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Retention and attrition during the preparation phase and after start of antiretroviral treatment in Thyolo, Malawi, and Kibera, Kenya: implications for programmes?

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ABSTRACT

Among adults eligible for antiretroviral therapy (ART) in Thyolo (rural Malawi) and Kibera (Nairobi, Kenya), this study (a) reports on retention and attrition during the preparation phase and after starting ART and (b) identifies risk factors associated with attrition. 'Retention' implies being alive and on follow-up, whilst 'attrition' implies loss to follow-up, death or stopping treatment (if on ART). There were 11 309 ART-eligible patients from Malawi and 3633 from Kenya, of whom 8421 (74%) and 2792 (77%), respectively, went through the preparation phase and started ART. In Malawi, 2649 patients (23%) were lost to attrition in the preparation phase and 2189 (26%) after starting ART. Similarly, in Kenya 546 patients (15%) were lost to attrition in the ART preparation phase and 647 (23%) while on ART. Overall programme attrition was 43% (4838/11 309) for Malawi and 33% (1193/3633) for Kenya. Restricting cohort evaluation to 'on ART' (as is usually done) underestimates overall programme attrition by 38% in Malawi and 36% in Kenya. Risk factors associated with attrition in the preparation phase included male sex, age <35 years, advanced HIV/AIDS disease and increasing malnutrition. Considerable attrition occurs during the preparation phase of ART, and programme evaluations confined to on-treatment analysis significantly underestimate attrition. This has important operational implications, which are discussed here.

1. Introduction

As several sub-Saharan African countries are engaged in scaling-up antiretroviral therapy (ART), the terms 'retention' in and 'attrition' from care are used to judge programme quality. A patient on ART is generally declared

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as being 'retained in care' if he/she is alive and on ART. 'Attrition' implies the discontinuation of ART for any given reason, namely loss to follow-up, death or stopping treatment.[1]

An important weakness of routine reporting and evaluation of HIV/AIDS programmes is that analysis generally focuses on those who are registered and start on ART. Thus, we do not know the situation among those who are eligible for ART yet who do not successfully complete preparatory activities such as counselling or management of opportunistic infections (OI). Programmes might thus be inadvertently presenting a skewed picture of success in reporting outcomes only of those who start ART. Attrition among people who have been identified as being eligible for treatment and are still in the ART preparation phase could be linked to factors such as late presentation reflecting severe illness resulting in prolonged treatment for OIs and possibly early death, and barriers linked to ART preparation at facility level such as poor quality of counselling, the need for repeated counselling visits, long distances to the health facility and cost of transport.

For these reasons, we hypothesised that attrition among ART-eligible patients during the preparation phase might be high and that by restricting cohort outcome reporting to only those who actually start ART we might be overestimating programme retention and, conversely, underestimating attrition. This would give a false evaluation of success of the programme. Although there are some reports from South Africa[2,3] and Uganda[4] reporting on pre-ART mortality, limited information exists on attrition during the preparation (pre-ART) phase of ART.

Thus, an analysis was conducted of routine data from two Médecins sans Frontières (MSF)-supported HIV/AIDS programmes in Malawi and Kenya in order (a) to report on retention and attrition rates among ART-eligible adults during the preparation phase for ART and after the start of ART and (b) to identify risk factors associated with attrition.

2. Methods

2.1. Study setting and population

The study involved retrospective programme data from Thyolo, a rural district in Malawi, and Kibera, an urban slum setting in Nairobi, Kenya. The two sites have estimated populations of approximately 600 000 and 700 000, respectively. For a number of years, MSF has been working in close collaboration with the Ministry of Health (MoH) in both settings, providing comprehensive HIV/AIDS care programmes, including ART. The management protocols in both projects have been approved by the MoH and are in line with WHO guidelines.[5] There are formal project agreements between MSF and the MoH in both countries. The study sites were the district hospital in Thyolo and three comprehensive primary care clinics in Kibera. Analysis included all ART-eligible adults presenting to the main ART facilities at the two sites during the period January 2004 to December 2008.

2.2. Antiretroviral therapy eligibility and regimens

All HIV-positive patients assessed as being in WHO clinical stage 3 or 4 or patients with a CD4 count <250 cells/mm^3 in Malawi or <200 cells/mm^3 in Kenya (irrespective of WHO staging) are considered eligible for ART.[6,7] Once patients are assessed as eligible for ART they undergo preliminary counselling, go home and are encouraged to return with a patient guardian (or next of kin) to prepare for ART initiation. Patients and guardians undergo group counselling and then individual counselling sessions where they are educated on HIV infection and the implications of ART. Once started on ART, patients are first reviewed back at the HIV/AIDS clinic after 2 weeks and from then on are given scheduled appointments for review and drug collection at fixed intervals.

The first-line ART regimen in Malawi[7] and Kenya[6] during the study period was a fixed-dose combination of stavudine (d4T), lamivudine and nevirapine (NVP) (Triomune). In case of d4T- and NVP-related side effects, the respective first-line alternatives are zidovudine or tenofovir and efavirenz. ART is offered free of charge.

2.3. Data collection, patient outcomes and statistical analysis

Data from the two settings were entered into standardised HIV/AIDS software (FUCHIA; Epicentre, Paris, France). Outcomes were defined as follows: (i) alive and being followed-up but not yet on ART (preparation phase), or alive and on ART—a patient who is alive and on ART at the facility where he/she is registered; (ii) lost to follow-up—a patient who has never been seen back at the ART facility for a period of $\geq$1 month after his/her last scheduled appointment date; this generally implies $\geq$2 months from the last clinic visit (this cut-off was used both for the preparation phase and for those on ART, as the greatest proportion of attrition is known to occur early, i.e. within 2 months of the last visit);[2,3] (iii) died—a patient who has died for any reason; (iv) stopped treatment—a patient who has been started on ART and has stopped treatment for any reason; and (v) transferred out—a patient who has been formally transferred out permanently to another treatment facility. For the purpose of this analysis, 'retention' was defined as being alive and on ART or alive in the preparatory phase and on follow-up (if not on ART) or formally transferred out to another facility,[8] whilst 'attrition' was defined as death, loss to follow-up or stopped treatment (if on ART) and as death or loss to follow-up (if not on ART). Retention during the preparation phase for ART included all patients 'alive and on follow-up' but yet to start ART as well as those who had completed the ART preparation phase and who had started treatment.

Data were collected from the two settings, and outcomes for patients not yet on ART and those on ART were censored on 31 December 2008. A patient whose next date of appointment fell after the censor date was considered as being retained in care. The χ^2 test for linear trend was used to verify linear trends. Measures of risk were determined by crude odds ratios (OR) and adjusted odds ratios. ORs were adjusted using multivariate logistic regression

Table 1
Baseline case registration characteristics of antiretroviral therapy (ART)-eligible adults in Malawi and Kenya

Variable	Malawi [*n* (%)]	Kenya [*n* (%)]
Total	11309	3633
Sex		
Female	6780 (60.0)	2367 (65.2)
Male	4529 (40.0)	1264 (34.8)
Unknown	0 (0.0)	2 (0.1)
Age		
15–34 years	5999 (53.0)	2266 (62.4)
≥35 years	5310 (47.0)	1367 (37.6)
Median (IQR) (years)	34 (30–41)	32 (27–39)
WHO clinical stage		
Stage 1 or 2 and with CD4 count <250 cells/mm^3[a] or <200 cells/mm^3[b]	1607 (14.2)	1140 (31.4)
Stage 3	6130 (54.2)	1923 (52.9)
Stage 4	3572 (31.6)	570 (15.7)
CD4 cell count		
<200 cells/mm^3	4973 (44.0)	1844 (50.8)
200–349 cells/mm^3	1659 (14.7)	667 (18.4)
≥350 cells/mm^3	1088 (9.6)	427 (11.8)
Unknown	3589 (31.7)	695 (19.1)
Median (IQR) (cells/mm^3)	143 (65–250)	159 (77–258)
BMI		
<16 kg/m^2	1427 (12.6)	225 (6.2)
16–16.9 kg/m^2	1079 (9.5)	193 (5.3)
17–18.4 kg/m^2	1927 (17.0)	420 (11.6)
≥18.5 kg/m^2	5213 (46.1)	1775 (48.9)
Unknown	1663 (14.7)	1020 (28.1)

Data are *n* (%) unless otherwise stated.
IQR: interquartile range; BMI: body mass index.
[a] For Malawi.
[b] For Kenya.

and all related *P*-values are based on the Wald test. CD4 count was left out in the multivariate analysis owing to the fact that patients in WHO stage 3 or 4 were eligible for ART on clinical grounds without necessarily having a CD4 count available. For this reason, baseline CD4 counts were unknown for a considerable proportion (almost 30%) of patients.

Cumulative probability of attrition over time was determined using the Kaplan–Maier method and was expressed graphically. Plots were compared using the Cox–Mantel (log-rank) test.

The same variables were adjusted for both in Malawi and Kenya. The level of significance was set at $P \leq 0.05$ and 95% CIs were used throughout. Data analysis was done using STATA 8.2 software (StataCorp., College Station, TX, USA).

3. Results

3.1. Characteristics of the study population

Between January 2004 and December 2008, a total of 15 503 adults were registered at the two ART sites in Malawi and Kenya and were considered eligible for ART. Of these, 561 (3.6%) did not have their next appointment date specified and were thus excluded from the analysis. Table 1 shows the case registration characteristics of the 14 942 adults included in the study (11 309 patients from Malawi and 3633 from Kenya).

3.2. Retention and attrition in patients in the preparation phase and while on antiretroviral therapy in Malawi and Kenya

Of 11 309 and 3633 ART-eligible adults, respectively, in Malawi and Kenya, 8421 (74%) and 2792 (77%) went through the preparation phase and started ART. Figure 1 shows cumulative retention and attrition rates for ART-eligible patients during the preparation phase (before starting ART) and while on ART for the study period.

Overall, in Malawi 2649 patients (23%) were lost to attrition in the preparation phase and 2189 (26%) while on ART. Among patients in the preparation phase of ART, loss to follow-up during the preparation phase constituted the main reason for attrition (2322/2649; 88%) (Figure 1A). Median time to attrition from eligibility during this preparation phase was 1.4 months [interquartile range (IQR) 0.6–3.0 months], whilst for those who started ART the median time to attrition was 4.1 months (IQR 1.5–12.2 months). Waiting time from eligibility to start of ART for patients who started ART was 0.4 months (IQR 0.2–1.1 months). In Malawi, there were a total of 1849 tuberculosis (TB) patients who were considered eligible for ART, of whom 812 (44%) were lost to attrition prior to starting ART. This constitutes 31% (812/2649) of all patients lost to attrition in the preparation phase.

In Kenya, 546 patients (15%) were lost to attrition in the ART preparation phase and 647 (23%) while on ART. Similar to Malawi, among patients in the preparation phase of ART loss to follow-up constituted the main reason for attrition (460/546; 84%) (Figure 1B). Median time from eligibility

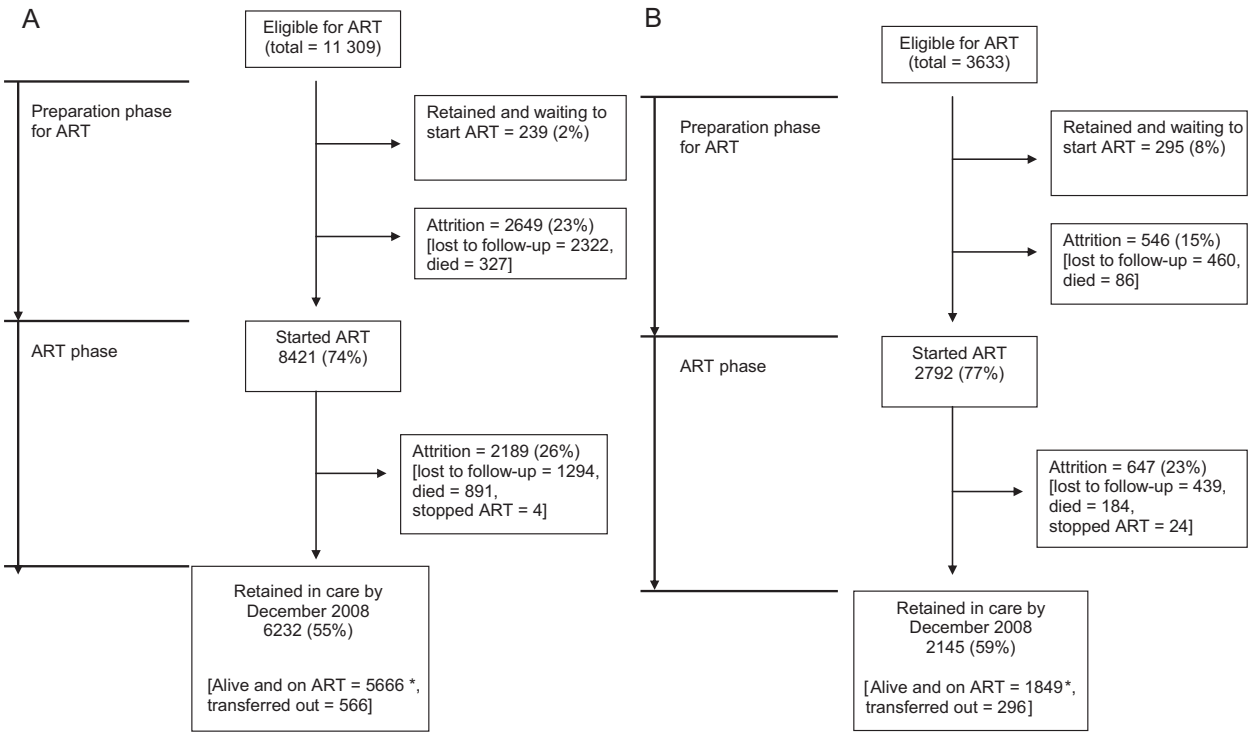

Figure 1. Cumulative retention and attrition during the preparation phase and after starting antiretroviral therapy (ART) in (A) Thyolo, Malawi and (B) Kibera, Kenya (2004–2008). * In the same facility.

to attrition during the preparation phase was 1.4 months (IQR 0.5–6.6 months), whilst for those who started ART the median time to attrition was 5.4 months (IQR 1.8–12.6 months). Waiting time from eligibility to start of ART for patients who started ART was 0.9 months (IQR 0.3–3.2 months).

3.3. Underestimation of overall programme attrition

Overall programme attrition including both the 'preparation phase' and 'on ART' was 43% (4838/11 309) and 33% (1193/3633) for Malawi and Kenya, respectively (Figure 1). This implies that programme analyses that do not include those 'in the preparation phase' will underestimate overall attrition among ART-eligible individuals by 38% in Malawi and 36% in Kenya.

Figure 2 shows the significantly higher cumulative incidence of attrition when 'overall' attrition for all ART-eligible patients is compared with 'on ART' attrition for patients who were registered and started ART in Malawi and Kenya.

3.4. Risk factors associated with attrition in the preparation phase and while on antiretroviral therapy in Malawi and Kenya

Tables 2 and 3 show risk factors associated with attrition for patients in the preparation phase and while on ART in the two countries. In Malawi, male sex, advanced disease (WHO stage 3 and 4) and increasing grades of malnutrition were significantly associated with attrition among both those in the preparation phase and those on ART. In addition, age <35 years was a risk factor for attrition in the preparation phase. Linear trends in attrition were observed in relation to WHO stage and varying grades of malnutrition (Table 2).

In Kenya, WHO stage 4 disease was significantly associated with attrition both among those in the preparation phase and those on ART. In addition, among those in the preparation phase significant risk factors for attrition included age <35 years and WHO stage 3 or 4 disease. A linear trend in attrition was observed in relation to WHO stage and increasing grades of malnutrition (while on ART) (Table 3). Conclusions regarding CD4 counts are limited by large proportions in the unknown category.

4. Discussion

This is one of the first studies assessing retention in care and attrition amongst ART-eligible individuals rather than ART-registered patients from two resource-limited countries, showing that close to one-quarter of all ART-eligible patients drop out during the preparation phase and do not start treatment.

Unique to this study was that all patients eligible for ART were included, even those who had not yet begun ART. This study shows that programme evaluations confined to 'on ART' analysis may significantly underestimate overall attrition among ART-eligible patients.

Significant risk factors associated with attrition in the preparation phase included advanced HIV/AIDS disease and increasing grades of malnutrition, i.e. vulnerable

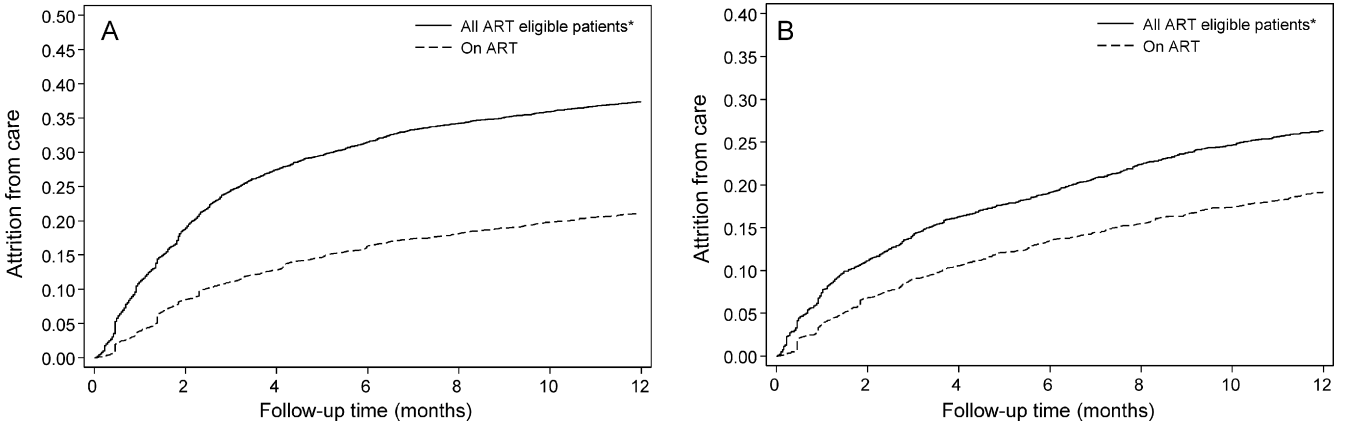

Figure 2. Cumulative incidence of attrition comparing attrition for all antiretroviral therapy (ART)-eligible patients with 'on ART' attrition in (A) Malawi and (B) Kenya. (A) Cox–Mantel (log-rank) test = 601.8, $P < 0.001$. (B) Cox–Mantel (log-rank) test = 64.4, $P < 0.001$. * All ART-eligible patients includes patients who are yet to start ART and patients who started ART during the study period. For all ART-eligible patients, follow-up time starts from the time of registration; for patients on ART, follow-up time starts from the time of ART initiation.

Table 2
Risk factors associated with attrition among antiretroviral therapy (ART)-eligible patients in the ART preparation phase and on ART by case registration characteristics in Malawi

Variable	Preparation phase (n = 11 309)				On ART (n = 8421)			
	Attrition				Attrition			
	n (%)	OR	AOR (95% CI) [a]	P-value	n (%)	OR	AOR (95% CI) [a]	P-value
Total	2649/11 309 (23.4)				2189/8421 (26.0)			
Sex								
Female	1411/6780 (20.8)	1	1		1169/5228 (22.4)	1	1	
Male	1238/4529 (27.3)	1.4 (1.3–1.6)	1.5 (1.3–1.6)	<0.001	1020/3193 (31.9)	1.6 (1.5–1.8)	1.6 (1.4–1.8)	<0.001
Age (years)								
15–34	1540/5999 (25.7)	1.3 (1.2–1.4)	1.3 (1.2–1.5)	<0.001	1113/4317 (25.8)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	0.67
≥35	1109/5310 (20.9)	1	1		1076/4104 (26.2)	1	1	
WHO stage [b]								
Stage 1 or 2 and with CD4 count <250 cells/mm^3	220/1607 (13.7)	1	1		157/1285 (12.2)	1	1	
Stage 3	1437/6130 (23.4)	1.9 (1.6–2.2)	1.7 (1.5–2.0)	<0.001	1205/4602 (26.2)	2.5 (2.1–3.0)	2.2 (1.8–2.6)	<0.001
Stage 4	992/3572 (27.8)	2.4 (2.1–2.8)	2.2 (1.9–2.6)	<0.001	827/2534 (32.6)	3.5 (2.9–4.2)	3.1 (2.6–3.8)	<0.001
CD4 cell count (cells/mm^3) [c]								
<200	432/4973 (8.7)	1			1236/4439 (27.8)	1.4 (1.1–1.7)		
200–349	174/1659 (10.5)	1.2 (1.0–1.5)			310/1448 (21.4)	1.0 (0.8–1.2)		
≥350	346/1088 (31.8)	4.9 (4.2–5.8)			151/696 (21.7)	1		
Unknown	1697/3589 (47.3)	9.4 (8.4–10.6)			492/1838 (26.8)	1.3 (1.1–1.6)		
BMI (kg/m^2) [d]								
<16	495/1427 (34.7)	2.5 (2.2–2.9)	2.4 (2.1–2.8)	<0.001	382/920 (41.5)	2.7 (2.3–3.1)	2.6 (2.2–3.1)	<0.001
16–16.9	284/1079 (26.3)	1.7 (1.5–2.0)	1.6 (1.4–1.9)	<0.001	244/779 (31.3)	1.7 (1.4–2.0)	1.7 (1.4–2.0)	<0.001
17–18.4	463/1927 (24.0)	1.5 (1.3–1.7)	1.4 (1.3–1.6)	<0.001	406/1422 (28.6)	1.5 (1.3–1.7)	1.4 (1.2–1.6)	<0.001
≥18.5	905/5213 (17.4)	1	1		883/4180 (21.1)	1	1	
Unknown	502/1663 (30.2)	2.1 (1.8–2.3)	2.0 (1.8–2.3)	<0.001	274/1120 (24.5)	1.2 (1.0–1.4)	1.2 (1.0–1.4)	0.01

OR: odds ratio; AOR: adjusted odds ratio; BMI: body mass index.

[a] Adjusted for age, sex, WHO stage and BMI.

[b] For patients in preparation phase, χ^2 test for trend = 122.3, $P < 0.001$; for patients on ART, χ^2 test for trend = 184.8, $P < 0.001$.

[c] For patients in preparation phase, χ^2 test for trend = 319.7, $P \leq 0.01$. CD4 cell count was left out in the multivariate analysis owing to the fact that patients in WHO stage 3 or 4 were eligible for ART on clinical grounds without necessarily having a CD4 count available.

[d] For patients in preparation phase, χ^2 test for trend = 174.1, $P < 0.001$; for patients on ART, χ^2 test for trend = 149.3, $P < 0.001$.

Table 3
Risk factors associated with attrition among antiretroviral therapy (ART)-eligible adults in the ART preparation phase and on ART by case registration characteristics in Kenya

Variable	Preparation phase ($n = 3633$)				On ART ($n = 2792$)			
	Attrition				Attrition			
	n (%)	OR	AOR (95% CI) [a]	P-value	n (%)	OR	AOR (95% CI) [a]	P-value
Total	546/3633 (15.0)				647/2792 (23.2)			
Sex								
Female	345/2367 (14.6)	1	1		416/1824 (22.8)	1	1	
Male	201/1264 (15.9)	1.1 (0.9–1.3)	1.1 (0.9–1.4)	0.26	231/968 (23.9)	1.1 (0.9–1.3)	1.0 (0.8–1.2)	0.82
Unknown	0/2 (0.0)	NA			0/0 (0.0)	NA		
Age (years)								
15–34	369/2266 (16.3)	1.3 (1.1–1.6)	1.4 (1.2–1.7)	0.001	402/1717 (23.4)	1.0 (0.9–1.2)	1.1 (0.9–1.3)	0.48
≥35	177/1367 (12.9)	1	1		245/1075 (22.8)	1	1	
WHO stage [b]								
Stage 1 or 2 and with CD4 count <200 cells/mm^3	91/1140 (8.0)	1	1		208/1026 (20.3)	1	1	
Stage 3	349/1923 (18.1)	2.6 (2.0–3.3)	2.5 (1.9–3.2)	<0.001	312/1345 (23.2)	1.2 (1.0–1.5)	1.1 (0.9–1.3)	0.38
Stage 4	106/570 (18.6)	2.6 (1.9–3.6)	2.4 (1.8–3.3)	<0.001	127/421 (30.2)	1.7 (1.3–2.2)	1.5 (1.2–2.0)	0.02
CD4 cell count (cells/mm^3) [c]								
<200	228/1844 (12.4)	1.8 (1.3–2.5)			357/1526 (23.4)	1.4 (1.0–1.8)		
200–349	48/667 (7.2)	1			112/586 (19.1)	1		
≥350	76/427 (17.8)	2.8 (1.9–4.1)			51/227 (22.5)	1.3 (0.8–1.8)		
Unknown	194/695 (27.9)	5.0 (3.6–7.0)			127/453 (28.0)	1.6 (1.2–2.2)		
BMI (kg/m^2) [d]								
<16	45/225 (20.0)	1.8 (1.3–2.6)	1.5 (1.0–2.1)	0.04	58/158 (36.7)	2.3 (1.6–3.3)	2.1 (1.5 –3.0)	<0.001
16–16.9	43/193 (22.3)	2.1 (1.4–3.0)	1.7 (1.2–2.5)	0.006	42/134 (31.3)	1.8 (1.2–2.7)	1.7 (1.1–2.5)	0.01
17–18.4	64/420 (15.2)	1.3 (0.9–1.8)	1.1 (0.8–1.5)	0.45	83/319 (26.0)	1.4 (1.0–1.8)	1.3 (1.0–1.7)	0.07
≥18.5	215/1775 (12.1)	1	1		281/1392 (20.2)	1	1	
Unknown	179/1020 (17.5)	1.5 (1.2–1.9)	1.4 (1.1–1.8)	0.002	183/789 (23.2)	1.2 (1.0–1.5)	1.2 (0.9–1.4)	0.18

OR: odds ratio; AOR: adjusted odds ratio; BMI: body mass index; NA: not applicable.

[a] Adjusted for age, sex, WHO stage and BMI.

[b] For patients in preparation phase, χ^2 test for trend = 59.3, $P \leq 0.001$; for patients on ART, χ^2 test for trend = 12.4, $P < 0.001$.

[c] For patients in preparation phase, χ^2 test for trend = 1.0, $P = 0.3$. CD4 cell count was left out in the multivariate analysis owing to the fact that patients in WHO stage 3 or 4 were eligible for ART on clinical grounds without necessarily having a CD4 count available.

[d] For patients on ART, χ^2 test for trend = 10.5, $P = 0.001$.

patients lost to follow-up constituted the great majority (>80%) of attrition during preparatory activities.

The strengths of this study are that: (i) it included two very large cohorts; (ii) the data come from two programme settings and the findings are thus likely to reflect the operational reality on the ground; (iii) missing data on outcomes were limited to 3.6%; and (iv) the STROBE guidelines were adhered to for reporting of observational data.[9]

The findings of this study have a number of programme-related implications. First, we have shown that confining cohort analysis only to patients on ART (on-treatment analysis) and not including those in the preparation phase of ART underestimates overall attrition (by 38% in Malawi and 36% in Kenya). This is very similar to the situation in global TB control where patients with smear-positive pulmonary TB who appear in the laboratory sputum register but not in the TB patient register (so-called 'initial defaulters') are not included in the cohort analysis of treatment outcomes.[10] By failing to include these patients with smear-positive pulmonary TB, treatment outcomes are always reported as better than they in fact are. As programmes in sub-Saharan Africa progress to scale-up ART, they should routinely report on (a) what proportion of those who meet the criteria to start ART eventually do so and (b) attrition that is inclusive of both pre-ART and on-ART.[11] Pre-ART patients are particularly important as they reflect those who have entered the system but who do not benefit from the treatment available. We would encourage the WHO to include such a recommendation in their monitoring and reporting guidelines.[12]

Second, the great majority of attrition among patients in the preparation phase who did not start ART was attributed to patients declared lost to follow-up. It is questionable whether this is indeed the true outcome of these patients. A study in Malawi assessing true outcomes of patients declared lost to follow-up after starting ART showed that 50% were dead, 27% could not be traced and 8% had silently transferred to another clinic.[13] It is possible that patients declared lost to follow-up in the preparation phase for ART might have a similar spectrum of outcomes. Since attrition was significantly associated with advanced disease and the most vulnerable, a large proportion of those declared lost to follow-up might actually be unascertained deaths. This is also supported by recent studies from South Africa and Uganda which showed that considerable pre-ART attrition is attributable to death.[4,14,15]

Third, a practical problem at programme level is that active tracing of those who do not turn up for scheduled appointments is applicable only for those who start ART. Thus, when an ART-eligible patient in the preparation phase of ART does not turn up for a scheduled appointment, no action is taken, i.e. this is not reported and existing patient tracing systems make no effort to find them. We suggest that a way forward in addressing this problem is (a) to agree on a standardised definition of loss to follow-up for those in the preparation (pre-ART) phase (we propose 'a patient not seen for $\geq$1 month after the date of scheduled appointment', as attrition occurs early and the commonly used cut-off of 3 months is 'simply too late to act'; however, this might need to be adapted according to the context);[16] (b) to routinely record those who do not turn up for scheduled appointments; and (c) to ensure that existing patient tracing systems are activated for all ART-eligible patients who miss scheduled appointments. In settings where community-based systems are well developed, expanding active tracing to include those yet to start ART should be considered.[17]

Fourth, the groups at risk of attrition before and after starting ART are generally similar and include the most severely ill patients, i.e. those in advanced WHO stages and who are malnourished. At a programme level this suggests that ART should be started as early as possible. In this study, the median ART waiting time prior to attrition was 1.4 months both in Malawi and Kenya and this needs to be reduced as mortality is known to be extremely high in the first 30 days from enrolment.[3] At the same time, trying to put patients on ART in haste should not be done at the cost of 'adequate' preparation for ART. Finding innovative and fast-track strategies to address this issue are needed.

Although we do not know the exact reasons for attrition among those still in the preparation phase for ART, there are several possible reasons.[4,16,18,19] They may include late presentation with severe illness, relatively long waiting times at the clinic, poor or ill-adapted counselling techniques, repeated appointments linked to ART preparation, cost of transport, migration (particularly in Kibera), malnutrition, undiagnosed TB and bacteraemias/septicaemias. Of particular interest in Malawi was the finding that one in three patients lost to attrition in the preparation phase were ART-eligible TB patients. Although this merits specific investigation, possible reasons might include (a) inadequate integration of TB–HIV services (TB is decentralised whilst ART is centralised, i.e. only offered at hospital level[20]) requiring patients to travel to two sites to access joint TB–HIV treatment, (b) that after 2 months or so of TB treatment, patients feel better and decide not to return for ART, (c) inadequate ongoing TB-HIV counselling and (d) patients dying. It is well known that once patients develop WHO stage 4 disease, or are malnourished, the risk of mortality is very high and by adding additional delays to accessing ART their chances of survival diminish. Many of these factors might be compounded by growing patient case loads and overburdened human resources associated with scaling-up ART.[21]

Some further possible ways forward, some of which would merit specific operational research, include (a) giving priority clinical attention to patients who are ART-eligible to fast-track patients onto ART, (b) developing more tailored and particularly 'faster' ART counselling techniques, (c) considering empirical TB treatment for those in whom TB cannot be reliably excluded, although the merits or otherwise of this approach would need a formal randomised controlled trial and (d) systematically treating with broad-spectrum antibiotics.[19] The recent WHO rapid advice aimed at starting ART earlier and at higher CD4 counts is supported by this study and should facilitate earlier access to ART for all patients, including those with TB.[22]

Finally, male sex was significantly associated with attrition and this is likely attributed to men seeking

medical care at more advanced disease stages or the fact that they are workers who can ill afford time off work to be compliant with visits.[23]

The limitations of this study are that: (i) patients declared lost to follow-up may include unascertained deaths or other outcomes; (ii) CD4 counts were not available for all patients as this was not necessary for starting ART; (iii) we do not know the exact cause of adverse outcomes, i.e. deaths and losses to follow-up; and (iv) we might have overestimated attrition since some patients declared as lost to follow-up might include undeclared, self-initiated transfers to other health facilities. There might also have been unknown gaps in data monitoring and reporting of decentralised patients within the central database, which needs to be verified.[13]

In two large independent cohorts in sub-Saharan Africa, attrition rates in the preparation phase of ART were high and contributed considerably to overall programme attrition. HIV programmes must count pre-ART (but eligible) patients in their evaluation if they wish to understand their true attrition rate. Addressing these patients' needs more aggressively should improve the overall retention rates in HIV programmes.

Authors' contributions: RZ, MMan, MMas, BM, JvG, IvE, EJS, FMC and ADH were involved in the conception and design of the study; RZ wrote the study protocol, which was improved by MMan, MMas, JvG EJS, FMC and ADH; MMas, BM and IvE were involved with implementation and overall study supervision; KT-S performed the initial analysis, which was supported by MMan and RZ; all the authors contributed to data interpretation and analysis; RZ and KT-S wrote the first draft of the paper, which was reviewed and improved by all co-authors, who all significantly contributed to the intellectual content of the final paper; RZ and KT-S handled the repeated revisions. All co-authors were involved with drafting, critically reviewing and finalising the final version of the manuscript. All authors have approved the final paper. RZ is guarantor of the paper.

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