Highlights

A task-shifted problem-solving therapy intervention for depression and barriers to antiretroviral therapy adherence for people living with HIV in Zimbabwe: Case Series

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- An integrated intervention for depression and ART adherence delivered by a lay adherence counselor in a low-income country is described
- Acceptability of the intervention as measured by patient's attendance was high
- The integrated intervention was feasible as indicated by the counsellor's ability to deliver the intervention
- The intervention was associated with a reduction in depression symptoms

A task-shifted problem-solving therapy intervention for depression and barriers to antiretroviral therapy adherence for people living with HIV in Zimbabwe: Case Series

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In Sub-Saharan Africa the prevalence of depression is twice as high in people living with HIV compared to those without HIV, as is the case globally (Brandt, 2009; Chibanda, Benjamin, Weiss, & Abas, 2014; Ciesla & Roberts, 2001). Zimbabwe has a prevalence of HIV of 14.6% and the prevalence of depression among adults with HIV is estimated to be 68.5% (Chibanda, Cowan, Gibson, Weiss, & Lund, 2016). As shown in systematic reviews and a meta-analysis, depression is one of the most important individual-level factors that adversely affects adherence to antiretroviral therapy (Langebeek et al., 2014; Gonzalez, Batchelder, Psaros, & Safren, 2011). Antiretroviral therapy (ART) adherence is the key driver to viral suppression, delaying progression to AIDS and reducing the likelihood of transmitting HIV to others (Chi et al., 2009; Cohen et al., 2011). Good adherence is critical for survival and for achieving the goal set by the Joint United Nations Programme on HIV/AIDS of 90% of people receiving ART having viral suppression by 2020 (Joint United Nations Programme on HIV/AIDS, 2015). Depression may affect adherence because it interferes with critical factors like information processing and problem-solving (Fisher, Amico, Fisher, & Harman, 2008; S.A. Safren et al., 2012).

A systematic review suggested that the treatment of depression can improve adherence to ART (Sin & DiMatteo, 2014). A recent randomized controlled trial (RCT) in the United States showed that antidepressants alone did not improve adherence (Pence et al., 2015), but other RCTs in high income countries (HICs) have shown that psychological interventions that integrate cognitive behavioral therapy for depression with adherence counselling can improve depression and ART adherence (Safren et al., 2015; Safren et al., 2012; Simoni et al., 2013). While these interventions have been developed and tested in high income HIC settings, they may have similar results in low and middle-income countries (LMIC) LMIC settings and be able to be taken to scale. There is preliminary evidence to suggest the acceptability and feasibility of this approach in South Africa (Andersen et al., 2016). However, especially in low-income countries such as Zimbabwe, it is important that interventions are feasible for non-specialists to deliver. A task-shifting approach has been recommended, by which non-specialists take on tasks that in high-income settings are normally provided by mental health specialists. Task-shifting for depression can be delivered through a stepped-care model by which clients are all offered a low-intensity treatment in the first instance, only 'stepping up' to intensive or specialist services as clinically required (Haaga, 2000).

In prior work, we described the initial phases of culturally and linguistically adapting a problem solving therapy-based intervention for ART adherence among people living with HIV (PLWH) in Zimbabwe (*'Nzira Itsva'* or 'New Map') (Bere et al., 2016), based on the original Life-Steps intervention (Safren et al., 2004). As a subsequent phase of this work, we sought to integrate Nzira Itsva with therapy for depression to address depression and ART adherence simultaneously. To integrate with Nzira Itsva, we picked a culturally adapted problem-solving therapy (PST) for depression and behavioural activation, known locally as 'Opening up the Mind' or *Kuvhura Pfungwa* (Abas et al., 2016). PST is a brief evidence-based therapy for depression in which patients are taught a structured approach to identifying problems and finding workable solutions (Mynors-Wallis, 1996; D'Zurilla & Nezu, 2007). Depression may affect adherence because it interferes with critical cognitive and emotional correlates like information processing and problem-solving (Safren et al., 2012, Fisher et al., 2008). The World Health Organisation is currently developing PST as part of its task-shifting toolkit for dealing with depression in low- and middle-income countries (Lima et al., 2009). This forms part of the stepped-care guideline: The Mental Health Gap Action Plan (mhGAP)(WHO, 2016).

The aim of this study is to assess the feasibility and acceptability of a culturally adapted, integrated 6-session psychological intervention based on PST and delivered by adherence counsellors to address ART adherence and depression among PLWH receiving care in a general clinic setting in Harare, Zimbabwe and to examine preliminary changes in depression following the adapted intervention. Three cases will be presented in this paper to show how this intervention can be implemented in routine HIV care.

Methods

Setting

All participants were recruited from Parirenyatwa General Hospital which has a large ART clinic in central Harare that provides ART to approximately 3000 patients and is a referral centre for complicated HIV management. When we initiated the intervention, there was no specific care at the clinic for depression. Only patients with suspected severe mental disorder could be referred to the psychiatrists.

Recruitment

We recruited participants with adherence problems for an open-label pilot trial through a number of methods which included referral from doctors, announcements in the waiting hall and in appointment queues. During the announcements, the research assistant gave a brief synopsis of the research study and asked that people with adherence problems who were willing to be screened come to the study room. An information sheet on the study was given to the participants and then informed consent was sought from the interested participants**.** Participants who met eligibility criteria and provided informed consent were given a baseline assessment and received the intervention.

Participants

Participants were included if they were aged 18 or over; had been on ART for at least 4 months as confirmed by pharmacy records and medical records; had adherence problems as assessed by one or more of the following: 1) one or more missed HIV clinic appointments in past 3 months, 2) referral from doctors due to falling CD4 count or detectable viral load or 3) self-reported adherence problems; and had probable depression as assessed by scoring 5 or above on the short version of the Shona Self Report Questionnaire (SRQ-8) (Patel & Todd, 1996) and through interview by a Shona-speaking clinical psychologist.

Participants were excluded if they had severe cognitive impairment defined as a score of ≤6 on the International HIV-Dementia Scale (IHDS) (Sacktor et al., 2005); hazardous alcohol use defined as a score of ≥5 on the short AUDIT-C screen for alcohol dependence (Bohn, Babor, & Kranzler, 1995); suicidal intent as determined by the P4 screener (Dube, Kurt, Bair, Theobald, & Williams, 2010) or were too unwell/agitated to take part.

Assessments

Acceptability. This was defined as participant therapy session attendance.

Depression symptoms*.* These were assessed using the Shona Self Report Questionnaire (SRQ-8) which assesses common mental disorders that include depression. The SRQ-8 is a questionnaire consisting of 8 questions that was developed and validated in Zimbabwe with a cut-point of 5 and above indicating probable depression (Patel & Todd, 1996).

The supervising psychologist went through the scores to confirm the diagnosis. The SRQ-8 was administered by the research assistant at baseline and after 6 months. At Session 4 and Session 6 the SRQ-8 was administered by the adherence counsellor.

ART adherence. This was measured using a real-time electronic adherence monitor called Wisepill (Wisepill Technologies, Cape Town, South Africa). Wisepill was used for 14 days at baseline and at 6 month follow up. Wisepill is a pill case, which looks like a cell phone and contains an SMS microchip that sends a signal to the Wisepill server of the date and time of each opening. The score is the percentage of pills taken on time (+/- 1 hour) over the past 14 days. To supplement Wisepill, self-reported ART adherence was also assessed using the AIDS Clinical Trials Group questionnaire (Chesney et al., 2000), which assessed any missed ART doses in the last 30 days.

HIV care-related outcomes were extracted from clinic records, including viral load and CD4 count*,* which were measured by routine clinic blood test monitoring. Undetectable viral load was defined as less than or equal to 200.

A trained research assistant collected the study data whhich was entered using REDCap electronic data capture tools hosted at the University of Zimbabwe, College of Health Sciences. The dataset was exported to Stata v14.0 for analysis. Ethical approval was obtained from the Medical Research Council of Zimbabwe (MRCZ/A/1936), the Joint Parirenyatwa Hospital Ethics Committee (JREC 18/13) and King's College London College Research Ethics Committee (PNM/13/14-158). Participants were reimbursed ($3) for travel and provided with a snack.

The Intervention

Insert Table 1 here.

The intervention was delivered by one adherence counsellor. Her educational qualifications were 5 subject passes in 11th grade. She had worked as a nurse aide and then did 6 months training in adherence counselling. She had 5 years of experience working as an adherence counsellor. She had received 5-day training in the culturally adapted, integrated behavioural intervention (Nzira Itsva). A local psychologist (TB) provided her with weekly face-to-face supervision.

The culturally adapted intervention was based upon problem-solving therapy (PST) for depression and adherence. The underlying assumption of this approach is that mental distress can be understood as the negative consequences of ineffectual or maladaptive coping strategies. PST assists individuals to adopt a more realistically positive perspective of coping, recognise the role of emotions more effectively, and develop action plans geared towards reducing distress and enhancing well-being. (D'Zurilla & Nezu, 2007; Lima et al., 2007; Nezu, 2004). PST does not require extensive training for delivery or complex skills from the therapist, and can therefore be delivered by lay counsellors using a task sharing approach. The 6-session intervention consisted of 1 session for PST for adherence barriers and then 5 sessions for PST for depression with some time spent at each session also reviewing adherence (Table 1). The first two sessions each take up to 50 minutes; sessions 3-6 last up to 30 minutes.

Session 1 - Nzira Itsva ('New Direction').

LifeSteps is a an adherence intervention based on cognitive behavioral principles that identifies barriers to ART medication adherence and uses a problem solving approach to identify potential solutions (Safren et al., 2001). The first session is *Nzira Itsva* (New Map) (Bere et al., 2016), the culturally and linguistically adapted Life-Steps adherence intervention (Steven A Safren, Otto, & Worth, 1999; Steven A Safren et al., 2001), a detailed description of which can be found elsewhere (Bere et al., 2016). LifeSteps is a an adherence intervention based on cognitive behavioral principles and uses a checklist to identify barriers to ART medication. The primary components include psycho-education, enhancing motivation for adherence, and teaching problem-solving skills to address culturally relevant barriers to adherence.

The subsequent five sessions follow the culturally adapted PST intervention for depression (Abas et al., 2016; Dixon Chibanda et al., 2011). This approach includes psycho-education about depression (information, advice and support) combined with problem-solving, positive activity scheduling, stress management and a 10-15 minute discussion of

adherence during each session, checking progress and assisting the participant to find solutions for additional barriers to adherence.

Session 2: Problem Solving for Depression.

Session 2 includes the following components:

Stage 1: The counsellor explains to the participant the meaning of their SRQ-8 scores.

Stage 2: The counsellor explains depression as a mental health condition, normalising depression and providing information about evidence based interventions including psychological therapy and antidepressants.

Stage 3 "*Kuvhura pfungwa/* (Opening up the mind)": The counsellor helps the participant understand what is happening in their lives, encouraging them to share what is going on and how they feel about it. The aim is to identify and formulate the nature of problems being experienced that could be contributing to the depressed mood. The adherence counsellor elicits, listens to and reflects back the problem list. The participant is then encouraged to categorise and rate each problem in terms of its importance and potential solvability, which supports them to take control of their problems and determine what is important to them. Next, patient and counsellor brainstorm a list of possible solutions.

Stage 4: *Kusimudzira (encouraging):* The participant is encouraged to consider the pros and cons of potential solutions. The counsellor helps them recognise potentially dysfunctional problem-solving style activities and helps them develop a SMART (Specific; Measurable; Achievable; Realistic; Timely) plan for the successful resolution of specific problems.

Stage 5: *Kusimbisa (Strengthening):* The participant is reassured and encouraged that the goals set can be achieved and discouraging certain attitudes or beliefs, which may inhibit or interfere with implementing the action plan. The participant is encouraged to see how depression and their problems might also have been contributing to non-adherence.

Session 3: Problem Solving Review.

The counsellor reviews progress with problem-solving solutions. If the participant reports that the plan went well, the counsellor praises, reinforces and reaffirms the plan. The counsellor also explores whether the participant wishes to work on identifying and generating solutions for additional problems. If the implementation plan did not

go well, the counsellor explores the possible reasons for this, unpacks potential obstacles, which may have arisen and repeats the various problem-solving tasks in order to determine where renewed efforts should be directed in order to solve the problem successfully.

Session 4: Positive Activity Scheduling and Deep Breathing.

This session introduces use of positive activities ('*Kusimudzira*') and social support networks to increase positivity and help improve mood and functionality. Here participants are encouraged to identify and schedule pleasant activities and task-oriented activities, particularly tasks that they have stopped or been avoiding because of depression. They are also urged to identify particular resources (individuals, agencies etc.) that may be able to offer potential practical or emotional support.

Sessions 5-6: Review and Relapse Prevention.

These sessions continue to support clients' application of problem solving, activity scheduling, relaxation exercises and addressing barriers to ART adherence following roughly the same format as session 3. The final session incorporates a depression relapse prevention component, which involves identifying personal warning signs of relapse, assessing participants' knowledge of strategies to prevent relapse and identifying future goals.

For patients failing to make progress after Session 3 or who remained depressed at Session 6, the counsellor could refer to the supervising psychologist for assessment and further treatment. The psychologist then provided extra support to the counsellor, or delivered the session together with the adherence counsellor or referred the patient to get an antidepressant from the clinic and this is the stepped care part of the intervention.

Results

We present detailed case histories for three participants to illustrate the application of the intervention. The supervising psychologist reviewed the cases to confirm the diagnosis.

Case 1

Herbert * was a 49 year old male, married with six children. He did not complete the final year of secondary school and had worked as a security guard for over 20 years, but became unemployed after the firm closed down. He was taking first line HIV medication and had been on ART for three years. He self-reported missing ART doses in the past 3 months.

He suffered from minor depression. Symptoms included sadness, thinking too much, poor appetite, fatigue, loss of interest and thoughts that he was a failure. Only some of his symptoms were present more than half the days in the previous month. His main stressors were financial problems, and worry about a blood test advised by his doctor that would cost USD10 which he could not afford. His fear was that the advice to have this test (which was actually just a routine test to monitor urea and electrolytes) meant that the doctor thought his liver was failing, because his HIV medication was "working against him".

During Session 1, the main adherence barrier he identified was forgetting to take medication. He stored his medication in a bag that he sometimes forgot to open, and his phone alarm reminder often failed due to lack of battery power. A second barrier was medication side effects, especially nausea. He made a plan to put stickers on his drug storage bag, to remind him to take his ART, charge his phone, and to write down questions for his doctor about side effects.

During Session 2, he prioritised working on the problem of finding USD10 for the blood test. He generated three solutions: finding a job as a security guard, buying goods in Lesotho to set up small-scale trading in Zimbabwe, or requesting the money from his eldest son. He decided to find a job as a security guard by visiting security firms to show his CV and request work. His actions were reviewed in Sessions 3 and 4. He had visited several firms and being offered an interview by one. He had also been offered a one-off piece of manual work which would earn enough for the blood test. He was remembering to take his ART with use of the stickers and phone alarm. During Session 5 it emerged that he had surrendered the money he had earned to cover a relative's funeral expenses. Further he had not been called back after his job interview.

He could not generate a new solution he thought was feasible. The counsellor referred him for Step 2 care of review by a clinical psychologist. The psychologist encouraged him to think of more solutions and he decided to try employment agencies and also to ask his son for the blood test money. At Session 6 he reported that his son had given him funds for the blood test, and that he had an appointment at an employment agency.

Case 4

Gift* was a 45 year old male, unemployed and married with one child, who had been on ART for 9 years and was currently taking second line HIV medication.- He suffered from major depression. Symptoms included loss of

interest, isolating himself from other men, feelings of being a failure, poor sleep, weight loss, repetitive worries about physical health and loss of hope.

He had suffered from tuberculosis in the past and had been told that he needed an operation. He had given up all hope in life because he could not afford the operation. He was also worried that he could not financially take care of his wife and child. He had stopped taking his ART medication a few weeks before recruitment into the study. He said he knew the consequences of not taking medication and felt like his behaviour was like "knitting a jersey and then undoing the stitches".

In Session 1, the counsellor reviewed his stressors and helped him understand that taking ART was a step he could take to improve his health, even if he could not afford the operation. He opted to re-start his ART and planned to set an alarm and ask his wife to remind him to take ART.

By the second session, his self-reported adherence had improved to 100%. He identified financial problems as his priority. He selected becoming an agent in mobile banking for a local telecommunication company as his solution. To do this he had to go to the telecommunications company to sign up. In the third session, the counsellor reviewed the solution and it had not worked because he did not have enough capital required by the telecommunications company. The client then tried a different solution: to cook and sell traditional food for lunches at a local business centre. During Sessions 4-6, reviews showed that he was making good progress with this solution. He was less worried about physical health and his adherence improved based on his self-report.

Case 7

Sarah* was a 41 year old widowed female with primary school education and 2 children. She was self-employed rearing and selling chickens. She was taking first line HIV medication and had been on ART for 8 years. She suffered from major depression. The symptoms were poor sleep, sadness, loss of interest, irritability, and poor concentration, lasting for several months. The main stressors were family conflict and desire to find a partner. She self-reported missing some ART doses in the last week.

During Session 1 the primary adherence barrier she identified was coping with side effects. She was on a tenofovir, lamuvidine and efavirenz regimen and thought it was causing some of her anger towards her children. Sarah came

up with the solution to talk to doctors and use a future session to learn about anger management. The second adherence barrier was forgetting to take her medication in the evening because she would be busy and tired. She came up with a solution to set an alarm for her evening medication. The third barrier was fear of taking medication after missing a dose, and as a solution to this, she talked to the doctors. She also identified missing appointments due to financial constraints and she decided to continue working on her small business that she was giving up on. During Session 2 she and the counsellor discussed anger management techniques, including taking a step back, thinking about what she would say, and counting to ten before reacting.

During Session 3 she reported still feeling depressed. She generated a solution to ask the doctors about the possibility of her mood being affected by her medication since her regimen had been changed that month.

During Session 4 attending church was Sarah's positive activity. She made a plan to start going to church again.

During Session 5 the client reported that church had gone well and she planned to continue attending and try to participate in more social activities, such as participating in church activities. The counsellor continued with psycho-education about depression and anger management.

During Session 6, the client reported some improvement in mood and anger. The patient was doing relatively well however at the 6 month follow up visit her depression scores had risen slightly. The participant did not attribute the depression symptoms to any life-event, but indicated that this could have been because of her medication regimen.

Insert Figure 1 here

Insert Table 2 here

Discussion

This study provides one of the first examples of a combined intervention to treat depression and address barriers to ART adherence in a resource-limited, sub-Saharan African setting. We used a stepped care intervention for depression, integrated with a culturally adapted version of an adherence intervention shown to be feasible, acceptable and effective in the USA (Safren et al., 2009).

The intervention was acceptable to participants as evidenced by their attendance to all 6 sessions and this is representative of the participants who received this intervention. This attendance was exceptional considering that the participants were given very minimum incentives because only travel to the clinic was reimbursed. A possible

reason for this high attendance to sessions could be that the participants viewed the intervention as helpful to them and attending the session would be an opportunity to review their progress from the previous problem solving session. The sessions were also scheduled at an agreed time that was convenient for the participant and this could have played a role in the high attendance to sessions. The intervention was also feasible. An adherence counsellor with a basic 6-month certificate in adherence counseling was able to deliver the intervention after being trained. The certificate in adherence counseling is a qualification that consists of basic training in HIV adherence counselling
For all the cases presented here, the participant and the counsellor were able to work collaboratively to brainstorm and identify barriers and generate solutions to those barriers. This is because the intervention is delivered in a collaborative approach with the participant actively involved. The goal is that the participants can apply the skills they learned in the sessions even after they had completed the intervention sessions.

Another reason why the collaborative approach worked well is because both the Nzira Itsva intervention and the Problem Solving therapy were culturally and lingusitically adapted and are appropriate to be used in this setting (Bere et al., 2016). Therefore these two combined provide an intervention that adherence counsellors can deliver and that participants can learn and implement in their day to day lives. One challenge in implementing this type of intervention is in emphasising the collaborative approach that the counselors must use. Generally, in this setting the adherence counsellor is trained to “instruct” the patients so that they adhere to medication. Training the adherence counsellor as well as checking fidelity of the counselling sessions ensured that this collaborative appraoch was maintained.

Strengths of this study include the cultural adaptation of evidence-based interventions that can be delivered by lay counsellors in this resource-limited setting, a focus on missed visits in addition to adherence to promote

engagement in care, integration of problem solving strategies for both adherence and depression and a stepped care model, which provides a parsimonious approach to treatment. This study has also indicated some promising outcomes regarding a change in depression symptoms for people living with HIV. This intervention is of public health relevance because in order to achieve the 90% target of those with HIV virally suppressed (Joint United Nations Programme on HIV/AIDS, 2015), depression has to be addressed in order to improve adherence. Other areas that could use this model are other chronic illnesses in which adherence to medication is an important part of treatment for example is diabetes. Future studies can be conducted to determine whether the intervention is

effective for clinical levels of depression, including major depressive disorder, as well as distress. Since depression is highly prevalent in people living with HIV clinicians should incorporate depression screening and implement subsequent interventions for patients who are depressed.

In summary, this pilot study suggests that interventions which integrate depression treatment with collaborative problem-solving around barriers to adherence can be associated with improved outcomes in both depression and adherence. Though this was not an effectiveness study we can say with caution that the findings are consistent with the evidence from high income countries that depression can be treated in PLWH (Sherr, Clucas, Harding, Sibley, & Catalan, 2011). This is consistent with the most recent WHO guidelines which recommend an integration of depression screening and management in routine care for people living with HIV (WHO, 2016). In light of these findings a larger randomized effectiveness-implementation trial is warranted.

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Tables and Figures

Table 1. Description of Integrated Intervention for Adherence and Depression

	Name	**Components**
Session 1	*Nzira Itsva* (New Direction) Adherence Intervention	• Psycho-education • Identification of barriers to adherence • Motivation to take medication
Session 2	Problem Solving Therapy	• Explanation of depression scores and psych-psychoeducation about depression • Identification of the problem • Brainstorming and evaluation of solutions • Identify one solution to work on
Session 3	Problem Solving Review	• Review of progress on the implementation of solution from previous session • Identify barriers faced and discuss solutions • Possible identification of another problem to work on
Session 4	Positive Activity Scheduling	• Identification of positive activities that the participant can engage in
Session 5 and 6	Review and Relapse Prevention	• Support application of problem solving • Encourage continuation of positive activities • Depression relapse prevention

Figure 1: SRQ-8, log of viral load and CD4 over time by individual

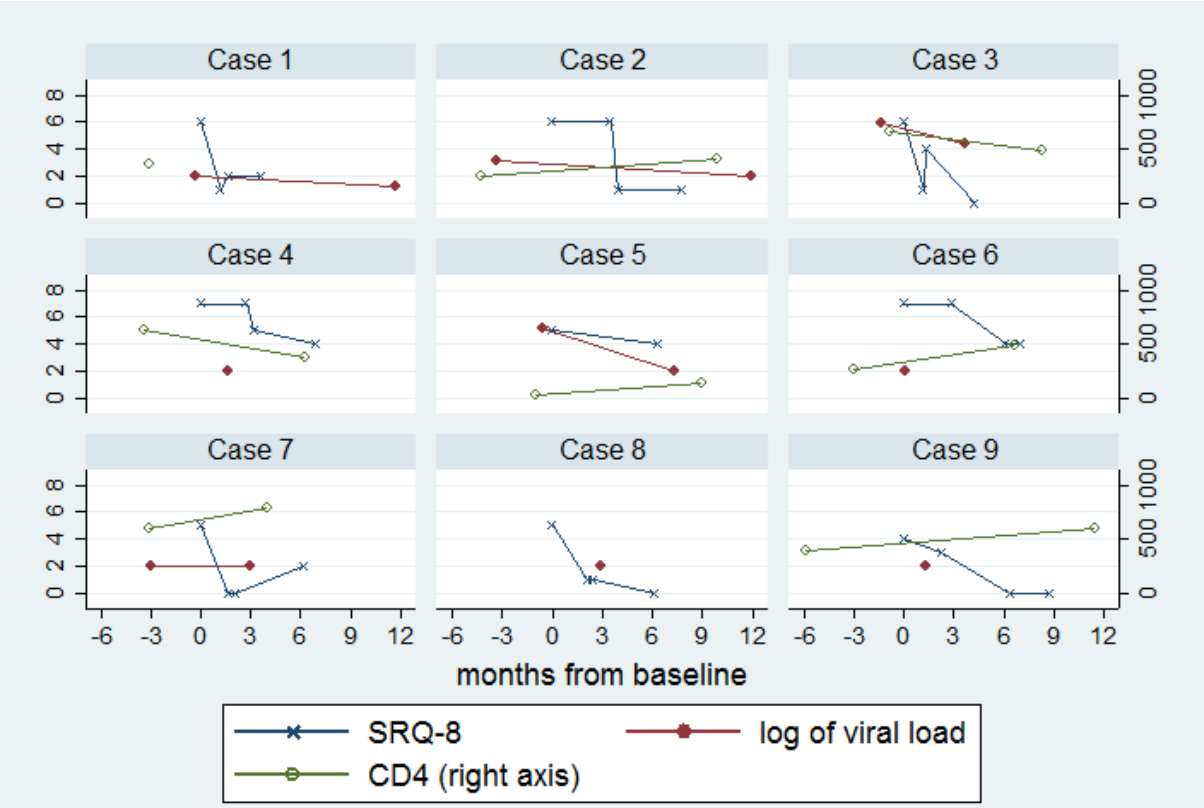

Table 2. Participant characteristics and outcomes

		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Gender		Male	Female	Female	Male	Male	Female	Female	Male	Female
Age		49	41	40	45	43	65	41	20	35
Marital status		Married	Widowed	Single	Married	Married	Widowed	Widowed	Single	Married
Years on ART		1.9	3.9	7.0	9.1	3.5	4.1	7.8	10.1	0.5
Regimen	**Baseline**	First line	First line	First line	Second line	First line	Second line	First line	Second line	First line
Regimen	**Follow-up**	First line	First line	First line	Second line	Second line	Second line	First line	Second line	First line
Number of sessions attended		6	6	6	6	1	6	6	6	6
Self-report % pills taken	**Baseline**	100	100	100	100	100	71.4	85.7	100	100
	Follow-up	81.0	100	100	100	-	100	100	100	100
Wisepill adherence	**Baseline**	100	100	96.7	93	100	-	-	-	100
	Follow-up	100	100	100	93	-	100	100	-	-
Self-report last missed	**Baseline**	1-3 months ago	In past week	Never	Never	Never	In past week	In past week	1-3 months ago	1-3 months ago

		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
medication dose	Follow-up	In past week	Never	Never	>3 months ago	> 3 months ago	Never	Never	Never	Never
CD4	**Baseline**	354	243	657	633	28	273	604	-	398
	Follow-up	-	415	490	382	136	485	784	-	604
Viral load	**Baseline**	<200	1300	750000	<200	150000	<200	<200	-	-
	Follow-up	<200	<200	27000	<200	<200	<200	<200	<200	<200
SRQ-8	**Baseline**	6	6	6	7	5	7	5	5	4
	Session 4	1	6	1	7	-	7	0	1	3
	Session 6	2	1	4	5	-	4	0	1	0
	Follow-up	2	1	0	4	4	4	2	0	0