

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



LSHTM Research Online

Burns, Rose; Borges, Joana; Blasco, Philippe; Vandembulcke, Alexandra; Mukui, Irene; Magalasi, Denview; Molfino, Lucas; Manuel, Rolanda; Schramm, Birgit; Wringe, Alison; (2019) 'I saw it as a second chance': A qualitative exploration of experiences of treatment failure and regimen change among people living with HIV on second- and third-line antiretroviral therapy in Kenya, Malawi and Mozambique. *Global Public Health*. ISSN 1744-1692 DOI: <https://doi.org/10.1080/17441692.2018.1561921>

Downloaded from: <http://researchonline.lshtm.ac.uk/4650229/>

DOI: <https://doi.org/10.1080/17441692.2018.1561921>

Usage Guidelines:

Please refer to usage guidelines at <http://researchonline.lshtm.ac.uk/policies.html> or alternatively contact researchonline@lshtm.ac.uk.

Available under license: <http://creativecommons.org/licenses/by-nc-nd/2.5/>

<https://researchonline.lshtm.ac.uk>

'I saw it as a second chance': A qualitative exploration of experiences of treatment failure and regimen change among people living with HIV on second- and third-line antiretroviral therapy in Kenya, Malawi and Mozambique

Rose Burns ^a, Joana Borges^b, Philippe Blasco^c, Alexandra Vandembulcke^c, Irene Mukui^d, Denview Magalasi^c, Lucas Molfino^b, Rolanda Manuel^e, Birgit Schramm^a and Alison Wringe^f

^aEpicentre, Paris, France; ^bMédecins sans Frontières, Geneva, Switzerland; ^cMédecins sans Frontières, Paris, France; ^dMinistry of Health, Nairobi, Kenya; ^eMinistry of Health, Maputo, Mozambique; ^fLondon School of Hygiene and Tropical Medicine, London, UK

ABSTRACT

Increasing numbers of people living with HIV (PLHIV) in sub-Saharan Africa are experiencing failure of first-line antiretroviral therapy and transitioning onto second-line regimens. However, there is a dearth of research on their treatment experiences. We conducted in-depth interviews with 43 PLHIV on second- or third-line antiretroviral therapy and 15 HIV health workers in Kenya, Malawi and Mozambique to explore patients' and health workers' perspectives on these transitions. Interviews were audio-recorded, transcribed and translated into English. Data were coded inductively and analysed thematically. In all settings, experiences of treatment failure and associated episodes of ill-health disrupted daily social and economic activities, and recalled earlier fears of dying from HIV. Transitioning onto more effective regimens often represented a second (or third) chance to (re-)engage with HIV care, with patients prioritising their health over other aspects of their lives. However, many patients struggled to maintain these transformations, particularly when faced with persistent social challenges to pill-taking, alongside the burden of more complex regimens and an inability to mobilise sufficient resources to accommodate change. Efforts to identify treatment failure and support regimen change must account for these patients' unique illness and treatment histories, and interventions should incorporate tailored counselling and social and economic support.

Abbreviations: ART: Antiretroviral therapy; HIV: Human immunodeficiency virus; IDI: In-depth interview; MSF: Médecins Sans Frontières; PLHIV: People living with HIV

ARTICLE HISTORY

Received 3 October 2018
Accepted 23 November 2018

KEYWORDS

Antiretroviral therapy; second-line treatment; treatment failure; adherence; sub-Saharan Africa

Background

The scale-up of antiretroviral therapy (ART) in sub-Saharan Africa over the past 15 years has dramatically reduced HIV-related mortality and morbidity, with HIV-attributable deaths declining by 51% between 2004 and 2017 (UNAIDS, 2018). Efforts are now focussed on achieving universal access to ART with a view to controlling the epidemic, whereby people living with HIV (PLHIV) receive

CONTACT Rose Burns  rose.burns@epicentre.msf.org  Epicentre, 55 rue Crozatier, 75012 Paris, France

© 2019 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

treatment as soon as they are diagnosed with HIV, and achieve sustained viral suppression through adherence to an effective regimen (WHO, 2015). This period in the HIV epidemic response is also characterised by the rise of a burgeoning population of patients who are failing first-line ART and face diminished treatment options, typically requiring more expensive protease inhibitor-based second-line ART (Cambiano et al., 2014; WHO, 2017). Virological failure rates amongst patients on first-line ART in treatment programmes across sub-Saharan Africa have been estimated at 24% after 12 months, and 33% after 24 months on treatment (Schuurman et al., 2010), and it has been predicted that up to three million patients in sub-Saharan Africa will be receiving second-line ART by 2020 (Estill et al., 2016).

With the rapidly increasing use of second-line regimens in sub-Saharan Africa, a new cohort of patients who are experiencing antiretroviral treatment failure for a second time is also emerging. A meta-analysis of treatment outcomes among patients on second-line regimens in resource-limited settings demonstrated relatively high virological failure rates of 23% at 12 months and 27% at 24 months, with virological failure largely associated with poor adherence (Ajose, Mookerjee, Mills, Boule, & Ford, 2012). In sub-Saharan Africa, third-line ART regimens remain costly (14 times more expensive than commonly used first-line regimens) and are not yet readily available in most settings, making second-line ART the last therapeutic option for most patients (WHO, 2017). Despite a growing number of patients on second-line treatment regimens, there are limited interventions tailored to their needs, partly reflecting the limited evidence base from qualitative studies pertaining to these patients' experiences and challenges they may face with adhering to advanced treatment regimens (Barnett et al., 2013).

Before the widespread availability of first-line ART in sub-Saharan Africa, PLHIV often experienced progressive states of ill-health, causing substantial disruption to their lives and those of their caregivers. Studies from this period have highlighted how the burden of caregiving and the associated costs of illness of a family member could induce extreme poverty for the whole household, or result in various strains on the main carer (Foster & Williamson, 2000; Kipp, Tindyebwa, Rubaale, Karamagi, & Bajenja, 2007). During sustained or repeated periods of ill-health, other social relationships based on reciprocity and mutual support may also be strained or disrupted, exposing individuals to illness-related stigma and leaving them struggling to mobilise resources to improve their situation (Bury, 1982; Ssekubugu et al., 2018). Furthermore, the lived experiences of chronic illness can trigger profound disruptions in a person's understanding of their place in society, leading them to reconsider their future plans and identity, particularly for diseases associated with disability or death (Bury, 1982).

The scale-up of ART led to the 'Lazarus' effect amongst PLHIV who came close to death, but who survived thanks to treatment availability (Pierret, 2007; Rofes, 1998; Trainor & Ezer, 2000; Whyte, 2014). This 'biogeneration' of PLHIV were marked by the shared experience of diagnosis and near-death followed by initiation of effective treatment (Whyte, 2014). Undergoing HIV testing and initiating first-line ART triggered changes in patients' lives and outlook, as they recovered from illness and were given a 'second chance' (Whyte, 2014) with re-shaped possibilities, opportunities, social roles and relationships, and the emergence of new identities (Davies, 1997; Frank, 1993; Hassin, 1994; Merten et al., 2010). For many PLHIV, these transformations brought a greater appreciation for life, as well as enabling them to develop coping mechanisms, re-evaluate behaviours around alcohol, drugs and sexual risks, and in some cases, adopt spirituality, religion, or participate in community services (Alexias, Savvakis, & Stratopoulou, 2016). However, PLHIV are positioned as part of an epidemic where life often cannot get 'back to normal' after receiving treatment (Shapiro, Angus, & Davis, 1997): they may need to rebuild livelihoods, support a family alone, navigate intimate relationships in the shadows of HIV, or face emotional hardship and perpetual stigma (Bonnington et al., 2017; Russell & Seeley, 2010; Wamoyi et al., 2017). As such, these 'social rebirths' are rarely linear, are often fraught with challenges especially as the years progress, and are usually dependent on PLHIV's access to economic and social support, including supportive relationships with their health providers (Ondenge et al., 2017; Russell et al., 2007; Russell & Seeley, 2010; Seeley & Russell, 2010).

Much of the literature on how PLHIV experience social disruptions and transformations relates to their HIV diagnosis, initiation of ART and their subsequent recovery (e.g. (Pierret, 2007; Seeley & Russell, 2010; Whyte, 2014; Wringe, Renju, Seeley, Moshabela, & Skovdal, 2017)). Little research has been undertaken to understand how PLHIV respond to *treatment failure* and the ways in which regimen change can shape their subsequent attitudes towards care-seeking. Although there may be parallels between patients' experiences of initiating second- or third-line ART treatment, and the social transitions that accompany recuperation from illness described in the early days of ART availability, there may also be several differences: patients on second-line regimens will often have long treatment histories and may have been living with an HIV diagnosis for well over a decade. Selection effects will also come into play whereby patients on second-line and third-line drugs are more likely to include those who were unable to address adherence challenges whilst on previous regimens. Initiation of second- or third-line ART may add to these challenges as a result of the greater complexity of the drug regimens, including the pill burden and associated side-effects, which persist, despite improvements over recent years (WHO, 2016, 2018). On the other hand, patients who experience treatment failure and eventually transition onto second or third-line regimens are 'survivors', and have often undergone multiple experiences of declining health followed by 'turning points' (Shapiro et al., 1997) where symptoms diminish after the initiation of a new, effective regimen, potentially giving rise to repeated or multiple social transformations (Russell & Seeley, 2010; Seeley & Russell, 2010).

In this paper, we explore patients' lived experiences of treatment failure and the transition to second- and in some cases, third-line antiretroviral therapy regimens in Kenya, Malawi and Mozambique, with a view to informing interventions to support this growing cohort of patients.

Methods

Study context

We draw on qualitative data collected as part of a multi-country study that investigated treatment failure among patients on second-line ART regimens in rural Malawi and Kenya, and urban Mozambique. The study took place in three sub-Saharan African countries where Médecins Sans Frontières (MSF) supports the Ministry of Health to run HIV care and treatment programmes: Chiradzulu in rural south-eastern Malawi, Homa Bay, located on the banks of Lake Victoria in rural Kenya, and Maputo, the capital city of Mozambique. The quantitative component of this study included a cross-sectional survey to assess virological failure and associated drug resistance in all three sites among patients receiving a boosted protease inhibitor-based second-line regimen for at least six months following a history of treatment failure on a standard first-line regimen (Schramm et al., 2016). The key characteristics of the study settings and their HIV programmes are shown in Table 1.

Data generation

Qualitative data generation took place between August 2016 and March 2017. Repeated in-depth interviews (IDI) were conducted with PLHIV on second- or third-line ART. Two interviews per participant were conducted, on average five days apart, in Dholuo, KiSwahili or English (Homa Bay), Chichewa (Chiradzulu), and Portuguese or Changana (Maputo) by locally-recruited, non-clinical, fieldworkers with social science qualifications, matched to the participant's gender. The first IDI lasted 25–60 minutes and aimed to develop rapport with the participants and covered their lived experiences of illness and their treatment-taking journeys. The second IDI lasted 30–75 minutes, and revisited the earlier topics as well as exploring patients' knowledge and understanding of different ART regimens, drug resistance and viral load results, and their views on treatment and care services. All interviews with PLHIV took place in a private location outside the clinic (such as a community building or school) depending on the participants' preferences.

Table 1: Study setting characteristics.

Site	Homa Bay	Chiradzulu	Maputo
<i>HIV prevalence</i>	24% (2012)	17% (2013)	17% (2010)
<i>Start date of MSF/MoH HIV intervention</i>	2000	1997	2001
<i>Health service setting</i>	County hospital	District hospital and 10 health facilities	Referral level clinic
<i>No. Patients (end 2016)</i>	7341	36,500	2348
<i>Year of second-line ART introduction</i>	2009	2005	2009
<i>Prescribed second-line regimen (2016)</i>	Lopinavir-based (twice-per-day)	Artazanavir (once-per-day)	Lopinavir-based (twice-per-day)
<i>No. Patients on second-line ART (end 2016)</i>	847	1780	1271
<i>Year of third-line ART introduction</i>	2011	2015	2014
<i>No. Patients on third-line ART (end 2016)</i>	26	17	37
<i>Appointment schedule (for second-and third-line)</i>	Monthly	Bi-monthly	Monthly
<i>Interventions (second-line patients):</i>			
<i>Enhanced adherence counselling</i>	Monthly (regardless of VL result)	Monthly (if high VL result)	Monthly (if high VL result)
<i>Viral load testing</i>	Every 12 months (and 6 months after regimen change)	Every 6 months	Every 12 months (and 6 months after regimen change)
<i>Differentiated model of care for second-line patients</i>	N/A	N/A	1. 'Risk of treatment failure' (clinician-lead and counsellor-lead counselling) 2. Fast track patient 'clubs' in case of undetectable VL (ART refill and group counselling)
<i>Additional services</i>	Home visits, transport reimbursements according to need.	N/A	Nutritional support, home visits according to need.

Three participants were no-shows for the second interview and could not be contacted, whilst 5 participants requested to undertake both interviews on the same day, usually because of travel or other commitments.

One-time IDIs were conducted with health workers across the three sites by the field workers or the lead author (RB) in English (with the exception of one IDI conducted in Portuguese in Maputo) and took place in a private room within the health facilities. Topic guides with health workers elicited their perceptions of the challenges faced by patients transitioning from first to second or second to third-line regimens, and their experiences of caring for these patients.

Observations took place in the HIV clinics during staff meetings, group counselling sessions, group education sessions and other activities. IDI were audio-recorded, transcribed and translated (where necessary) into English. Fieldworkers wrote up interview summaries and recorded their observations in study diaries, and discussed these during debriefing and on-the-job training sessions.

Sampling strategy

In each site, PLHIV were sampled for IDI from among those participating in the cross-sectional survey component of the study. Sampling took place between 17–20 months following the survey, depending on the site. Additional inclusion criteria for the qualitative study included being 18 years of age or over. A purposive sampling strategy was used to ensure maximum diversity in terms of viral load results during and following the cross-sectional survey, and ART regimen at the time of the sampling (second-line, optimised second-line, third-line).

Table 2: Participant characteristics.

Group			Kenya	Malawi	Mozambique	Total
PLHIV	VL <1000 ¹	Receiving second-line regimen	5	4	4	13
		Stayed on second-line regimen	0	2	3	5
	VL ≥1000 ²	Switched to simplified/optimised second-line regimen	6	2	2	10
		Switched to third-line regimen	5	5	5	15
		Female	10	7	8	25
Health workers	Clinical staff Counsellors and support staff	Male	6	6	6	18
			2	4	2	8
			3	1	3	7
Total\			21	18	19	58

¹at most recent viral load test and ~12 months before IDI;

²at viral load test ~12 months before IDI.

Across the three sites, 43 PLHIV on second- or third-line ART and 15 health workers participated in the study (Table 2). PLHIV participants had a median age of 43 years, reflecting the fact that they were generally highly treatment-experienced with a median time on ART of 9 years. The number of male and female participants approximately reflected the gender distribution of second and third-line patients in each setting. Among 18 participants receiving second-line ART, the median duration on second-line ART was 2.8 years at the time of their interview. Among 25 participants who experienced virological failure on second-line and changed regimens, their median duration on a modified second-line regimen (simplified or optimised) was 12 months, and the median duration on third-line regimens was 11 months, at the time of their interview.

Data management and analysis

Transcripts and notes were coded inductively by site, using NVivo11 software as an aid. Codes were initially inductive and phenomenological, prioritising the meaning that participants themselves gave to their experiences. A thematic analysis was conducted, drawing on the principles of grounded theory, whereby codes were raised to a conceptual level considering their underlying meaning and their inter-relationship. Constant comparison between new codes and sites and existing codes took place, with 'deviant' cases, or those cases which ran counter to the emerging theory, also examined (Glaser & Strauss, 1967). Data were collected until saturation was reached, meaning new themes were no longer emerging from the analysis. Analytic memos were used to aid the process of deriving second and third-order themes, and to compare across respondent types (e.g. patients with or without treatment failure on second-line ART). Experiences over time were also considered in order to reflect on the processes of change including perspectives before and after treatment failure. Coding frameworks and analytical memos were discussed regularly between the study researchers and fieldworkers, ensuring that consideration was given to the interpretation of categories that had local meanings attached.

Ethics

Ethical approval for the study was granted from the Kenya Medical Research Institute in Kenya (KEMRI/RES/7/3/1), the National Health Sciences Research Committee in Malawi (1578), the National Committee on Health and Bioethics in Mozambique (94/CNBS/2016) and the London School of Hygiene and Tropical Medicine in the United Kingdom (11298).

Results

Three distinct themes emerged from the analysis reflecting the chronology of PLHIV's lived experiences of treatment failure and regimen change: firstly, social disruptions associated with ill-health

related to first-line treatment failure; secondly, social transformations that occurred following a switch to a new treatment regimen; and thirdly PLHIVs' engagement with new treatment regimens following these transformations.

'I was about to die': living with treatment failure

When recalling their experiences of failing first-line ART, many participants referred to the resurgence of HIV illnesses. For some participants, this fear was palpable through their feelings of certainty that they would not survive, leading them to question the relevance of continued drug-taking:

I was sick, doctor, I was very sick, and I couldn't even stand up, I was not even talking. Now my heart was still calculating, I was thinking that: why should I now take these drugs when I was about to die ... ? [Woman receiving second-line ART, Kenya]

Others recalled the circumstances that may have contributed to first-line treatment failure, and some acknowledged the emotional burden of living with HIV, or earlier denial of their HIV status which was overcome as ill-health came to the forefront of their daily lives:

There was a time I stopped taking them (ART). I said to myself 'why do I have this illness? I would rather die.' But later I realized that, I just can't think that way, and then I kept on taking pills again. **Why did you feel this way?** I did not believe I have HIV [Man receiving second line ART, Mozambique]

Other participants recalled having endured long stays in hospital, or with relatives, and the significant toll that these illnesses had taken on their social lives and economic activities, with some having to completely change their lifestyle and jobs. For some participants, this change of lifestyle could be less enjoyable, or represented a constant reminder of the fact that they were unwell:

Ok, can you talk about your daily routine? ... as I am ill, as soon as I take my meal, I generally go to bed, I get up and watch TV, I do nothing at all. **What did you used to do before you were sick?** I used to do the cleaning in the house ... **Where do you usually go to chill out, especially at the weekends?** As I am sick, I do not enjoy, I just stay home. When I feel better I only go out to parties where I am invited to. I was a dancer, I used to dance at parties, and weddings. [Man receiving second-line ART, Mozambique]

Periods of illness were often prolonged as some patients experienced delays in being switched to second-line ART, extending the duration and consequences of social and economic disruptions caused by treatment failure.

They said that the treatment I was taking was over; it was not working in a good way. But that was when I was sick in hospital because of tuberculosis ... it took me a while to get those pills and when they changed, I felt fine. [Man receiving third-line ART, Mozambique]

In this context, treatment failure often prompted reflection or provoked blame among PLHIV as they struggled to find meaning to their predicament, as one Kenyan health worker explained:

At times they blame themselves, at times they blame it on drugs and at times it is blamed on the health care workers. [Health worker, Kenya]

'My drugs shaped my lifestyle': new treatment brings social transformations

After experiencing life-threatening illnesses due to treatment failure, many patients felt they were given a second chance at life when switched to a second-line regimen that would provide effective treatment. This was even more notable for patients who had switched to third-line ART and were acutely aware of their limited treatment options, as one Malawian man explained:

To tell the truth, I felt I was going to go back home and wait for my death. So, when I heard about the research for third-line I saw it as a second chance. So I joined and I was given the drugs. They told me there was not any other drugs and no fourth-line, so I was glad it worked otherwise I would be dead now. [Man receiving third-line ART, Malawi]

Changing treatment catalysed transformations for many participants as they reflected on earlier ‘mistakes’ that had contributed to poor adherence, and made changes or found compromises in their lives to accommodate more regular pill-taking. For example, some participants reported how they could only accommodate daily pill-taking routines through changing their source of livelihood, which some participants appeared to accept and even embrace.

..my drugs shaped my lifestyle and it shaped it permanently ... I had to organize my duties and my responsibilities in accordance to my time of taking drugs. I was an ardent fisherman, but nowadays I am an ardent gardener [Man receiving second-line ART, Kenya]

However, other participants expressed regret and reluctance when faced with the need to change their livelihoods in order to accommodate the requirements of regular treatment-taking or appointment attendance. In some cases, this prompted regret over their past attitudes or behaviours towards their drugs, expressed through self-blame and the sense of an opportunity lost.

Now I am limited, I cannot go to South Africa. That’s where I used to earn the living ... I can only earn the living around here in the city waiting for the 14th to go and to refill the pills ... because I am needed at the hospital for tests ... and this affects me ... On the first line, after having felt better, I went abroad to work. That’s where I ruined everything. I stayed two years without taking them [Man receiving second-line ART, Mozambique]

Other changes that occurred to participants’ lives as a result of incorporating regular pill-taking were often perceived positively. Some participants described themselves as being more appreciative of treatment than in the past, while others reported overcoming community stigma, including disclosing their HIV status to other people, or overcoming denial in order to stay alive to bring up their children and fulfil their social roles as a mother. Nevertheless, these transformations sometimes required interventions from family members or health workers, often desperate for their relatives or clients to respond to this ‘second chance’ at life. One participant recounted how her husband, who was her treatment supporter, and also on ART, helped her through her denial:

My CD4 decreased and viral load went up to 2000 copies. So that’s when they [the health workers] called my husband, they said ‘it’s better you talk to your wife, because your wife is going to die’. And I was about to die. So then, in the hospital, my husband talked to me, I swore right there ‘never again’. From that day, I was going to start taking the pills. And I started taking them normally, no problem ... He would say ‘... I am pleading. Continue and never give up! Take the pills, because we have these children here to look after, they still need us a lot, especially the little one ... look at your baby, and think: between the pill and the baby, what do you want?’ [Woman recently switched to third-line ART, Mozambique]

Some patients reported changing their attitudes towards their intimate relationships in the wake of treatment failure: several men declared they had reduced ‘womanising’ and some women divorced husbands that they believed to be promiscuous.

They [health workers] said the drugs were failing, the viruses were still multiplying ... I said that since my husband refuses to use condoms it was better for me to dump him. [Woman recently switched to third-line ART, Malawi]

In some cases, these changes were encouraged by health workers through their counselling of the patients, where they often attributed treatment failure to high-risk sexual behaviours (through ‘re-infection’) rather than as a result of sub-optimal ART adherence, and thereby shifted responsibility for high viral load results away from the patient’s own treatment-taking:

Mostly of course those with high viral loads we send them to the counsellors to discuss with the patient in terms of how she sees the husband and if he is faithful to you or do you trust him ... ? Re-infection comes because husbands may go to sleep with other women and then come to sleep with the wife who has maybe been trying to take medicine properly ... then he re-infects the poor lady [Health worker]

‘Nowadays we are used to it’: maintenance or relapse of social transformations

Although many participants expressed their commitment to more regular pill-taking with their new ART regimen, some adherence challenges were not always easily surmountable. Changes to

behaviours and lifestyles could be precarious and difficult to enact and sustain over time, such that initial, good intentions could sometimes fade as one man explained:

Sometimes when things start, they start nicely. When a person buys a car, he thinks about cleaning it before he leaves. It is like pills, a person takes them regularly on the first days, then he says ‘ahh I will take them tomorrow’. [Man receiving second-line ART, Mozambique]

A fluctuating sense of hope was also common among participants who, on the one hand often felt a sense of optimism regarding the future following regimen change, but on the other had already experienced the psychological burden of sustaining treatment:

Okay, I have accepted to take the drugs, and again I have accepted that I am sick and I have started a new walk. Now, what can I do to make me continue going for care without losing hope? In my case, I have accepted to come for care, but sometimes maybe I can start losing hope: now what is it that can keep me moving and going on so that I don’t go backwards? [Woman receiving third-line ART, Kenya]

However, other participants described how they found it progressively easier to adhere to their drugs over time, as they became more ‘experienced’ with taking their treatment, more used to attending HIV clinics and more familiar with treatment messages. Furthermore, in each of the settings, patients mentioned how the counselling helped them to understand the causes of treatment failure, allowing them to potentially address the problems that had caused it. Patients often cited building up a strong personal rapport with counselling staff, or becoming engaged with group counselling activities which encouraged them to make transformations in their lives that were more conducive to regular pill-taking. In some cases, participants attributed counselling as the main reason that they were able to overcome emotional and psychological struggles that had undermined their previous engagement in care, as one Kenyan woman explained:

Only one of the twins survived ... I had a lot of thoughts, I stopped taking drugs for two years. [name of counsellor] kept on teaching us, she taught me ... I joined the support group and you could hear people had challenges more than what you are going through, I listened to them then I gathered courage and started taking drugs. [Woman receiving second-line ART, Kenya]

Over the years, many patients reported building resilience to community stigma:

Earlier I used to feel bad, but nowadays even the people who used to walk tip toe when going to take the drugs so that you don’t see them. So someone can laugh at you today ... tomorrow you are in the queue with them! Nowadays we are used to it even if people talk. [Woman receiving second-line ART, Kenya]

They cared less about what other people thought, and may have disclosed their status to their partners, families or in some cases publicly. This often facilitated pill-taking inside households or workplaces, as family members could remind them to take their doses, or support them emotionally.

Some participants in Maputo described how maintaining their transformed lives was facilitated through access to differentiated models of care offered to patients on second-line treatment with undetectable viral loads. Patient clubs with fast-track refills, for instance, were appreciated given they allowed participants to re-enter employment or re-engage in other activities that some had stopped following treatment failure:

Clubs save time and we do not have to wait long in the pharmacy, and check-up ... we no longer have to ask for permission at work to go to hospital ... [Man receiving second-line ART, Mozambique]

However, other patients risked not being able to maintain their renewed desire to adhere to their drugs given the persistence of multiple and interrelated social, economic, health system and medication challenges that had previously undermined their adherence on first-line regimens. Once initiated on second-line ART, there were usually a greater number of pills, a twice-daily prescription, and more significant side effects, all of which could conflict with participants’ work or family obligations. Patients navigated these challenges in different ways, sometimes modifying their dosing schedule, to cope with side-effects.

I used to take my drugs once a day, I decided it on my own because I could hear some people say that the drugs can be taken once ... when I was walking I felt some dizziness and that was preventing me from going to the garden, that is how I started taking drugs once (per day) **Did you tell the doctor?** ... when he asked how am taking the drugs I said 8 in the morning and 8 in the evening. I never told him that am taking the drugs once. [Woman receiving third-line ART, Kenya]

This account also illustrates how some participants navigated different sources of information, from other PLHIV as well as health workers, in order to make their treatment-taking decisions, which they may then choose to conceal from health workers.

For other patients, challenges that they had experienced whilst on first-line ART remained unaddressed and continued to blight their efforts to take their pills regularly, particularly those that were related to structural issues such as poverty.

My social position is not good as I am not working, I sometimes have appetite of eating fruits, many other things. Nonetheless I can't afford: the same difficulties I used to go through when I was on the first line [ART]. Regarding difficulties, nothing has changed. [Man receiving second-line ART, Mozambique]

Discussion

This study explored the narratives of biographical disruptions and social transformations in the accounts of PLHIV who had experienced treatment failure prior to being transitioned onto second-, and in some cases, third-line treatment regimens, in one urban and two rural African settings. We found that when faced with ill-health as a result of treatment failure (typically on first-line regimens), PLHIV often gave up hope, fearing an imminent death, mirroring the despair that was often observed among PLHIV in the era prior to widespread ART availability (Pierret, 2007; Trainor & Ezer, 2000; Whyte, 2014). Prolonged illnesses due to delays in switching regimens could exacerbate the suffering and despair of PLHIV, although this may be improving with recent scale-up of routine viral load monitoring. Being transitioned onto a more effective treatment regimen often restored hope and engendered a sense of optimism for these patients. Our findings support calls for timely regimen switching for patients with treatment failure and align with those of other researchers who have identified hope as a central element of patients' experiences of life on ART (Nixon et al., 2018; Rhodes, Bernays, & Terzić, 2009), confirming the importance of interventions that help to sustain patients' hope and optimism for promoting their engagement with HIV treatment programmes (Bernays, Rhodes, & Barnett, 2007; Nixon et al., 2018).

Initiation of second- or third-line regimens was often also experienced by patients as an opportunity for redemption and a second chance to try and adhere to the strict behavioural codes that were seen as necessary for adequate pill-taking. Other scholars have noted similar responses from PLHIV after witnessing the death of a peer or loved one which may also act as a trigger to overcome denial or adherence challenges (Skovdal et al., 2017). Our participants were often able to make substantial changes to their working arrangements or social circumstances in order to address previous challenges that had undermined their ability to take their drugs as prescribed. Several researchers have also noted how social relationships may be modified, or behaviours re-evaluated among people living with chronic illnesses including HIV, often leading to the development of new identities and coping mechanisms (Davies, 1997; Frank, 1993; Hassin, 1994; Merten et al., 2010; Russell & Seeley, 2010; Seeley & Russell, 2010). In accord with previous studies, our findings suggest that the ability of PLHIV to effectively incorporate these changes into their biographies with a sense of progression, rather than disruption, is likely to be paramount to sustained engagement to treatment in the long-term (Alexias et al., 2016; Wekesa & Coast, 2013).

A sense of regret, remorse and self-blame were commonly expressed among our participants as they reflected on the circumstances that led to their treatment failure, particularly when they considered that second- or third-line treatment regimens would require additional sacrifices or compromises to their lifestyle. Other researchers have also shown that PLHIV often blame themselves for dis-engaging from care, and that this sense of guilt and fault need to be carefully navigated by health

care workers as they move forward in their treatment journeys (Layer et al., 2014). In addition, the precarity of the social transformations that accompany regimen change that we observed echo the findings in Russell and Seeley's research in Uganda among individuals who initiated first-line ART following HIV-related illnesses (Russell & Seeley, 2010; Seeley & Russell, 2010) and recall the complexity of achieving sustained engagement with HIV care and treatment in the context of pervasive stigma and challenging social circumstances (Ondenge et al., 2017; Skovdal et al., 2017; Stern, Colvin, Schutz, Burton, & Meintjes, 2017; Wamoyi et al., 2017). Other researchers have also noted apparent contradictions or paradoxes in the experiences of patients who have very long treatment histories, whereby optimism and hope often co-exist alongside new challenges that arise from sustained treatment-taking, and which may risk undermining treatment-taking (Nixon et al., 2018).

Our findings chart various unique challenges and supportive influences for maintaining a commitment to treatment over time amongst these patients. In line with other studies, we found that patients' transformations were closely linked to their social and economic circumstances which are often gendered (Merten et al., 2010; Russell & Seeley, 2010; Seeley & Russell, 2010). As such, economic as well as social support may help some patients to better cope through periods of livelihood disruptions arising from their treatment and care routines.

The themes that emerged from our analysis were very similar across the three sites, likely reflecting the fact that all three programmes were supported by MSF and therefore provided similar services and standard of care to second- and third-line patients. Tailored and patient-centred counselling proved valuable to many participants in our study as they transitioned through regimen-changing processes. Counselling interventions should recognise that patients who experience treatment failure may need support to prepare for transitioning onto second- or third-line regimens, including messages and skill development tailored to this cohort in order for them to understand and address the underlying causes for treatment failure. Furthermore, the needs of patients on second-line treatment are likely to be fluid, and those who struggle to address previous challenges to adherence may need more counselling support including access to support groups to trigger social changes in their lives that are conducive to more regular pill-taking. However, counselling is poorly supported or in decline in many sub-Saharan African settings. In the three countries included in this study there is no dedicated counselling cadre within the Ministry of Health workforce and counselling is left to clinical staff unless services are provided by partner organisations. As a result, these needs may go unmet unless greater national-level guidance and commitment to quality patient-centred counselling is forthcoming.

Our results also showed that patient clubs were important in catalysing or maintaining patients' 'transformations'. There is a growing recognition of the need for patient clubs offered through differentiated care strategies, including for patients on second-line regimens (ICAP, 2017). National guidelines on differentiated care in Kenya, Malawi and Mozambique are starting to make provisions for patients on second-line regimens, although their implementation is not yet widespread (Grimsrud, Barnabas, Ehrenkranz, & Ford, 2017; Ministry of Health Kenya, 2015; Ministry of Health Malawi, 2016).

These findings need to be considered in light of various limitations that are inherent to qualitative studies exploring experiences of adherence to ART. Patients may have overstated the significance of 'transformations' if they felt pressure from health services to 'repent' previous mistakes and justify their access to scarce regimens through exemplary adherence behaviour. Furthermore, although researchers were non-clinical, their association with a medical organisation may have influenced the participants' accounts. We tried to mitigate this by carrying out extensive fieldworker training, and by conducting repeat interviews with PLHIV wherever possible in order to build rapport and trust over time. Similarly, we used 'vignettes' a tool that allowed PLHIV to explain their adherence experiences and challenges through a hypothetical third person which may allow them to speak more freely about socially undesirable behaviour (Gourlay et al., 2014). Only patients who were currently engaged in HIV care were recruited into the study, and as such, the views of patients with the greatest

challenges with respect to receiving care, including those who did not manage to successfully transition to second- or third-line regimens would not have been captured.

An important strength of our study was our ability to draw on data from three different study sites, enabling us to document the similarity in the experiences of patients across diverse settings. To our knowledge, this is one of the first published qualitative studies among patients on second- and third-line treatment regimens and is valuable in providing insights into the challenges that may undermine the effectiveness of these regimens in these three sub-Saharan African settings. These findings are particularly timely as current efforts to scale up routine viral load monitoring and reduce the prices of second-line antiretroviral therapy regimens are likely to result in several million patients being transferred from first to second-line regimens over the coming decade (Estill et al., 2016). There is a short window of opportunity to learn from the experiences of patients on second-line treatments in order to design interventions that are likely to maximise the duration and effectiveness of increasingly wide-spread salvage regimens.

Conclusion

In conclusion, we found that patients on second- and third-line treatment regimens may initially experience transformations regarding social and economic aspects of their lives and their attitudes towards treatment, in many cases allowing re-engagement with treatment. However, the risk of relapse may be high unless prior challenges to adherence are addressed. Interventions should recognise the unique experiences of this growing population and deliver psychosocial support, treatment messages and models of care that are tailored and aimed towards promoting transformations and sustaining changes. This can aid in prolonging the life-span of second and third-line regimens.

Acknowledgements

We would like to thank the patients and health workers who participated in the study; the fieldworkers, transcribers and translators who worked on data collection; and the MSF teams in Homa Bay, Chiradzulu and Maputo for their excellent support to the study.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by Médecins Sans Frontières.

ORCID

Rose Burns  <http://orcid.org/0000-0002-4135-2403>

References

- Ajose, O., Mookerjee, S., Mills, E. J., Boulle, A., & Ford, N. (2012). Treatment outcomes of patients on second-line antiretroviral therapy in resource-limited settings. *Aids*, 26(8), 929–938. doi:10.1097/QAD.0b013e328351f5b2
- Alexias, G., Savvakis, M., & Stratopoulou, I. (2016). Embodiment and biographical disruption in people living with HIV/AIDS (PLWHA). *AIDS Care*, 28(5), 585–590. doi:10.1080/09540121.2015.1119782
- Barnett, W., Patten, G., Kerschberger, B., Conradie, K., Garone, D. B., Van Cutsem, G., & Colvin, C. K. (2013). Perceived adherence barriers among patients failing second-line antiretroviral therapy in Khayelitsha, South Africa. *Southern African Journal of HIV Medicine*, 14(4), 170–176. doi:10.7196/SAJHIVMED.981
- Bernays, S., Rhodes, T., & Barnett, T. (2007). Hope: A new way to look at the HIV epidemic. *Aids*, 21(Suppl 5), S5–11. doi:10.1097/01.aids.0000298097.64237.4b

- Bonnington, O., Wamoyi, J., Ddaaki, W., Bukenya, D., Ondenge, K., Skovdal, M., ... Wringe, A. (2017). Changing forms of HIV-related stigma along the HIV care and treatment continuum in sub-Saharan Africa: A temporal analysis. *Sexually Transmitted Infections*, 93(Suppl 3), doi:10.1136/sextrans-2016-052975
- Bury, M. (1982). Chronic illness as biographical disruption. *Sociology of Health and Illness*, 4(2), 167–182. doi:10.1111/1467-9566.ep11339939
- Cambiano, V., Bertagnolio, S., Jordan, M. R., Pillay, D., Perriens, J. H., Venter, F., ... Phillips, A. (2014). Predicted levels of HIV drug resistance: Potential impact of expanding diagnosis, retention, and eligibility criteria for antiretroviral therapy initiation. *Aids*, 28(Suppl. 1), doi:10.1097/QAD.0000000000000082
- Davies, M. L. (1997). Shattered assumptions: Time and the experience of long-term HIV positivity. *Social Science and Medicine*, 44(5), 561–571. doi:10.1016/S0277-9536(96)00177-3
- Estill, J., Ford, N., Salazar-Vizcaya, L., Haas, A. D., Blaser, N., Habiyambere, V., & Keiser, O. (2016). The need for second-line antiretroviral therapy in adults in sub-Saharan Africa up to 2030: A mathematical modelling study. *The Lancet HIV*, 3(3), doi:10.1016/S2352-3018(16)00016-3
- Foster, G., & Williamson, J. (2000). A review of current literature of the impact of HIV/AIDS on children in sub-Saharan Africa. *Aids*, 14(Suppl. 3), S275–S284.
- Frank, A. W. (1993). The rhetoric of self-change: Illness experience as narrative. *The Sociological Quarterly*, 34(1), 39–52. doi:10.1111/j.1533-8525.1993.tb00129.x
- Glaser, B. G., & Strauss, A. L. (1967). *The Discovery of grounded theory: Strategies for qualitative research*. Chicago: Transaction.
- Gourlay, A., Mshana, G., Birdthistle, I., Bulugu, G., Zaba, B., & Urassa, M. (2014). Using vignettes in qualitative research to explore barriers and facilitating factors to the uptake of prevention of mother-to-child transmission services in rural Tanzania: A critical analysis. *BMC Medical Research Methodology*, 14(1), 21. doi:10.1186/1471-2288-14-21
- Grimsrud, A., Barnabas, R. V., Ehrenkranz, P., & Ford, N. (2017). Evidence for scale up: The differentiated care research agenda. *Journal of the International AIDS Society*, doi:10.7448/IAS.20.5.22024
- Hassin, J. (1994). Living a responsible life: The impact of AIDS on the social identity of intravenous drug users. *Social Science and Medicine*, 39(3), 391–400. doi:10.1016/0277-9536(94)90136-8
- ICAP. (2017). *Differentiated Care for Adults at High Risk of HIV Disease Progression: A Call to Action*.
- Kipp, W., Tindyebwa, D., Rubaale, T., Karamagi, E., & Bajenja, E. (2007). Family caregivers in rural Uganda: The hidden reality. *Health Care for Women International*, 28(10), 856–871. doi:10.1080/07399330701615275
- Layer, E. H., Brahmabhatt, H., Beckham, S. W., Ntongwisangu, J., Mwampashi, A., Davis, W. W., ... Kennedy, C. E. (2014). 'I Pray that they accept me without scolding:' experiences with Disengagement and Re-engagement in HIV care and treatment services in Tanzania. *AIDS Patient Care and STDs*, 28(9), 483–488. doi:10.1089/apc.2014.0077
- Merten, S., Kenter, E., McKenzie, O., Musheke, M., Ntalasha, H., & Martin-Hilber, A. (2010). Patient-reported barriers and drivers of adherence to antiretrovirals in sub-Saharan Africa: A meta-ethnography. *Tropical Medicine and International Health*, 15(Suppl. 1), 16–33. doi:10.1111/j.1365-3156.2010.02510.x
- Ministry of Health Kenya, National AIDS and STI Control Programme. (2015). *Toolkit for third-line antiretroviral therapy in Kenya*. Nairobi: NASCOP.
- Ministry of Health Malawi. (2016). *Clinical Management of HIV in children and Adults: Malawi integrated guidelines and standard operating procedures*. Lilongwe: Department for HIV and AIDS.
- Nixon, S. A., Bond, V., Solomon, P., Cameron, C., Mwamba, C., Hanass-Hancock, J., ... Yates, T. (2018). Optimism alongside new challenges: Using a rehabilitation framework to explore experiences of a qualitative longitudinal cohort of people living with HIV on antiretroviral treatment in Lusaka, Zambia. *AIDS Care*, 30(3), 312–317. doi:10.1080/09540121.2017.1363365
- Ondenge, K., Renju, J., Bonnington, O., Moshabela, M., Wamoyi, J., Nyamukapa, C., ... Skovdal, M. (2017). 'I am treated well if i adhere to my HIV medication': Putting patient-provider interactions in context through insights from qualitative research in five sub-Saharan African countries. *Sexually Transmitted Infections*, 93), doi:10.1136/sextrans-2016-052973
- Pierret, J. (2007). An analysis over time (1990–2000) of the experiences of living with HIV. *Social Science & Medicine*, 65(8), 1595–1605. doi:10.1016/J.SOCSCIMED.2007.06.017
- Rhodes, T., Bernays, S., & Terzić, K. J. (2009). Medical promise and the recalibration of expectation: Hope and HIV treatment engagement in a transitional setting. *Social Science & Medicine*, 68(6), 1050–1059. doi:10.1016/j.socscimed.2008.12.017
- Rofes, E. (1998). *Dry bones breathe*. New York: Haworth Press.
- Russell, S., & Seeley, J. (2010). The transition to living with HIV as a chronic condition in rural Uganda: Working to create order and control when on antiretroviral therapy. *Social Science and Medicine*, 70(3), 375–382. doi:10.1016/j.socscimed.2009.10.039
- Russell, S., Seeley, J., Ezati, E., Wamai, N., Were, W., & Bunnell, R. (2007). Coming back from the dead: Living with HIV as a chronic condition in rural Africa. *Health Policy and Planning*, 22(5), 344–347. doi:10.1093/heapol/czm023

- Schramm, B., Carnimeo, V., Rakesh, A., Ardiel, D. L., Cossa, L., Bouchaud, O., ... Szumilin, E. (2016). *Cross-sectional assessment of virological failure, drug resistance and third-line regimen requirements among patients receiving second-line ART in 3 large HIV programmes in Kenya, Malawi and Mozambique*. 21st International AIDS Conference, Durban, South Africa.
- Schuurman, R., Wensing, J., Barth, A. M., E, R., van der Loeff, S., Schuurman, M. F., ... M, A. (2010). Virological follow-up of adult patients in antiretroviral treatment programmes in sub-Saharan Africa: A systematic review. *The Lancet Infectious Diseases*, 10, 155–166. doi:10.1016/S1473-3099(09)70328-7
- Seeley, J., & Russell, S. (2010). Social rebirth and social transformation? Rebuilding social lives after ART in rural Uganda. *AIDS Care*, 22 Suppl 1(1998), 44–50. doi:10.1080/09540121003605054
- Shapiro, S., Angus, L., & Davis, C. (1997). Identity and meaning in the experience of Cancer: Three Narrative themes. *Journal of Health Psychology*, 2(4), 539–554. doi:10.1177/135910539700200410
- Skovdal, M., Wringe, A., Seeley, J., Renju, J., Papanini, S., Wamoyi, J., ... Bonnington, O. (2017). Using theories of practice to understand HIV-positive persons varied engagement with HIV services: A qualitative study in six Sub-Saharan African countries. *Sexually Transmitted Infections*, 93(Suppl. 3), doi:10.1136/sextrans-2016-052977
- Ssekubugu, R., Renju, J., Zaba, B., Seeley, J., Bukenya, D., Ddaaki, W., ... Wringe, A. (2018). 'He was no longer listening to me': A qualitative study in six Sub-Saharan African countries exploring next-of-kin perspectives on caring following the death of a relative from AIDS. *AIDS Care*, doi:10.1080/09540121.2018.1537467
- Stern, E., Colvin, C., Schutz, N. G. C., Burton, R., & Meintjes, G. (2017). Conceptions of agency and constraint for HIV-positive patients and healthcare workers to support long-term engagement with antiretroviral therapy care in Khayelitsha, South Africa. *African Journal of AIDS Research*, 16(1), doi:10.2989/16085906.2017.1285795
- Trainor, A., & Ezer, H. (2000). Rebuilding life: The experience of living with AIDS after Facing imminent death. *Qualitative Health Research*, 10(5), 646–660. doi:10.1177/104973200129118705
- UNAIDS. (2018). *Global HIV and AIDS statistics-2018 factsheet*. Retrieved from <http://www.unaids.org/en/resources/fact-sheet>.
- Wamoyi, J., Renju, J., Moshabela, M., McLean, E., Nyato, D., Mbata, D., ... Wringe, A. (2017). Understanding the relationship between couple dynamics and engagement with HIV care services: Insights from a qualitative study in eastern and southern Africa. *Sexually Transmitted Infections*, 93(Suppl 3), doi:10.1136/sextrans-2016-052976
- Wekesa, E., & Coast, E. (2013). Living with HIV postdiagnosis: A qualitative study of the experiences of Nairobi slum residents. *BMJ Open*, 3(5), e002399. doi:10.1136/bmjopen-2012-002399
- WHO. (2015). *Guidelines on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*. [http://doi.org/978 92 4 150956 5](http://doi.org/978%2092%204%20150956%205).
- WHO. (2016). *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection recommendations for a public health approach- second edition*. Geneva.
- WHO. (2017). *HIV drug resistance report 2017*. Geneva.
- WHO. (2018). *Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidance*. Geneva.
- Whyte, S. R. (2014). *Second Chances: Surviving AIDS in Uganda*. Durham: Duke University Press.
- Wringe, A., Renju, J., Seeley, J., Moshabela, M., & Skovdal, M. (2017). Bottlenecks to HIV care and treatment in sub-Saharan Africa: A multi-country qualitative study. *Sexually Transmitted Infections*, doi:10.1136/sextrans-2017-053172