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ORIGINAL ARTICLE

Advanced HIV disease and associated attrition after re-engagement in HIV care in Myanmar from 2003 to 2019: a retrospective cohort study

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Background: The burden of advanced HIV disease (AHD) and predictors of outcomes among people living with HIV (PLHIV) re-engaging in care are not well known.

Methods: We conducted a retrospective cohort study of PLHIV who re-engaged in care after being lost to follow-up (LFU), from 2003 to 2019, in Myanmar. We calculated the incidence rates of attrition after re-engagement and performed Cox regression to identify risk factors for attrition.

Results: Of 44 131 PLHIV who started antiretroviral treatment, 12 338 (28.0%) were LFU at least once: 7608 (61.6%) re-engaged in care, 4672 (61.4%) with AHD at re-engagement. The death and LFU rates were 2.21-fold (95% CI 1.82 to 2.67) and 1.46-fold (95% CI 1.33 to 1.61) higher among patients who re-engaged with AHD ($p>0.001$). Death in patients who re-engaged with AHD was associated with male sex (adjusted HR [aHR] 2.63; 95% CI 1.31 to 5.26; $p=0.006$), TB coinfection (aHR 2.26; 95% CI 1.23 to 4.14; $p=0.008$) and sex work (aHR 7.49, 95% CI 2.29 to 22.52; $p<0.001$). History of intravenous drug use was identified as a predictor of being LFU.

Conclusions: Re-engagement in HIV care in Myanmar is frequent and those who re-engage carry a high burden of AHD. As AHD at re-engagement is associated with higher attrition rates, implementation of differentiated interventions that enable earlier linkage to care and prompt identification and management of AHD in this population is necessary.

Keywords: advanced HIV disease, attrition, key populations, Myanmar, re-engagement.

Introduction

The world has achieved progress in controlling the HIV epidemic and out of 38 million people living with HIV (PLHIV), 73% (56–88%) were receiving antiretroviral treatment (ART) by the end of 2020.[1] In 2015, countries started to implement the 'Test and Treat' strategy that recommends starting ART regardless of the CD4 cell count. Still, 680 000 (480 000–1 000 000) people died of HIV in 2020.[1] HIV-related mortality was declining but plateaued due to a persistent burden of advanced HIV disease (AHD), defined as having either a CD4 cell count of <200 cells/mm^3 or clinical stage III or IV disease, or being a child aged <5 y with HIV infection.[2] Data from various contexts show that more than one-third of PLHIV start ART with AHD.[3–5] In the early stage of ART roll-out, patients with AHD were mostly ART-naïve 'late presenters', who were diagnosed with HIV and started ART in an advanced

stage of their infection. At present, an increasing proportion of patients who present with AHD had started ART, interrupted treatment and then re-engaged in care.[3] A South African study showed that the proportion of ART-experienced patients returning to care with a CD4 cell count of <50 cells/mm^3 increased from 14.3% to 56.7%.[5] Patients with AHD are at a higher risk of dying.[2] Two reported leading causes of death are TB and cryptococcal meningitis, although data on the specific cause of mortality are not usually reported.[6] Since 2017, the WHO has recommended a package of interventions that include enhanced prophylaxis, screening and diagnosis of the most prevalent opportunistic infections, rapid (re)initiation of ART in patients with AHD and adherence support.[2] However, most programmes do not have clear targets for the implementation of these specific recommendations. Furthermore, there is a lack of standardised indicators to systematically monitor and evaluate the burden of AHD or the effect of intervention on morbidity or mortality associated with the presence of AHD. Some experts therefore recommend adding AHD indicators to the already existing '95–95-95' Joint United Nations Programme on HIV/AIDS (UNAIDS) targets.[7]

Myanmar has the second highest HIV prevalence in Southeast Asia. About 0.57% of the general population was estimated to be infected with HIV, although key populations and their partners were the most affected; the HIV prevalence among people who inject drugs (PWID), sex workers (SWs) and men having sex with men (MSM) was 28.5%, 25% and 20%, respectively.[8] In 2018, Myanmar counted an estimated 220 000 PLHIV.[1] The National AIDS Programme, Ministry of Health and Sports, Myanmar (NAP) successfully scaled up ART, reaching 77% coverage by the end of 2019.[9] However, a study published in 2018 by Aung et al. reported a 58% burden of AHD upon enrolment to HIV care and high rates of early mortality and loss to follow-up. This study identified AHD as one of the risk factors for unfavourable treatment outcomes in the large Myanmar cohort.[10]

Since 2003, Médecins Sans Frontières (MSF), in collaboration with the NAP, has been providing HIV care at the primary healthcare level in Yangon, Kachin and Shan States in Myanmar. Before 2014, due to the high volume of patients needing to start ART, only those with severe immunosuppression (CD4 cell count<200 cells/mm^3) were enrolled for treatment. From 2014 onwards, after the NAP successfully scaled up access to ART through decentralisation, and following updates from the WHO and national guidelines, the ART enrolment criteria became more inclusive. The threshold to start ART increased stepwise, from CD4 cell count<200 cells/mm^3 to 'Test and Treat' in 2016. By 31 December 2018, 58 470 PLHIV aged >5 y were enrolled in HIV care in MSF programmes. Since 2014, to provide good quality of care in a setting with a health workforce gap and to maximally focus clinical care on the needs of patients with AHD, MSF implemented differentiated service delivery, spacing appointments for patients stable on ART and introducing the concept of task sharing.[11] Since 2009, AHD management included the full package of systematic prophylaxis, screening and treatment of opportunistic infections, as recommended by the WHO.[2] Studies from China, Cambodia and Myanmar report that despite the gradual improvement observed in earlier ART initiation, a large proportion of patients starting ART have AHD.[10,12,13] Re-engagement with healthcare after treatment interruption has been studied in a limited number of contexts and studies report that 11–77% of patients enrolled in HIV care temporarily disengage.[14–16] However, the burden of AHD after re-engagement has not yet been studied in detail. In the present study, we describe the proportion of PLHIV presenting with AHD at the time of re-engagement in HIV care in MSF's programme in Myanmar. We compare attrition after re-engagement in those with and without AHD and assess predictors of attrition among those with AHD.

Methods

Design and study population

This was a retrospective cohort study of PLHIV aged >5 y at the time of ART initiation, who received ART in the Myanmar MSF HIV programme from 1 January 2003 to 1 January 2019 and who re-engaged in care after being declared lost to follow-up (LFU).

Data collection and analysis

The study used routine programme data collected from standardised patient forms and encoded in the MSF HIV programme database (Follow-up and Care of HIV Infection and AIDS). The dataset was exported into the statistical software RStudio (version 3.5.1; RStudio, Boston, MA, USA) for statistical analysis. Independent variables included age, gender, marital status, profession, binary variables to show belonging to a subgroup (SWs, PWID, MSM, imprisonment, economic migration, mother-to-child transmission, blood transfusion), having an HIV-positive partner, opportunistic infections (cryptococcal meningitis, TB, talaromycosis [formerly penicilliosis], cytomegalovirus infection), baseline CD4 cell count (cells/mm^3) and baseline WHO clinical stage. Outcome variables included LFU (disengaged from care from the next planned appointment for >60 d), death (all-cause mortality while on ART) and attrition (either LFU or death). Prevalence of severe opportunistic infections was reported for the first 60 d after the day of re-engagement. Baseline characteristics were described using frequencies and percentages for categorical variables. For continuous variables, the distribution of data was assessed by histograms. When the distribution was normal, means with their SDs were calculated, otherwise medians with IQR would be presented. The follow-up time was expressed in person-years and defined as the difference between the date of ART start and the date the patient had an event (either LFU or death) or the date the patient was censored (date of transfer out or, if active on ART, the date of the end of the observation period). Incidence rates of death and LFU were calculated as the number of participants who experienced the event (death, LFU) divided by total person-years of follow-up time. Incidence rate ratios were calculated as ratios of incidence rates in exposed (with AHD) and non-exposed (without AHD) populations. Kaplan–Meier survival analyses were performed to assess time to death, LFU and attrition, yielding survival probability for AHD patients vs those without AHD. The log-rank test was used to determine if the differences between survival curves were significant. In separate survival analyses, LFU and death were considered as censoring events. To identify predictors of attrition among patients with AHD after re-engaging in care, univariate Cox regression was used to assess the association between exposure variables and attrition and

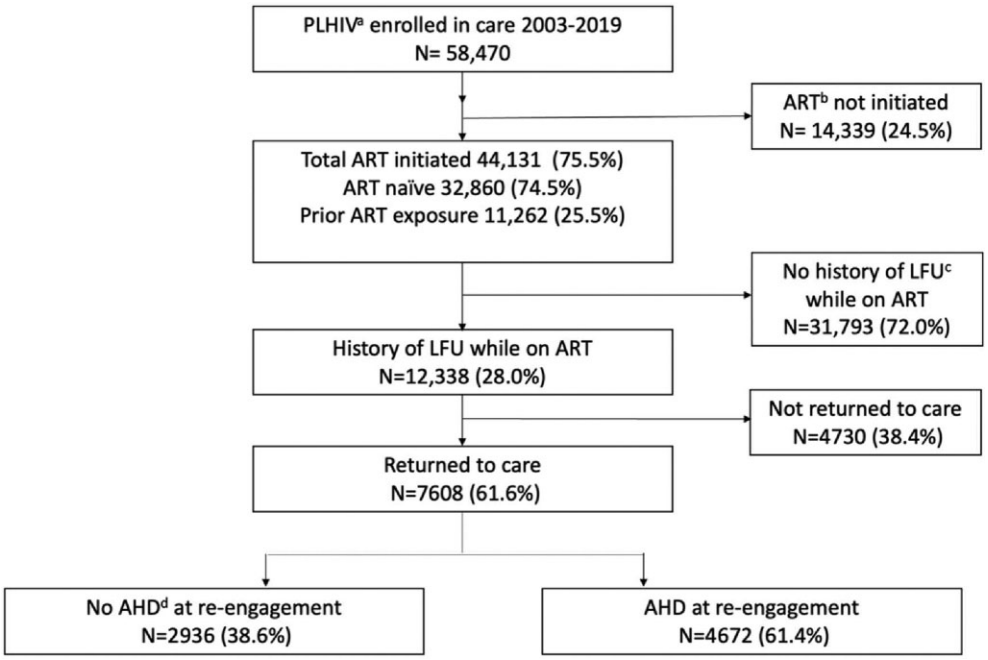

Figure 1. Flowchart of inclusion pathway in the study. [a]People living with HIV; [b]antiretroviral treatment; [c]lost to follow-up; [d]advanced HIV disease.

those where association resulted in p<0.10 together with gender and age were included in the multivariable Cox regression model. A multiple Cox regression model was constructed using a hierarchical approach. First, we created a saturated multivariable model, including all explanatory variables. The model was then simplified by stepwise backwards elimination until only variables that improved fit of the model were included in the final analysis.

Results

From 2003 to 2019, 58 470 PLHIV aged >5 y were enrolled in care and 44 131 (75.5%) were initiated on ART: 32 869 (74.5%) were ART-naïve and 11 271 (25.5%) had been exposed to ART before enrolment in the MSF programme. Among ART-naïve patients, 24 791 (75.4%) had AHD. Of 44 131 PLHIV who started ART, 12 338 (28%) were LFU at least once: 7608 (61.6%) re-engaged in care, among whom 4672 (61.4%) had AHD at the time of re-engagement (Figure 1). Among those who re-engaged and were diagnosed with AHD, 460 (9.84%) had not been diagnosed with AHD before, and they progressed to AHD while being LFU.

Demographic and clinical characteristics of PLHIV re-engaging in care are presented in Table 1. Among PLHIV who re-engaged with AHD, 547 (11.7%) and 86 (1.84%) did not have a baseline CD4 cell count or WHO clinical stage reported, respectively. Among those for whom data were available, 1839 (44.5% of 4125) had a CD4 cell count of <200 cells/mm^3 and 3995 (87.1% of 4586) presented with WHO clinical stage III or IV disease. Among PLHIV with AHD, 1800 (38.5%) had a CD4 cell count and WHO stage status showing AHD, 39 (0.83%) had AHD based on having a CD4 cell count of <200 cells/mm^3 and 2833 (60.6%) of PLHIV were diagnosed based on their WHO clinical status. TB, cryptococcal meningitis, cytomegalovirus and talaromycosis were diagnosed in 30%, 1.7%, 1.2% and 0.1% of patients re-engaging in care with AHD, respectively.

Attrition after re-engagement

The mean time to re-engagement was shorter among PLHIV with AHD than among those without AHD (541.4 (SD 579.7) vs 907.8 (SD 804.3) d; p<0.001). Of 7608 patients who re-engaged in care, 2617 (34.4%) either died (N=605; 8.0%) or were subsequently LFU again (N=2012; 26.4%) (Table 2). The death rates in patients with and without AHD were 2.95 (95% CI 2.70 to 3.22) and 1.33 (95% CI 1.13 to 1.58) per 100 person-years, respectively. The LFU rates in patients with and without AHD were 8.81 (95% CI 8.38 to 9.26) and 6.01 (95% CI 5.56 to 6.49), respectively. The death and LFU rate were 2.21-fold (95% CI 1.82 to 2.67) and 1.46-fold (95% CI 1.33 to 1.61) higher, respectively, among patients who re-engaged with AHD (p>0.001). Based on survival statistics after re-engagement in care, retention in care at 1, 2, 4 and 6 y in patients with and without AHD was 78.1% (95% CI 77.9 to 78.3%) vs 88% (95% CI 87.6 to 88.2%), 69.4% (95% CI 68.8 to 70.2%) vs 81.4% (95% CI 81.1 to 81.9%), 60.6% (95% CI 59.9 to 61.3%) vs 74.1% (95% CI 73.5 to 74.6%) and 54.2% (95% CI 53.1 to 55.0%) vs 69.8% (95% CI 68.8 to 70.9%) (p<0.001), respectively, as demonstrated in Figure 2.

Predictors of attrition among patients who re-engage with AHD

Among PLHIV who re-engaged in care with AHD, being male (adjusted HR [aHR] 2.63, 95% CI 1.31 to 5.26; p=0.006), working

Table 1. Demographic characteristics of the study population (n=7608)

Characteristics	Categories	n	%
Gender	Male	4218	55.4
	Female	3390	44.6
Age categories (y)	6–15	380	5.0
	16–40	5424	71.3
	41–65	1794	23.6
	>65	10	0.10
Marital status	Married	4551	59.7
	Separated	514	6.8
	Single	1686	22.2
	Widow	654	8.6
	Missing	203	2.7
Profession	Business	813	10.7
	Transportation	228	3.0
	Administration	220	2.9
	Manual labour	1131	14.9
	Student	118	1.6
	Unemployed	1598	20.9
	Other	2943	38.7
	Missing	557	7.3
SW[a]	No	4774	62.7
	Yes	129	1.7
	Missing	2705	35.6
PWID[b]	No	4213	55.4
	Yes	947	12.4
	Missing	2448	32.2
MSM[c]	No	4769	62.7
	Yes	57	0.75
	Missing	2782	36.5
Economical migrant	No	7468	98.2
	Yes	140	1.8
Imprisonment	No	7468	98.2
	Yes	140	1.8
History of blood transfusion	No	7508	98.7
	Yes	100	1.3
Mother-to-child prevention	No	7458	98.0
	Yes	150	2.0
HIV positive partner	No	6967	91.6
	Yes	641	8.4

[a]Sex worker.
[b]People who inject drugs.
[c]Men having sex with men.

as a SW (aHR 7.49, 95% CI 2.29 to 22.52; p<0.001) or having a diagnosis of TB when re-engaging in care (aHR 2.26, 95% CI 1.23 to 4.14; p=0.008) predicted mortality (Table 3). Those with a history of intravenous drug use were identified as having an almost twofold higher hazard of being LFU (aHR 1.94; 95% CI 1.54 to 2.46; p<0.001) compared with those with no history of intravenous drug use (Table 4). In comparison with those who were aged 16–40 y, children who re-engaged with AHD aged 6–15 y and those re-engaging aged 41–65 y had a lower hazard of being LFU (aHR 0.24, 95% CI 0.009 to 0.66 and aHR 0.77, 95% CI 0.62 to 0.95; p=0.016).

Discussion

Almost one-third of PLHIV in our cohort were LFU at least once during the 15 y of the follow-up period. More than one-half of the LFU cohort re-engaged in care. At the time of the re-engagement, they were presenting with a high burden of AHD. Our study results demonstrate consistently higher attrition rates over time for those re-engaging with AHD. Death and LFU rates among PLHIV who re-engaged with AHD were significantly higher when compared with those who re-engaged in a better immunological and clinical condition.

In most HIV programmes, the frequency of treatment interruptions is very likely underestimated. A study from South Africa showed that one-quarter of PLHIV disengaged from care at least once during a study period of >10 y and that one-third re-engaged in care.[14] In Uganda, during 7 y of follow-up, disengagement from care was less frequent (11.2%) and >70% returned to care. The authors explain the high proportion of re-engagement by the performance tracing system.[17] Similarly, in our setting, tracing of LFU patients was established from the start of the programme and it contributed to re-engagement. A study from a rural community in Kenya reported that 77% of PLHIV disengaged at least once from care, with some patients interrupting treatment up to seven times.[15] In our study, we observed up to two episodes of being LFU. After re-engaging in care, about one-quarter disengaged from care again. The majority of the study participants were diagnosed with AHD before interrupting care. Another 10% experienced clinical and/or immunological deterioration after disengaging from care, which on average lasted >500 d. Repetitive disengagement and a high burden of AHD show that barriers to care are not yet well addressed. Patients on lifelong ART need to overcome psychosocial and structural barriers to pill intake on a daily basis.[18] Even when appointments are spaced, patients still must invest time and money to stay in care. Besides health system-driven interventions, such as spacing and tracing, programmes may also need to consider patient-driven interventions that build on social networks within communities.[19] Experiences from high HIV prevalence settings show that retention in community-based HIV programmes is high.[20,21] Various interventions have been suggested as enablers for linkage to HIV care among those diagnosed with HIV, but there is a lack of evidence on the specific interventions for those who disengaged from care.[22] Additional evidence is needed to identify reasons for delayed re-engagement. Tailored but feasible and cost-effective approaches for earlier linkage to care need to be evaluated. In a study from Zambia, Zanolini et al. reported a negative impact of health providers' attitudes, described as unfriendly or disrespectful, on retention and re-engagement in care.[23] Therefore, some programmes started with the implementation of 'Welcome Back' differentiated services specifically targeting those who are re-engaging in care.[4,24]

Among those who re-engaged with AHD, key populations were at risk of having an unfavourable outcome. People with a history of drug use had an almost two times higher hazard of being LFU after re-engagement and SWs were seven times more at

Table 2. Attrition, lost to follow-up and death rates per 100 person-years, by advanced HIV disease status

	AHD[a] at re-engagement (15 983 person-years)		No AHD[b] at re-engagement (10 051 person-years)			
	N	Rate (95% CI)	N	Rate (95% CI)	Incidence rate ratio (95% CI)	p
Death	471	2.95 (2.70 to 3.22)	134	1.33 (1.13 to 1.58)	2.21 (1.82 to 2.67)	<0.001
LFU[c]	1408	8.81 (8.38 to 9.26)	604	6.01 (5.56 to 6.49)	1.46 (1.33 to 1.61)	<0.001
Attrition	1879	11.76 (11.27 to 12.26)	738	7.34 (6.85 to 7.87)	1.61 (1.47 to 1.74)	<0.001

[a]Advanced HIV disease (N=4672).
[b]No advanced HIV disease (N=2963).
[c]Lost to follow-up after re-engagement.

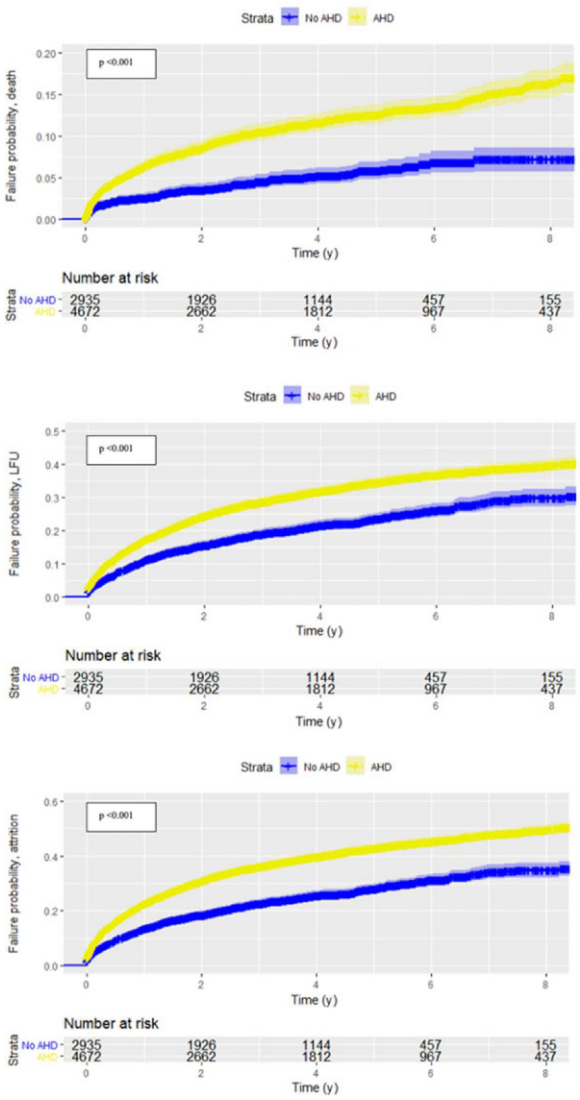

Figure 2. Kaplan–Meier curves for death, lost to follow-up (LFU) and attrition by advanced HIV disease status (n=7608).

risk of dying. Stigma, discrimination, criminalisation of sex work and drug use challenge adherence may delay re-engagement among those LFU, and consequently increase the risk of AHD and higher attrition after re-engagement, as recently reported in a review by Chen et al.[25] Our programme was not designed to provide differentiated care adapted to the specific needs of key populations. Furthermore, in our context, key populations are often mobile and their working hours impede easy access to care. There is a longstanding debate whether HIV care for key populations should be provided integrated, as part of HIV services for the general population, or whether they would be better served by a vertical set-up, involving peer healthcare workers and providing care at a venue where they feel most comfortable.[26]

Myanmar reports a high burden of HIV among key populations.[26] The National HIV Strategic Plan recommends differentiated service delivery models adapted to both health and social needs of key populations, while building on community engagement and peer support.[27] Implementation of those interventions should be seen as a priority by the national programme and its partners in Myanmar.

Effective AHD management requires diagnostic capacity. CD4 testing remains critical for the diagnosis of AHD and subsequent screening, prophylaxis, diagnosis and treatment of opportunistic infections. Since the implementation of 'Treat All', access to CD4 testing has reduced in many HIV programmes.[4] A study from Uganda reported a persistent high burden of AHD, which can only be identified by measuring the number of CD4 cells (24% of tested with a CD4 cell count of <200 cells/mm^3 and 83% presenting with WHO stage I or II). Unfortunately, CD4 testing coverage at enrolment decreased from 73% in 2013 to 21% in 2018, following the introduction of the 'Test and Treat' policy.[28] In our cohort of PLHIV re-engaging with care with AHD and available baseline results, 44.5% had a CD4 cell count of <200 cells/mm^3, but the majority were diagnosed with WHO stage III or IV at the same time, which could be explained by the ART experience and WHO stage diagnosis from the first ART initiation.

To achieve '95–95-95' UNAIDS targets, it is important to continue the scale-up of access to decentralised HIV care in Myanmar and to expand access to AHD care services. As ART cohorts in Myanmar grow and age, differentiated service delivery will allow

Table 3. Risk factors for dying among PLHIV re-engaged in care with advanced HIV disease

	Died (n=471)[a]		Univariable Cox regression		Multivariable Cox regression	
	n	%	HR	p	Adjusted HR	p
Gender						
Female	129	7.5	Reference		Reference	
Male	342	11.6	1.72 (1.41–2.13)	<0.001	2.63 (1.31–5.26)	0.006
Age group (y)						
6–15	4	2.7	0.24 (0.09–0.63)	<0.001	NA[b]	NS[c]
16–40	333	10.0	Reference		Reference	
41–65	1172	11.4	1.21 (0.99–1.48)		1.82 (1.01–3.28)	
>65	0	0.0	NA[b]		NA[b]	
Marital status						
Married	258	9.9	Reference	0.059	Reference	NS[c]
Separated	51	12.9	1.43 (1.06–1.94)		1.11 (0.43–2.87)	
Single	105	9.4	1.02 (0.81–1.28)		1.02 (0.53–1.95)	
Widow	45	9.8	0.93 (0.68–1.28)		0.52 (0.16–1.75)	
Profession						
Business	50	9.9	Reference	0.179	NA[d]	
Transportation	17	10.5	1.12 (0.65–1.95)			
Administration	16	11.7	1.30 (0.74–2.28)			
Manual labour	90	11.7	1.38 (0.98–1.95)			
Student	3	4.9	0.48 (0.15–1.54)			
Unemployed	90	9.9	1.03 (0.73–1.45)			
Other	171	9.4	1.05 (0.77–1.44)			
PWID[e,f]	20	3.0	2.08 (1.23–3.50)	0.006	0.66 (0.27–1.61)	NS[c]
Imprisonment[e]	3	2.8	0.26 (0.08–0.80)	0.019	1.74 (0.40–7.50)	NS[c]
SW[e,g]	14	17.1	10.84 (6.03–19.5)	<0.001	7.49 (2.29–22.52)	<0.001
Economical migrant[e]	5	5.2	0.54 (0.23–1.31)	0.175	NA[d]	
Blood transfusion[e]	2	3.6	0.31 (0.08–1.23)	0.095	0.85 (0.12–6.32)	NS[c]
HIV positive partner[e]	3	0.9	0.07 (0.02–0.22)	<0.001	0.56 (0.16–1.94)	NS[c]
TB[e]	118	15.8	1.82 (1.48–2.24)	<0.001	2.26 (1.23–4.14)	0.008
Cryptococcosis[e]	3	14.3	2.74 (1.02–7.32)	0.045	NA[b]	
Cytomegalovirus[e]	4	26.7	1.56 (0.50–4.84)	0.446	NA[d]	

[a]Death was not observed among participants with talaromycosis, men having sex with men and those registered through the mother-to-child prevention programme.
[b]Not applicable due to a small number of events.
[c]Not significant (p>0.05).
[d]Not applicable due to p>0.10.
[e]Binary variable.
[f]People who inject drugs.
[g]Sex worker.

stable patients to access ART closer to home, while clinic-based care can prioritise AHD management.[3,29]

In our cohort, one-third of PLHIV were diagnosed with TB at the time of their re-engagement. TB is known to be the most frequent cause of mortality among PLHIV and, in our study, the mortality hazard was twofold higher in those coinfected with TB.[3,6] Cryptococcal meningitis, another important cause of mortality, was registered in a small number of study participants, lower than what was reported in other resource-limited settings.[5,6] We speculate that the real prevalence in our cohort was much higher than reported. It is probable that this diagnosis was not rigorously recorded in the electronic database. To monitor and evaluate and subsequently adapt HIV services, it is necessary for national programmes to set targets and develop indicators focusing on the implementation of an AHD package of care.[30]

Our study has some important strengths. The findings represent the reality of a large, long-term HIV programme in the southeast Asian context. We focus our reporting outcomes on PLHIV re-engaging in care, which was not extensively studied in this region. However, there are also several limitations. First, our retrospective study used routinely collected programme data, which may have introduced information bias. This was mitigated

Table 4. Risk factors for being lost to follow-up among PLHIV re-engaged in care with advanced HIV disease

	Lost to follow up (N=1408)[a]		Univariable Cox regression		Multivariable Cox regression	
	n	%	HR	p	Adjusted HR	p
Gender						
Female	462	26.9	Reference		Reference	
Male	946	32.0	1.32 (1.18–1.48)	<0.001	1.05 (0.85–1.29)	NS[b]
Age group (y)						
6–15	23	15.3	0.42 (0.28–0.63)	<0.001	0.24 (0.09–0.66)	0.016
16–40	1091	32.6	Reference			
41–65	293	25.0	0.8 (0.7–0.91)		0.77 (0.62–0.95)	
>65	1	25.0	NA[c]		NA[c]	
Marital status						
Married	746	28.7	Reference	<0.001	Reference	NS[b]
Separated	150	38.0	1.45 (1.22–1.73)		1.46 (1.09–1.95)	
Single	368	32.9	1.24 (1.09–1.4)		1.15 (0.94–1.42)	
Widow	120	26.1	0.87 (0.72–1.06)		0.84 (0.61–1.15)	
Profession						
Business	134	26.5	Reference	0.04	Reference	NS[b]
Transportation	43	26.5	1.05 (0.74–1.48)		0.61 (0.31–1.21)	
Administration	37	27.0	1.11 (0.77–1.6)		0.99 (0.55–1.81)	
Manual labour	252	32.6	1.43 (1.16–1.76)		1.17 (0.84–1.62)	
Student	13	21.3	0.77 (0.43–1.36)		0.61 (0.21–1.71)	
Unemployed	256	28.2	1.09 (0.88–1.34)		1.06 (0.77–1.45)	
Other	591	65.0	1.33 (1.1–1.61)		1.20 (0.89–1.61)	
PWID[d,e]	250	38.1	2.6 (2,23–3.04)	<0.001	1.95 (1.54–2.46)	<0.001
Imprisonment[d]	25	22.9	0.71 (0.48–1.06)	0.093	0.77 (0.48–1.28)	NS[b]
MSM[b,d]	9	28.1	1.27 (0.66–2.45)	0.48	NA[d]	
SW[d,f]	26	31.7	1.64 (1.11–2.43)	0.013	1.22 (0.54–2.76)	NS[b]
Economic migrant[d]	36	37.1	1.33 (0,96–1.85)	0.091		
Blood transfusion[d]	9	16.4	0.47 (0.24–0.9)	0.022	0.71 (0.35–1.45)	NS[b]
Mother-to-child prevention[d]	4	6.1	0.16 (0.06–0.44)	<0.001	NA[c]	
HIV positive partner[d]	68	19.9	0.55 (0.43–0.7)	<0.001	0.69 (0.22–2.15)	NS[b]
TB[d]	241	32.3	1.12 (0.98–1.29)	0.100	0.98 (0.76–1.25)	NS[b]
Cryptococcosis[d]	6	28.6	1.03 (0.46–2.29)	0.949	NA[g]	
Cytomegalovirus[d]	3	20.0	0.67 (0.22–2.09)	0.446	NA[g]	

[a]There were no events observed among participants with talaromycosis.
[b]Not significant (p<0.05).
[c]Not applicable due to a small number of events.
[d]Binary variable.
[e]People who inject drugs.
[f]Sex worker.
[g]Not applicable due to p>0.10.

by involving a team of data clerks in data management, including prospective data encoding and periodic data cleaning. Reporting bias might have occurred as PLHIV in this setting tend to under-report certain risk behaviours due to stigma and criminalisation of these activities. This may have resulted in an underestimation of the frequency of such risk behaviours, which in turn may have affected our regression analyses. Data collection on opportunistic infections was disproportionally affected by missingness. We may have underestimated disengagement from care, as short interruptions were not identified, and we may have underestimated re-engagement in care, as those who silently returned to care in the same health facility (as newly registered patients) or self-transferred to another health provider were not accounted for. The study highlights areas of future research to investigate predictors of AHD among PLHIV who re-engage in care, to help identify at-risk groups who can be targeted or prioritised in provision of an AHD package of care. Furthermore, studies to assess specific reasons for unfavourable outcomes within these

specific populations (children, older people, key populations) to gain information on how to tailor AHD and re-engagement interventions would support health providers.

Conclusions

An adequate response to AHD remains an important component of controlling the HIV epidemic. Our study shows that re-engagement in HIV care, after a period of temporary disengagement, is frequent, and that those who re-engage carry a high burden of AHD in this context. In this population, interventions that enable earlier linkage to care, followed by prompt identification and management of AHD, are necessary because having AHD is associated with a higher risk of attrition. As key populations may be disproportionally affected by HIV, in settings where the HIV prevalence is high in this group, HIV care needs to include differentiated approaches, adapted to their specific needs. Such approaches will need to include a comprehensive clinical and social care package for the prevention, diagnosis and management of AHD.

Authors' contributions: The authors wish it to be known that, in their opinion, the first two authors should be regarded as joint First Authors. AM, TH, AL and TD conceptualised and designed the study. AM and TH contributed to study implementation. AM, TH, PT, HTM, TTT, AAK, MP and SS contributed to implementation of the study. TH was responsible for the data analysis. All authors participated in the data interpretation. AM drafted the original manuscript. All authors made major contributions to manuscript writing and all approved the final version of the manuscript.

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Competing interests: The authors have no competing interests to declare.

Ethical approval: The study was approved by the Institutional Review Board, Ministry of Public Health and Sports, Myanmar (Ethics/DMR/202/128). It fulfilled the exemption criteria set by the MSF independent Ethical Review Board (ERB)[31] for a posteriori analyses of routinely collected clinical data and thus did not require MSF ERB review. Exemption from the review by the MSF ERB for retrospective analyses of routinely collected data requires informed consent for secondary use of their data to have been given by patients in the MSF programme at the time of the enrolment in care. All medical records and data were fully anonymised before we accessed them for this analysis.

Data availability: The study was set up in the Médecins Sans Frontières' (MSF) HIV Program in Myanmar. MSF's ability to work in all settings, including unstable and conflict-affected countries, is based on impartiality and trust. Relinquishing control of sensitive patient data from named countries/regions to be used in non-approved ways, with no oversight around how this data may be interpreted, may jeopardise MSF relationships and thus our ability to access all contexts. Furthermore, MSF are a data controller subject to the EU GDPR and UK GDPR. This regulation requires that MSF adhere to the principles of data protection, including: fair, lawful and transparent processing, and purpose limitation. In order to adhere to these requirements, all processing must have a lawful basis (and condition for special categories data), which need to be assessed on a case-by-case basis prior to sharing any information. The principle of purpose limitation requires that any further processing of the data collected needs to have a similar purpose/objective to the original project/purpose. Again, this requires an assessment on a case-by-case basis. In order to adhere to the 'transparent' aspect of the first principle, MSF need to communicate to data subjects how their information will be shared, and open access repositories are not included in the information about potential data sharing.

This study used data from the MSF HIV Program in Myanmar—a vulnerable population in a named programme, involving highly sensitive data that has the potential to cause real harm to individuals if it was to get into the wrong hands. Whilst we have taken steps to fully anonymise the dataset, this anonymisation process has different levels and has not been undertaken with the aim of making these datasets open access.

MSF is committed to evidence-based practice, and strongly believes in ethical and lawful data sharing if that sharing will ultimately benefit wider society, which will need to be assessed per request. Requests for this data can be made via data.sharing@msf.org. The requestor will be required to complete a form detailing the proposed use of the data, and this will be reviewed by the MSF Research Committee on a case-by-case basis.

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