally the number of adolescents living with HIV (ALHIV) is growing. In 2018 there were an estimated 1.6 million ALHIV aged 10-19, 85% of whom live in sub-Saharan Africa. Adolescence is a time of considerable neurodevelopmental, psychosocial and physical change. In addition, ALHIV in LMIC often need to contend with orphaning, poverty, separation from siblings, school discontinuation, changing households and caregivers, stigma and discrimination.

ALHIV have higher rates of HIV treatment failure, morbidity and mortality than children or adults. While there is widespread recognition of the need for better support and care, there is currently relatively sparse evidence for cost effective, psychosocial, community-based support for adolescents with HIV.

Between 2016 and 2018, CeSHHAR Zimbabwe and research collaborators, funded by Viiv Healthcare's Positive Action for Adolescents, conducted a cluster randomized trial of Africaid's Zvandiri Programme in rural Zimbabwe to evaluate the impact of the programme on HIV treatment, retention and prevention outcomes among ALHIV.

The Zvandiri Programme

Zvandiri is a differentiated service delivery programme for children, adolescents and young people living with HIV, established in Zimbabwe in 2004. The programme has been adopted by Zimbabwe's Ministry of Health and Child Care (MoHCC). The programme is implemented primarily by CATS (Community Adolescent Treatment Supporters), who are young people living with HIV, aged 18-24 years old, who are adhering well to ART and are willing to be CATS. They have completed school and are able to read and write.

CATS are selected and recruited by Africaid and trained for two weeks including a clinical attachment, using a standardised curriculum. They receive weekly supervision at the clinic with a designated nurse or counsellor as well as on site mentorship visits from a Zvandiri Mentor and monthly training and mentorship at CATS Coordination meetings.

Beneficiaries of the Zvandiri programme are allocated to a CATS. CATS provide information, counselling and support to them at clinic visits, home visits, monthly support group meetings and through regular SMS messages. The level of care provided to individual beneficiaries is differentiated by their level of vulnerability and is reassessed 3 monthly. Caregivers of Zvandiri beneficiaries are invited to attend a 12 session caregivers support group meeting.



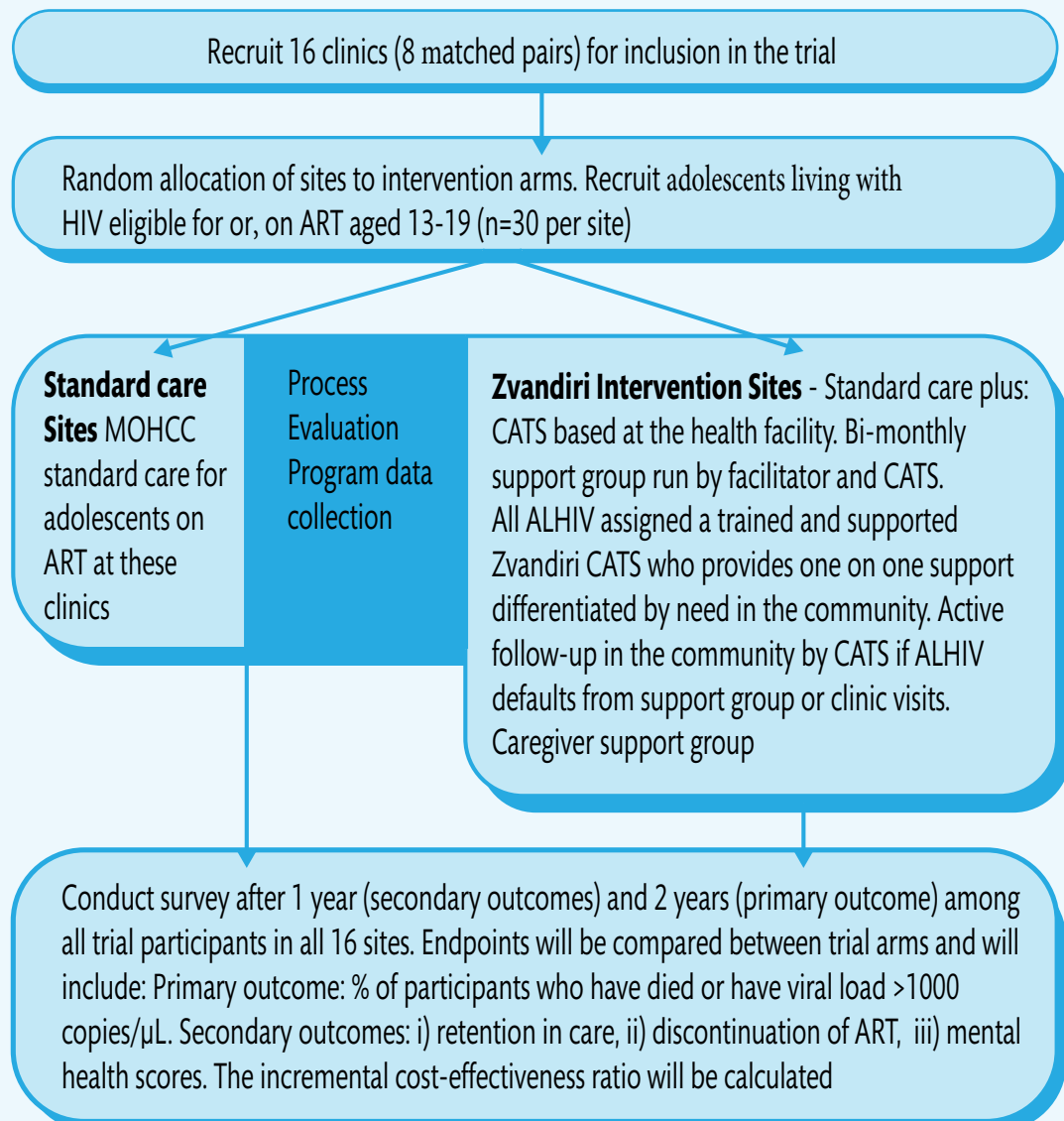
The Zvandiri Cluster Randomised Trial – overview and methods

The Zvandiri Trial was conducted by CeSHHAR Zimbabwe, King's College London, Liverpool School of Tropical Medicine, London School of Hygiene and Tropical Medicine, Ministry of Health and Child Care, Zimbabwe University of Sydney, and the University of Zimbabwe, College of Health Sciences

Sixteen rural clinics in two districts (Bindura and Shamva selected by MoHCC because of low treatment uptake among ALHIV in 2015) were randomised in 2016 to MoHCC standard of care or the Zvandiri programme. We hypothesised that ALHIV who received care at clinics supported by the Zvandiri programme would have better HIV treatment, retention and prevention outcomes than those attending clinics without Zvandiri support.

ALHIV were eligible for the trial if they were 13-19 years old, were on or starting antiretroviral therapy (ART), and had caregiver consent and were able to provide written consent or assent (those <18 years old). Six ALHIV who were too unwell to make clinic visits were excluded from enrolment. A process evaluation was conducted and in-depth qualitative study to better understand the lived experiences of ALHIV, including those of the CATS and their experiences of the Zvandiri programme.

Figure 1: Trial Overview

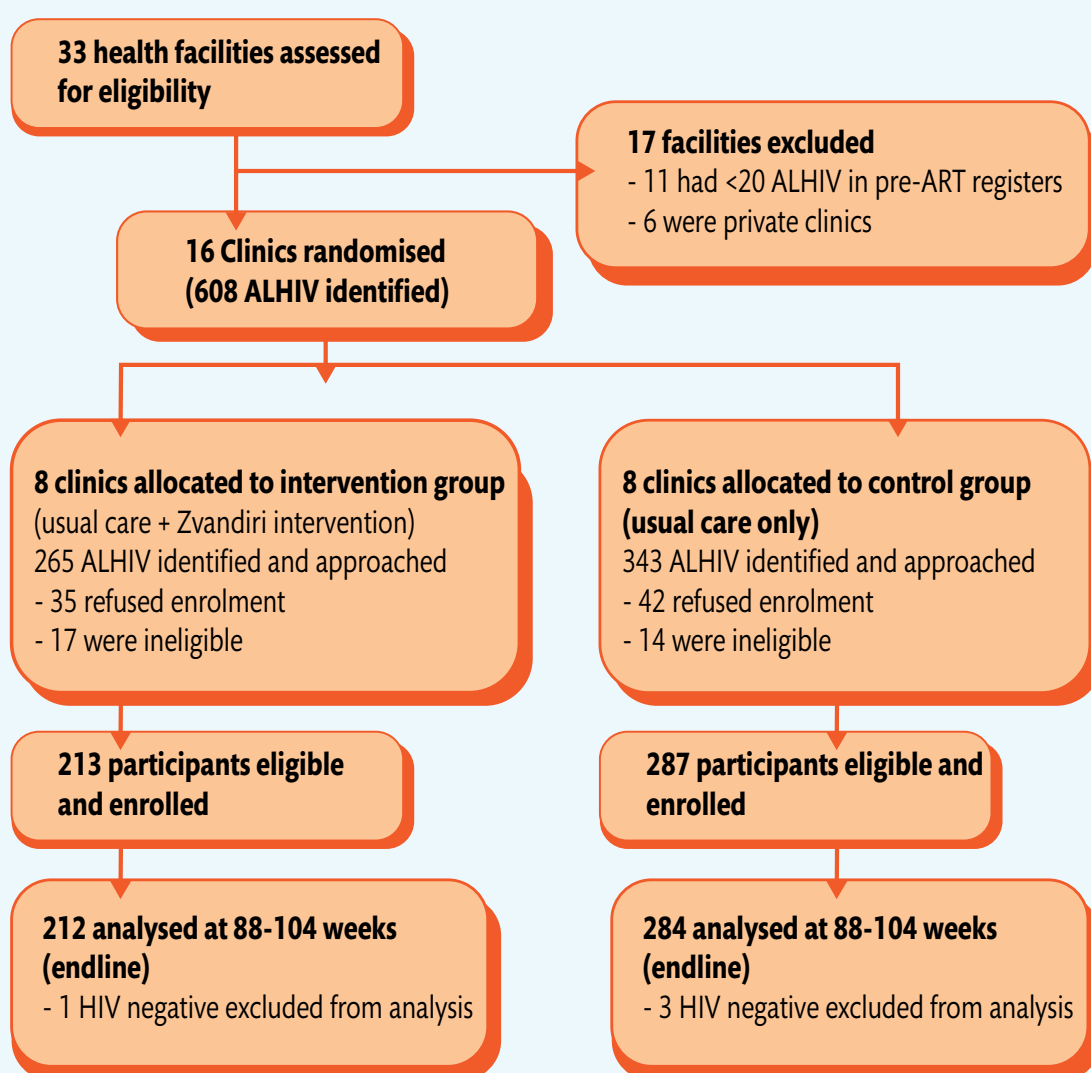


The primary outcome of the trial was the proportion of participants who had died or had a viral load >1000 copies/μL at 96 weeks. Secondary outcomes included i) not retained in clinic services (<80%) ii) who discontinued ART (completely stopping taking ART for ≥3 months) iii) at risk of depression (scoring ≥10/27 on PHQ-9 scale) iv) at risk of CMD (scoring ≥8/14 on SSQ-14) v) with poor quality of life (Shona version of EQ-5D scale. Trial outcomes were measured at midline (48-60 weeks) and at endline (96 ±8 weeks). A costing and cost effectiveness study is also being conducted.

Statistical analyses were conducted according to CONSORT guidelines for cluster randomised trials and followed a pre-specified analysis plan. The primary analyses were complete-case, modified-intention-to-treat. Cluster-level summary measures were used due to the small number of clusters per group. Secondary analyses examined effect-modification by baseline viral load, age group, gender, duration on treatment, and SSQ and PHQ-9 scores. The sample size of 500 participants provided 80% power to detect a difference in detectable viral load of 35% among participants in the standard care arm versus 18% in the intervention arm assuming 20% loss to follow-up and a coefficient of variation (k) between clusters of 0.25.

We used standard costing guidelines to estimate the annual cost per adolescent treated on ART and the cost per adolescent virally suppressed on ART through the intervention and control health facilities. All cost estimates included: staff salaries and training; drugs and other consumables; equipment; overheads. The trial is registered with Pan African Clinical Trial Registry, number PACTR201609001767322.

Figure 2: Flow Diagram ITT Analysis



Results

Sixteen clinics were randomised 1:1 to Zvandiri intervention or standard MoHCC care. Between August 2016 and March 2017, 608 ALHIV aged 13-19 years from the 16 clinics were identified and invited to enrol; 77 (13%) refused enrolment and 31 (5%) were ineligible, leaving 500 (82%) enrolled into the trial. Four (<1%) of the 500 cRCT participants, had their data excluded from final analyses after repeat testing using several assays found they were in fact HIV negative. The trial population included in analysis were 211 in the intervention group and 285 in the control group (see consort diagram Figure 2)

At enrolment, the median age of participants was 15 years, 52% were female, 82% were orphans, and 47% had a viral load ≥ 1000 copies/ μ L. There was some imbalance between groups at enrolment, with participants in the intervention arm more likely to be female, older, not in school, with a more positive caregiver attitude, less likely to have experienced stigma or to have CMD or depression, more likely to have an unsuppressed viral load and with a shorter duration on ART. Age, gender, being in school, and baseline viral load, SSQ-14 and PHQ-9 scores were adjusted for in subsequent analyses.

Of the 496 eligible participants enrolled, 479 (97%) had primary outcome data at endline. There was strong evidence of an intervention effect on the primary outcome of virological failure or death at endline (adjusted prevalence ratio (aPR)=0.58, 95%CI 0.36-0.94; p=0.03) – see Table 1.

Table 1: Primary Outcome at 2 years	Zvandiri intervention	Usual care	Unadjusted PR (95%CI)	Adjusted PR (95%CI)	p-value
	%(n/N)	%(n/N)			
HIV viral load ≥ 1000 copies/mL or death (primary outcome)	21.6% (52/209)	35.5% (97/270)	0.61 (0.38-0.97)	0.58 (0.36-0.94)	0.03

Table 2: Secondary outcomes at 2 years	Zvandiri group	Usual Care group	Unadjusted PR or mean difference	Adjusted PR or mean difference	p-value
	%(n/N) or mean (SE)	%(n/N) or mean (SE)	(95% CI)		
Discontinuation of ART for ≥ 3 months	6.7% (16/209)	10.5% (30)	0.64 (0.28-1.48)	0.68 (0.23-1.99)	0.45
Attended <80% of scheduled visits	12.7% (28/207)	15.2% (39/269)	0.83 (0.38-1.82)	0.80 (0.32-2.02)	0.62
SSQ-14 score >8	27.5% (60/192)	35.0% (86/259)	0.79 (0.52-1.19)	0.86 (0.60-1.23)	0.35
PHQ-9 score ≥ 8	9.9% (22/192)	16.0% (38/259)	0.69 (0.32-1.48)	0.80 (0.38-1.69)	0.53
Mean SSQ-14 score	5.42 (0.42)	5.90 (0.55)	-0.48 (-2.06,1.10)	-0.31 (-1.70,1.08)	0.64
Mean EQ-5D Index (SD)	0.91 (0.01)	0.92 (0.01)	0.00 (-0.04,0.03)	-0.01 (-0.04,0.03)	0.65

There was no statistical evidence of an effect on secondary outcomes at endline, although the direction of effect was in favour of the intervention for all secondary outcomes – see Table 2. There was also no evidence of an intervention effect on the exploratory outcomes (self reported disclosure to sexual partners or perceived stigma).

The process evaluation suggested that the Zvandiri intervention improved the quality of adolescents' lives through a focus on shared experiences, role modelling and supportive friendship (CATS visits and support group), as well as improving their own and their caregivers' HIV and treatment literacy (support group, CATS visits and caregiver workshops) which in tandem enabled them to better manage adherence and build their self-esteem. ALHIV described the transformative effect of a more sympathetic household environment, where caregivers, benefitting from the workshops, were better educated about the limited transmission risk of HIV in ordinary daily activities and more responsive in meeting the nutritional and physical needs of ALHIV. These changes were experienced by ALHIV as being better cared for and more cared about. They described the intervention as puncturing their sense of isolation and reducing their fear of the present and future implications of their HIV status. CATS were hosted within local clinics and overtime, this influenced the attitudes of health-care workers towards ALHIV, which was reported by health-care workers, CATS, ALHIV and caregivers to create a more open and receptive environment in which to seek care and support, producing a health system strengthening effect. The SMS, alongside the other support provided by the CATS, provided practical reminders which improved ALHIV's capacity to habituate treatment adherence.

The Zvandiri intervention increased the cost of delivering ART to ALHIV from \$163/year to \$992/year. The cost per HIV failure averted (ie ALHIV virally suppressed) was \$1342 with Zvandiri compared to \$450 with MoHCC standard of care. A cost effectiveness analysis to look at longer term outcomes is underway.

CASE STUDY

Rachel's story

Rachel is 15 years old. She wants to be a doctor. She was diagnosed with HIV when she was 7. She lives with her grandmother. Her mother has died, her father's whereabouts are unknown. Although her grandmother is very committed to providing support for Rachel, Rachel did not want it and was withdrawn. She was also not taking her ART and had a high viral load.

Then she became involved with Zvandiri and a CATS started visiting her at home. Initially, she didn't want him there though, giving him the cold shoulder.

In our interview she explains about trying unsuccessfully to contact her Dad. She has unmet costs for school, but her relatives have no money to help. She says she does not want to be reminded everyday about her mother's death, her HIV status or to take pills.

The CATS keep going to see her but as she will not talk to him, he instead talks to her grandmother. This improves the environment at home, making it more supportive for Rachel. In time, Rachel begins opening up to the CATS during home visits. The CATS encourages her to go to a peer support group. By spending time with other young people in a similar situation, Rachel starts to feel less alone.

The CATS help her when she comes to the clinic. Her treatment is switched to second line ART, but only once the clinician has confidence that her relational environment has changed and will support her adherence.

Rachel's poor adherence is not because she does not know that she needs to take her drugs, nor how to. But is a manifestation of all the concerns that she is trying to manage. Zvandiri was able respond to Rachel's particular situation, improving the household environment, providing a safe space for her to meet other ALHIV, listen to her needs and not focus only on adherence, but consider adherence in relation to other priorities in her life.

Discussion

Our trial found that the Zvandiri programme resulted in 42% lower prevalence of virological failure or death at 96 weeks among participants compared to those only receiving MoHCC standard of HIV care at rural clinics. This reinforces the need for clinical care for ALHIV to be complemented by interventions actively supporting adherence to treatment and well-being more generally.

This is the first youth-led trial of a multi-component intervention focusing on both adolescents' HIV-related and psychosocial outcomes. An important explanation for the Zvandiri intervention's success was the multi-component aspect which addressed the inhibiting context in which ALHIV navigate adherence, by providing them with a supportive peer network and a more receptive household environment. Even though each component played a specific role in improving the quality of ALHIV's lives, the various intervention components positively reinforced each other. Consequently, ALHIV receiving the Zvandiri intervention were able to benefit from continual support to drive and sustain behaviour change.

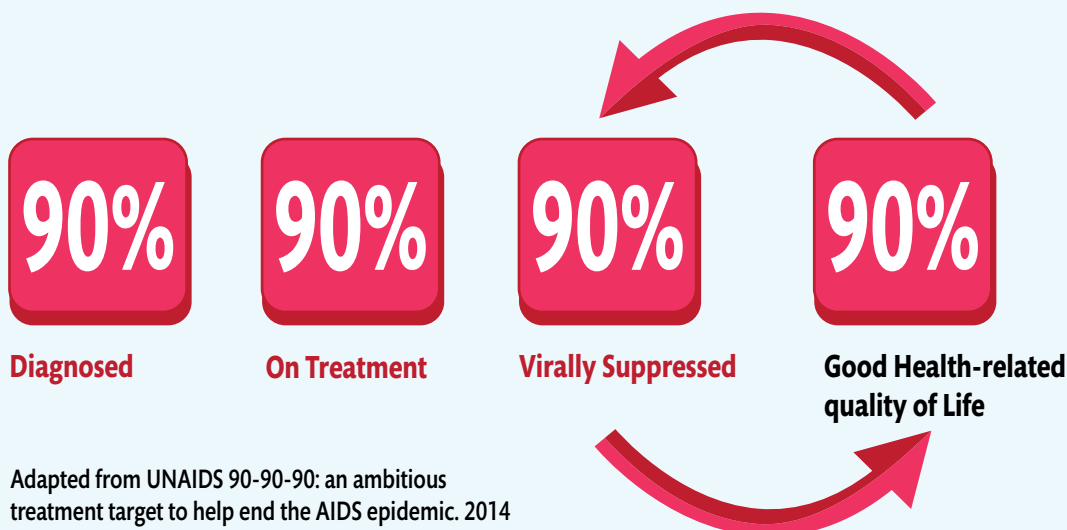
As illustrated by Rachel's story and our qualitative data more broadly the Zvandiri intervention addresses *intersecting concerns* and has the *flexibility and responsiveness* to adapt to the evolving circumstances of individual ALHIV, supporting ALHIV over *time*. The CATS are central to the success of the programme. They are themselves young people living with HIV and not only need support and mentoring to undertake their CATS role, but also to support their own health and well-being.

Our cost analysis suggests adding the Zvandiri intervention into current standard of care would increase the cost of providing HIV treatment to adolescents by approximately four-fold. The majority of this additional cost was due to the additional staff needed to deliver the counselling and adherence support at the clinics and in the community. Each of the intervention health facilities had three additional staff; who could have provided the same level of care to many more adolescents than the 30 or fewer adolescents accessing treatment at each facility over the course of the trial and already do so within the context of programme scale up.

A major strength of this trial is that it evaluated the Zvandiri programme as delivered in a real world and resource-constrained setting. The finding that it reduces rates of treatment failure strengthens support for further scale-up across the region more widely.

Community-based interventions to support ALHIV are likely to make a significant contribution to the UNAIDS 90-90-90 targets if they offer differentiated services, are youth-led, and multi-component. The recently coined 4th 90- "ensure that 90% of people with viral load suppression have good health-related quality of life" is critical – but not as drawn here – it is likely that achieving the 4th 90 is a catalyst for securing the third 90 (viral suppression).

Fig 3: The fourth 90: proposed revision to the UNAIDS 90-90-90 targets





Recommendations

Policy makers and implementers need to recognise the complex lives of ALHIV and the broader determinants of adherence and viral suppression. Programmes need to be designed to address these challenges flexibly and in a way that is aligned with the priorities of individual young people to maximise their incentive to adhere and become untransmissible.

More research is required to better understand why despite substantial reductions in virological failure, 20% of ALHIV in the Zvandiri arm died or continued with virological failure.

More research is required to determine how best to address issues of poor mental health among ALHIV. Although our qualitative data found ALHIV reporting improvements in quality of life we did not demonstrate this quantitatively. Zvandiri as currently implemented does not have a specific mental health component although ALHIV with severe depression are referred for services

Investments should be made in the development of systems which ensure peer support cadres are adequately trained, mentored and supervised both for their roles as peer supporters and for their own health and well-being, recognizing that this support may need to be differentiated. CATS come from different educational background and have variable levels of relational support.

Analyses to determine cost effectiveness over a longer time horizon is critical and planned.

We have presented the quantitative results complemented by our qualitative data, allowing us to better explain and understand the nuance behind these results. We recommend this approach for presentation of trial results of complex interventions.

For further information, contact:

Frances Cowan, *Principal Investigator*, frances@lstmed.ac.uk

Webster Mavhu, *Co-principal Investigator*, webster@ceshhar.co.zw

Nicola Willis, *Africaid Director and co-investigator*, nicola@zvandiri.org

Designed by Baynham Goredema