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Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique

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Abstract

OBJECTIVE Community ART groups (CAG), peer support groups involved in community ART distribution and mutual psychosocial support, were piloted to respond to staggering antiretroviral treatment (ART) attrition in Mozambique. To understand the impact of CAG on long-term retention, we estimated mortality and lost-to-follow-up (LTFU) rates and assessed predictors for attrition.

METHODS Retrospective cohort study. Kaplan–Meier techniques were used to estimate mortality and LTFU in CAG. Individual- and CAG-level predictors of attrition were assessed using a multivariable Cox proportional hazards model, adjusted for site-level clustering.

RESULTS Mortality and LTFU rates among 5729 CAG members were, respectively, 2.1 and 0.1 per 100 person-years. Retention was 97.7% at 12 months, 96.0% at 24 months, 93.4% at 36 months and 91.8% at 48 months. At individual level, attrition in CAG was significantly associated with immunosuppression when joining a CAG, and being male. At CAG level, attrition was associated with lack of rotational representation at the clinic, lack of a regular CD4 count among fellow members and linkage to a rural or district clinic compared with linkage to a peri-urban clinic.

CONCLUSIONS Long-term retention in this community-based ART model compares favourably with published data on stable ART patients. Nevertheless, to reduce attrition, further efforts need to be made to enrol patients earlier on ART, promote health-seeking behaviour, especially for men, promote a strong peer dynamic to assure rotational representation at the clinic and regular CD4 follow-up and reinforce referral of sick patients.

keywords antiretroviral therapy, community participation, health services accessibility, HIV, peer support

Introduction

In the past decade, the scale-up of antiretroviral therapy (ART) was spectacular. In low- and middle-income countries, 9.7 million people were reported on ART at the end of 2012. But still, it is not enough. Still 1.7 million people died because of AIDS in 2011 (WHO 2013a). To reduce AIDS-related deaths, WHO recommends a new target of 25.9 million receiving ART in low- and middle-income countries, an unprecedented public health challenge (WHO 2013b). A major bottleneck is attrition on ART, which includes patients who died or who are lost to follow-up (LTFU). A meta-analysis from more than 17 countries revealed a patient attrition of 30.0% and 35.4% at 24 and 36 months, respectively (Fox & Rosen 2010). Transport costs and distance are the most frequently cited barriers to adherence (Govindasamy *et al.* 2012).

In Mozambique, with a prevalence of 11.5% among adults, more than 1.5 million Mozambicans are living with HIV (Ministry of Health Mozambique 2010). At the end of 2012, only 42% (308 577) of the 690 000 estimated in need were on ART (WHO 2012). Meanwhile, almost one-third of the people living with HIV/AIDS (PLWHA) who had started ART were either dead or LTFU (Ministry of Health Mozambique 2012a). The decentralisation of ART care, which aimed to decrease the burden on overloaded clinics and increase accessibility for the patients, was hampered by a lack of infrastructure, a lack of human resources for health and

organisational problems, including the drug supply (Decroo *et al.* 2009; Ministry of Health Mozambique 2012b). Subsequently, attrition at rural clinics was almost twice as high as at urban clinics (Lambdin *et al.* 2013).

To reduce the attrition, community ART groups (CAG), peer support groups of up to six members, were started in the rural province of Tete since February 2008. Monthly, on the day of ART refill, CAG members meet in the community. During the meeting, they verify each other's adherence and choose a representative to collect ART for all members. At the health facility, the group representative has a consultation, relates any important events that occurred in the lives of the other members and receives a treatment refill for all members of the CAG. The most frequently prescribed ART regimen contains zidovudine, lamivudine and nevirapine. For each CAG, a group card, containing data about the members and the dates of refill, is updated, with one copy held at community level and one copy held at clinic level. Then, the group representative returns to the community to distribute the ART to the fellow group members. One month later, another group member is chosen to represent the CAG at the health facility. Early results showing a retention of 97.5% after a median follow-up time of 13 months convinced the national Ministry of Health to expand CAG first within Tete Province and then at national level (Decroo *et al.* 2011, 2013). In this study, we analyse long-term retention in CAG, estimate individual- and CAG-level risk factors associated with attrition and describe the circumstances in which CAG members died.

Methods

Study design and data collection

This retrospective study used programme data to describe and analyse the retention among adult members who joined the CAG programme between February 2008 and December 2012. Data were encoded in an electronic database (Excel) from February 2008 onwards. The sources were clinic-held copies of the group cards and patient files. Every month, a data technician met one of the providers (nurse or counsellor) of each clinic, who gave an update based on the information he/she had obtained from the CAG representatives. Variables were updated monthly, including recent CD4 results and the next day for ART refill. Periodically, a file review was organised to verify the data from the database with the data recorded in the files.

The treatment outcomes reported were as follows: active, dead, LTFU, transferred and returned to individual/routine care. LTFU was defined as being more than 2 months late for the last appointment or date for refill. Return to individual/routine care was defined as the exit of a member from a CAG and the return to normal individual/routine care, on the initiative of the patient or the clinician. In individual care, the patient would have to visit the clinic monthly for ART refill. The type of clinics on which CAG members depend for ART provision were categorised as peri-urban clinics (CAG members living in the vicinity of a referral hospital providing specialised care with medical specialists, referral laboratory and radiology available), district clinics (CAG members living in the vicinity of a district hospital with a medical doctor and small laboratory available) or rural clinics (CAG members living in the vicinity of a health centre providing primary health care with nurse-based care). To understand better the circumstances in which some of the patients died or were LTFU, the health staff (counsellor or nurse) tried to obtain information from the fellow group members or the treating clinician; this was digitised as a short narrative in the database.

Data analysis

Explanatory variables included in this analysis are either at individual or at CAG level. Some numeric variables were categorised to facilitate the analysis. The median and interquartile ranges (IQR) were calculated for numeric variables and proportions for categorical variables. Mortality and LTFU rates were calculated per 100 person-years. Kaplan–Meier techniques were used to estimate survival in CAG. Predictors of mortality were assessed using a multivariable Cox proportional hazards model, adjusted for site-level clustering. Missing data were handled using the missing indicator method. Adjusted hazard ratios (aHR), 95% confidence intervals (CI) and *P*-values were calculated to estimate the association between attrition (mortality or LTFU) and variables at individual and CAG levels. Patients alive on ART were censored on 31 December 2012. Members transferred to another clinic were censored on the date of transfer. Patients who returned to individual care and who were active on ART 3 months after leaving the CAG were censored on the day they left the group, independent of their final treatment outcome. Patients who returned to individual care and who died or were LTFU within 3 months after leaving the CAG were considered as having experienced the event.

A multiple Cox regression model was constructed using a hierarchical approach, including first individual-level (P-value < 0.1) and subsequently CAG-level (P-value < 0.1) characteristics. The model was simplified

by stepwise backwards elimination until all individual-level variables had a *P*-value < 0.05 and consequently further simplified by deletion of CAG-level variables until all CAG-level variables had a *P*-value of < 0.05. Analyses were performed with Stata (version 11.2).

Results

Characteristics of study population

Between February 2008 and December 2012, 6158 patients joined the CAG, of whom 5729 were adults. A total of 380 dependent children and 49 patients who were the only adult member of a CAG were excluded from the analysis (Figure 1). Of the 5729 adult members, 5507 were active (including 207 members who were transferred), 208 (3.6%) died and 14 (0.2%) were LTFU after a median follow-up time of 19 months (IQR 10–29).

The main characteristics of members in CAG are summarised by outcome in Table 1. Median age when joining a group was 36 years (IQR 30–43), and 30% of group members were male. The median CD4 count had improved since patients started ART and improved more while they were members of a CAG. Median CD4 counts at ART initiation, at group enrolment and the last value obtained were, respectively, 185 cells/μl (IQR 114–248), 385 cells/μl (IQR 258–560) and 421 cells/μl (IQR 277–593).

One-fourth (28%) of the members shared the cost of transport to get to a clinic for the monthly ART refill.

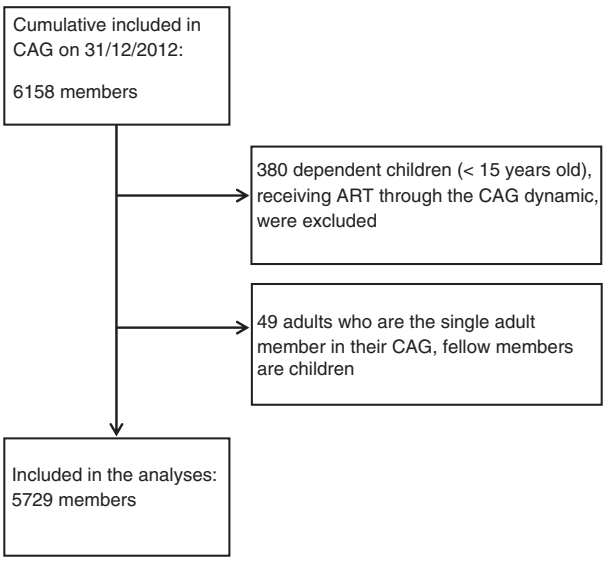

Figure 1 Members included in the analuysis. ART, antiretroviral therapy; CAG, community ART group.

Table 1 Characteristics of CAG members

	N = 5729 CAG members
At individual level	
Male: *n* (%)	1746 (30)
Age when joining a group (years): median (IQR)	36 (30–43)
CD4 when starting ART (cells/μl): median (IQR)	185 (114–248)†
CD4 when joining CAG (cells/μl): median, (IQR)	385 (258–560)‡
Last CD4 (cells/μl): median (IQR)	421 (277–593)§
At CAG level: member of a CAG	
With transport fee to go to the clinic: *n* (%)	1608 (28)
Without a recent CD4 count for all fellow members: *n* (%)*	4401 (77)
Without fluent rotational representation at the clinic: *n* (%)	2838 (50)
Consisting for more than 50% of young adults (<30 year): *n* (%)	1166 (20)
Linked to a: *n* (%)	
Peri-urban clinic	3394 (59)
District clinic	1666 (29)
Rural clinic	669 (12)

N, number; IQR, interquartile range; CAG, community ART group.
*Recent CD4 = during last 24 months.
†Data for 4406 (77%) members.
‡Data for 3983 (70%) members.
§Data for 4020 (70%) members.

Half (50%) of the members were members of a group without a working rotational representation at the clinic. Moreover, 77% of the members belonged to groups in which not all members had an updated CD4 count. Twelve percentage of the members depended on rural clinics, run by nurses only, and without possibility of hospitalisation.

Characteristics of members were similar at peri-urban, district or rural clinics (Table 2), except that at rural clinics, members joined CAG earlier, after a median of 7 months on ART. Furthermore, at district clinics and rural clinics, close to half of the members had to pay for transport to access the clinic, much more than the 7% of members at the peri-urban clinics.

Retention

On 31 December 2012, retention among CAG members at 1 year on ART was 97.7% (95% CI 97.4–98.2); at 2 years, 96.0% (95% CI 95.3–96.6); at 3 years, 93.4% (95% CI 92.3–94.3); and at 4 years, 91.8% (95% CI

Table 2 Characteristics of CAG members by clinic type

	Peri-urban 3394 members 840 CAG	District 1666 members 389 CAG	Rural 669 members 162 CAG
Male, *n* (%)	1019 (30%)	500 (30%)	227 (34%)
Age, median (IQR)	36 (30–44)	35 (28–41)	35 (29–42)
CD4 when starting ART, median (IQR)	189 (118–253)	186 (117–246)	162 (91–226)
CD4 when joining CAG, median (IQR)	411 (283–584)	375 (251–547)	303 (173–468)
Months of ART when joining CAG	27 (12–44)	17 (7–32)	7 (3–20)
N of members per CAG, median (IQR)	4 (2–6)	4 (2–6)	4 (2–6)
CAG depending on transport to get refill, *n* (%)	140 (7%)	168 (43%)	72 (44%)

N, number; IQR, interquartile range; CAG, community ART group.

Table 3 Factors associated with attrition among CAG members

Characteristics of members at individual or community ART group level	*N* (%)	Attrition (death or LTFU) (%)	HR (95% CI)	*P*	aHR (95% Cl)	*P*
Total, *n* (%)	5729 (100.0)	222 (100.0)				
Male, *n* (%)	1746 (30.5)	106 (47.8)	2.07 (1.59–2.70)	<0.001	1.93 (1.48–2.51)	<0.001
CD4 when starting ART, *n* (%)						0.057
≥200 cells/μl	1931 (33.7)	55 (24.8)	1		1	
<200 cells/μl	2475 (43.2)	140 (63.1)	1.76 (1.29–2.42)	<0.001	1.33 (0.96–1.82)	0.086
Missing data	1323 (23.1)	27 (12.2)	1.20 (0.70–2.05)	0.495	0.86 (0.53–1.40)	0.547
CD4 when joining CAG, *n* (%)						<0.001
≥200 cells/μl	3402 (59.4)	96 (43.2)	1		1	
<200 cells/μl	581 (10.1)	57 (25.7)	2.97 (2.12–4.17)	<0.001	2.28 (1.60–3.24)	<0.001
Missing data	1746 (30.5)	69 (31.1)	2.83 (2.05–3.91)	<0.001	2.65 (1.92–3.66)	<0.001
Member of a CAG without a recent CD4 for all fellow members, *n* (%)*	4401 (76.8)	201 (90.5)	2.49 (1.56–3.97)	<0.001	1.88 (1.18–3.00)	0.008
Member of a CAG without a fluent rotational representation at the clinic, *n* (%)	2838 (49.5)	153 (68.9)	2.00 (1.48–2.71)	<0.001	1.72 (1.27–2.33)	<0.001
Linked to which type of clinic, *n* (%)						<0.001
Peri-urban	3394 (59.2)	84 (37.8)	1		1	
District	1666 (29.1)	78 (35.1)	1.56 (1.13–2.13)	0.006	1.57 (1.14–2.16)	0.006
Rural	669 (11.7)	60 (27.0)	2.85 (2.00–4.06)	<0.001	2.59 (1.81–3.70)	<0.001

N, number; LTFU, lost to follow-up; HR, Hazard Ratio; aHR, adjusted Hazard Ratio; CAG, community ART group.
*Recent CD4 = during last 24 months.

90.1–93.2) (Figure 2). Overall, the attrition rate was 2.2 per 100 person-years among the 5729 adult members. The mortality rate was 2.1 per 100 person-years, and the LTFU rate was 0.1 per 100 person-years.

Factors associated with attrition

Factors associated with attrition in CAG were estimated. Table 3 shows the final multivariate model and the adjusted hazard ratios for each of the factors (at individual or group level) associated at level 0.05 with mortality among members in CAG. Risk factors associated with attrition at individual level were having a low CD4 count (below 200 cells/μl) when joining a group (aHR 2.28, 95% CI 1.60–3.24), and being male (aHR 1.93, 95% CI 1.48–2.51). Risk factors at group level were being a member of a group without a working rotational representation at the clinic to get a refill (aHR 1.72, 95% CI 1.27–2.33), being a member of a group without a recent CD4 for all fellow members (aHR 1.88,

95% CI 1.18–3.00) and being a member of a group linked with a rural clinic (aHR 2.59, 95% CI 1.81–3.70) or district clinic (aHR 1.57, 95% CI 1.14–2.16) rather than with a peri-urban clinic.

Retention rates among CAG members were 98.8%, 97.1% and 94.7% at the peri-urban clinics; 97.2%, 95.4% and 93.7% at the district clinics; and 95.8%, 92.2% and 87.3% at the rural clinics at 1, 2 and 3 years, respectively (Figure 2). The log-rank test for strata according to clinic type was significant (P-value < 0.05).

Circumstances of stopping or dying in CAG care

Of the 5729 adult CAG members, 208 (3.6%) died and 14 (0.2%) were LTFU after a median follow-up time of 19 months (IQR 10–29). The most frequent cause for stopping treatment was travel, often to look for work. Some female members feared to disclose their sero-status to a new partner and preferred to stop ART.

When the patient died in the community, in most cases the members of the CAG network were able to give feedback to the health workers. Only for 6 (3%) group members who died, no explanation at all was reported. However, the information obtained on the circumstances in which patients died was mostly non-specific. The majority of patients (73%, 151 patients) died after a prolonged period of illness, most likely due to an AIDS-related condition. Major causes were treatment failure, tuberculosis and anaemia. For 42% (64/151), a variety of non-specific symptoms were reported, and in most cases, there was no clear diagnosis.

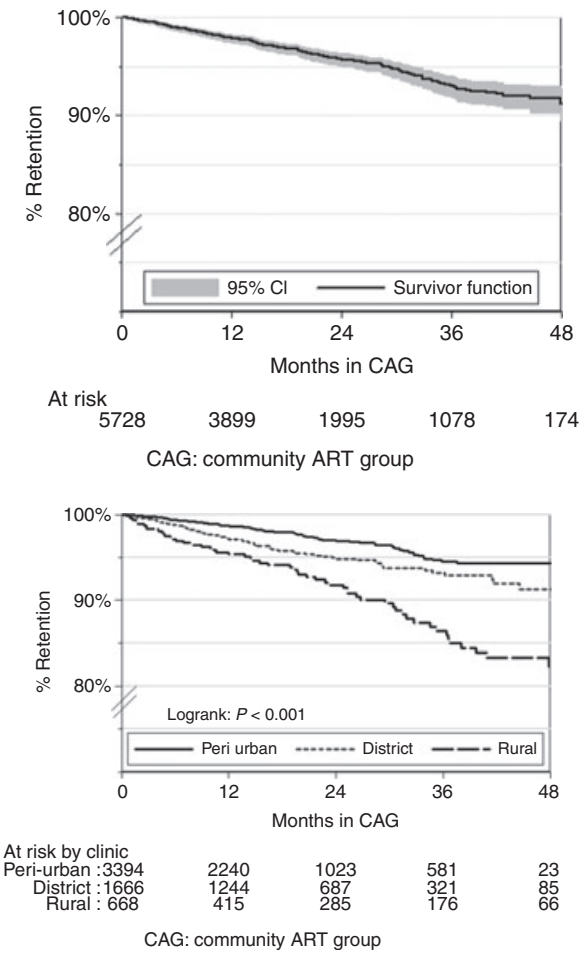

Figure 2 Retention among CAG members, overall and by clinic type.

Discussion

The attrition among 5729 adult members stable on ART, who joined a CAG between February 2008 and December 2012, was 2.2 per 100 person-years; mortality and LTFU rates were 2.1 and 0.1 per 100 person-years, respectively. The social network of CAG members and their close relatives was a very useful source for obtaining information on the few patients LTFU. For the few patients LTFU, mainly practical reasons (travel to work) and social behaviour (secrecy towards new husband) interfered with compliance with ART care. The majority of the deaths occurred after a prolonged period of disease. The data suggest that mortality is mainly HIV related and often caused by preventable or curable conditions. The very low LTFU rates among patients in CAG are very convincing in a context where 48.6% attrition at 3 years ART was reported (respectively, 17.4% and 31.0% were dead and LTFU at 3 years ART) (Wandeler *et al.* 2012). In another Mozambican study, overall attrition since the start of ART was 19.8 per 100 person-years. After the first 3 months, attrition on ART was 13.2 per 100 person-years (Auld *et al.* 2011).

How to interpret retention and attrition among CAG members? CAG consist mainly of stable patients on ART, and participation is voluntary (about 50% of patients on ART choose to join at the ART sites where the ART group dynamic was rolled out). It is probable that the patients who joined CAG have different psychosocial and biomedical characteristics than patients who chose to remain in individual care. First, patients were thought to be clinically stable on ART and immunologically recovering when they joined a CAG, and second they might have had a different adherence profile than those who preferred to stay in individual care. Subsequently, findings cannot be generalised, and one has to

be cautious when comparing outcomes of members in CAG with outcomes of other cohorts. A meta-analysis of attrition in sub-Saharan countries documented an attrition of five per 100 person-years among patients more than 2 years on ART (Fox & Rosen 2010), which can be considered as a threshold for attrition among stable patients. The outcomes among members in CAG, with 2.2 attritions per 100 person-years, compare favourably.

Attrition among CAG members depended on the immunological status, gender, the peer dynamic in the community and the level of care offered at the clinic. Members who joined the CAG with a CD4 below 200 cells/μl were at higher risk of attrition (aHR 2.28, 95% CI 1.60–3.24). Immunosuppression is a known risk factor for attrition among PLWHA on ART (Gupta *et al.* 2011). Patients need to be enrolled on ART earlier, so they would join a CAG with a less depressed immunological status. Another risk factor at individual level was being male (aHR 1.93, 95% CI 1.48–2.51). This finding confirms what was described by other studies and in a review (Auld *et al.* 2011; Mills *et al.* 2011; Druyts *et al.*2013). If men were to prioritise utilisation of healthcare services in an earlier stage of HIV infection and early during new episodes of illness, the attrition among men could diminish (Auld *et al.* 2011). Moreover, treatment strategies are not yet adapted to the specific needs of men, while for women antenatal care services are an opportunity to increase uptake into care (Mills *et al.* 2011; Druyts *et al.* 2013). An opportunity could be the roll-out of male circumcision, as part of a care package that could include a proposal for HIV testing (Mills *et al.* 2011).

At group level, attrition was associated with a lack of rotational representation at the clinic (aHR 1.72, 95% CI 1.27–2.33) and a lack of a regular CD4 count among fellow members (aHR 1.88, 95% CI 1.18–3.00). Risk factors associated with the functioning of the CAG confirm that the CAG has to be more than a distribution system for ART. Interestingly, dependency on a transport fee to access ART (aHR 0.97, 95% CI 0.72–1.31) was not significantly associated with mortality. This finding suggests that CAG were able to overcome the barrier of transport cost, as members share this cost.

Attrition among CAG members was also associated with linkage to a rural clinic (aHR 2.59, 95% CI 1.81–3.70) or a district clinic (aHR 1.57, 95% CI 1.14–2.16) compared with linkage to a peri-urban clinic. Retention in CAG at the rural clinics at 1, 2 and 3 years on ART was, respectively, 95.8%, 92.2% and 87.3%. Attrition was 4.8 per 100 person-years. In our study, attrition was mainly due to mortality, which is strongly associated with the type of clinic on which CAG members depend for clinical care. This association did not alter once adjusted for individual- or CAG-level factors, which suggests that the association between attrition and clinic type is mainly explained by health system factors, or the lower quality of care provided at rural clinics. Our findings are consistent with a recent Cochrane review, which reported a higher mortality among ART patients attending rural clinics (Kredo *et al.* 2013). Another Mozambican study reported 23 attritions per 100 person-years among patients more than 6 months on ART at rural clinics in Mozambique, which was twice as high as the attrition at urban clinics (Lambdin *et al.* 2013). However, the roll-out of simplified and standardised ART care compares favourably with no care at all. From a public health perspective, the reduction in overall HIV-/AIDS-related deaths at population level through ART decentralisation to nurse-based clinics outweighs the eventual loss due to a lower quality of clinical care at rural clinics (Kredo *et al.* 2013). Furthermore, when communities partner with rural clinics to deliver a standardised package of HIV care, improved uptake, linkage and retention in care can be achieved (Rasschaert *et al.* 2011; WHO 2013b).

Some limitations affect the interpretation of our findings. First, WHO clinical stage and history of tuberculosis are known risk factors associated with attrition, but data were unavailable for the analysis (Caluwaerts *et al.* 2009). Data for some variables were not available for all patients, such as CD4 counts and the date patients started ART. Many patients had no recent CD4 due to a limited access to CD4 (only three machines for the 32 ART sites in Tete Province) and the periodical breakdown of the machine at the central site. Second, patients were able to choose between joining a CAG and remaining in individual care. Selection and confounding bias would occur if one would compare the outcomes of patients in CAG with those of patients in individual care. An ongoing quantitative study will allow adjustment for collected biomedical variables; however, adjustment for psychosocial factors will be difficult. Finally, as the data were collected from members in CAG and from the counsellors, observation bias could have occurred. Files were rigorously reviewed in 2010 and periodically thereafter to assure that reported outcomes were true outcomes. During this repetitive process, no discrepancies were found regarding reported treatment outcomes. Frequent visits of the counsellors and a multidisciplinary supervision team to the communities also allowed to understand well the dynamic and to verify what was reported.

Conclusion

Long-term retention in CAG was exceptionally high: 91.8% at 4 years of follow-up. To reduce further

attrition among CAG members, efforts should be made to include patients earlier on ART, and earlier in CAG, with a less suppressed immunological status. Strategies should be piloted to reach male patients earlier and to support them to seek health care earlier when sick. The peer dynamic (rotating representation at the clinic, mutual follow-up of CD4) is associated with the treatment outcomes and is a potential resource to build future strategies on, and promote uptake of HIV testing, linkage to care and retention in care.

The findings of our study confirm the results of other recent studies that documented how community and peer support for ART care improve ART outcomes in sub-Saharan countries (Fatti *et al.* 2012; Wouters *et al.* 2012; van Rooyen *et al.* 2013). The recently proposed large-scale ART roll-out in high-prevalence countries with few financial means will only be possible if all available human potential, including community health workers and PLWHA, is engaged to reach the target of sustained ART coverage.

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