## Title

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## Authors

Hickey, Matthew D
Omollo, Dan
Salmen, Charles R
et al.

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# Movement between facilities for HIV care among a mobile population in Kenya: transfer, loss to follow-up and re-engagement

**Matthew D Hickey**[1,2,3], **Dan Omollo**[2], **Charles R Salmen**[2,3,4], **Brian Mattah**[2], **Cinthia Blat**[5], **Gor Benard Ouma**[2], **Kathryn J Fiorella**[2,6], **Betty Njoroge**[7], **Monica Gandhi**[8], **Elizabeth A Bukusi**[7], **Craig R Cohen**[5,9], and **Elvin H Geng**[8]

[1]Division of General Internal Medicine, University of California, San Francisco (UCSF), San Francisco, CA

[2]Mfangano Island Research Group, Organic Health Response, Homa Bay County, Kenya

[3]Microclinic International (MCI), San Francisco, CA

[4]Department of Family and Community Medicine, University of Minnesota, Minneapolis, MN

[5]Global Health Sciences, UCSF, San Francisco, CA

[6]Atkinson Center for a Sustainable Future, Cornell University, Ithaca, NY

[7]Centre for Microbial Research, Kenya Medical Research Institute, Nairobi, Kenya

[8]HIV-ID-Global Medicine Division, UCSF, San Francisco, CA

[9]Department of Obstetrics, Gynecology and Reproductive Sciences, UCSF

## Abstract

HIV treatment is life-long, yet many patients travel or migrate for their livelihoods, risking treatment interruption. We examine timely reengagement in care among patients who transferred-out or were lost-to-follow-up (LTFU) from a rural HIV facility. We conducted a cohort study among 369 adult patients on antiretroviral therapy between November 2011 and November 2013 on Mfangano Island, Kenya. Patients who transferred or were LTFU (i.e. missed a scheduled appointment by ≥90 days) were traced to determine if they re-engaged or accessed care at another clinic. We report cumulative incidence and time to reengagement using Cox proportional hazards models adjusted for patient demographic and clinical characteristics. Among 369 patients at the clinic, 23(6%) requested an official transfer and 78(21%) were LTFU. Among official transfers, cumulative incidence of linkage to their destination facility was 91% at three months (95%CI 69–98%). Among LTFU, cumulative incidence of reengagement in care at the original or a new clinic was 14% at three months (95%CI 7–23%) and 60% at six months (95%CI 48–69%). In the adjusted Cox model, patients who left with an official transfer reengaged in care six times faster than those who did not (aHR 6.2, 95%CI 3.4–11.0). Patients who left an island-based HIV clinic in Kenya with an official transfer letter reengaged in care faster than those who were LTFU, although many in both groups had treatment gaps long enough to risk viral rebound. Better coordination of transfers between clinics, such as assisting patients with navigating the process or improving inter-clinic communication surrounding transfers, may reduce delays in treatment during transfer and improve overall clinical outcomes.

## Introduction

Individuals receiving care and treatment for HIV in resource-limited settings face a unique challenge: while they must engage in care over long periods of time to optimize health outcomes, they often require a high degree of mobility to meet livelihood demands.(Camlin, Snow, & Hosegood; Marson et al., 2013; Ware et al., 2013) Furthermore, the increasing numbers of 'decentralized' clinics opening in rural areas present patients with new choices in care and incentives to transfer, such as shorter transit times, shorter waiting times, or friendlier staff.(Geng et al., 2010; Ware et al., 2013) Thus, the reality of treatment for HIV infected patients often includes accessing multiple sites for clinical services over time. (Nglazi et al., 2011)

Patient movement between sites can occur in ways that are either known (i.e. through official transfer request) or unknown (i.e. patients are 'lost to follow-up' or LTFU) to the original clinic. There is considerable interest in understanding outcomes among patients who cease accessing care through either of these mechanisms.(Brinkhof, Pujades-Rodriguez, & Egger, 2009; Geng et al., 2013; Geng et al., 2011; Yu et al., 2008) Though it is clear that substantial numbers of patients who discontinue care will access care at other sites, many do so only after their health has deteriorated,(Hallett & Eaton, 2013) with resulting increases in morbidity and mortality.(Kranzer, Govindasamy, Ford, Johnston, & Lawn, 2012) Irrespective of the conditions of departure from a particular HIV clinic, the success, timeliness, and ultimate safety of connection to care at other sites is not well known.

This study examines outcomes among HIV-infected patients who stopped accessing care at a rural primary health center located on an island in Lake Victoria that serves a population in which mobile livelihoods are particularly common.(Kwena, Camlin, Shisanya, Mwanzo, & Bukusi, 2013) We examine patients who left this clinic with official documentation of transfer as well as patients who left without documentation (i.e. LTFU). We followed these patients after clinic departure to determine whether they reengaged in care and the timing of any clinic-to-clinic movement. Our intention is to understand patterns of patient movement between clinic sites, identify gaps in care that could compromise patient safety, and explore reasons for these gaps.

## Methods

### Patients

This study was based at the Sena Health Center, a rural public-sector clinic on Mfangano Island in Homa Bay County, Kenya. This health center is the largest of six facilities on the island, serving a population of approximately 21,000.(*Mbita Division Population Projection*, 2009) All adult HIV-infected patients on combination antiretroviral therapy (cART) were first invited to enroll in a parent study known as the Mfangano Island Healthy Networks Impact Study (MIHNIS), a quasi-experimental trial to evaluate a social support strategy for engagement in care.(Hickey et al., 2015; Hickey et al., 2014) Patients in the MIHNIS trial were followed for two years, from 11/2011–11/2013. For the present analysis, we included

all MIHNIS participants who transferred out or were LTFU at any point during these two years of follow-up.

### Procedures and Measurements

Patient demographics, travel time to clinic, perceived HIV-related stigma in the community(Visser, Kershaw, Makin, & Forsyth, 2008) and HIV knowledge(Carey & Schroder, 2002) were measured at study enrollment through surveys administered by study staff. Clinic data, including CD4 counts, date of ART initiation, and both scheduled and attended visit dates were captured from the clinic's OpenMRS electronic medical record maintained by FACES.(Kulzer et al., 2012) At the end of study follow-up, patients who had left care were traced to ascertain whether they had re-engaged in HIV care. Re-engagement was defined as return to the original or another clinic to resume HIV care. For patients reporting transfer to other facilities, chart abstraction was conducted at those facilities to determine dates of linkage. Patients who returned to the Sena Health Center after initially meeting LTFU criteria were identified through the electronic medical record. The MIHNIS study was approved by the KEMRI Ethical Review Committee and the UCSF Committee for Human Subjects Research.

### Analyses

We plotted the cumulative incidence of re-engagement in care following the last attended visit at the Sena Health Center for patients who left with an official transfer versus those who were LTFU. The date of last attended appointment at the Sena Health Center was taken to be time zero for all time-to-event analyses. Cumulative incidence estimates and 95% confidence intervals (CIs) were calculated using the cumulative incidence function, treating death as a competing risk.(Satagopan et al., 2004) We also report the proportion of patients in each group who experience a gap in ART adherence, based on the amount of medication dispensed at patient's last clinic appointment at Sena. We evaluated demographic and clinical factors associated with re-connection to care, and compared rates of reengagement, using a Cox proportional hazards model. Each predictor of interest was included in a univariable Cox model to evaluate association between the predictor and re-engagement in care. The multivariable model included all variables with $p<0.1$ in the univariable models.

## Results

Of 369 patients on ART at the Sena Health Center at enrollment, 23 (6%) obtained an official transfer letter to another facility and 78 (21%) missed a clinic visit for ≥90 days without requesting transfer. All patients were traced to confirm whether and when they had accessed care at a different health facility.

Among the 23 patients making an official transfer, 15 (65%) filed for a transfer to another health facility on Mfangano or neighboring Takawiri islands, while 8 (35%) filed for transfer to a facility elsewhere in Kenya. Ninety six percent reached their destination facility, with a cumulative incidence of reaching the destination facility by three months after their last appointment at the Sena Health Center of 91% (95% CI 69–98%). (Figures 1&2) Standard practice at Sena is to dispense either 28 or 56 days of cART upon transfer. Among this

sample, 8 (35%) were given 28 days of cART, 8 (35%) were given 56 days of cART and 7 (30%) had missing data regarding the amount of cART dispensed. Thus, conservatively assuming that those with missing data were given 28 days of therapy, 7 (30%) made the transfer without any treatment gap (i.e. medication supply given by Sena exceeded time until connection to new clinic), 6 (26%) sustained a treatment interruption of 14 days or less, and 10 (43%) sustained a treatment interruption of more than 14 days during the transfer.

Among the 78 patients who were LTFU without official transfer (missed a clinic visit by ≥90 days), 38 (49%) eventually returned to care at the Sena Health Center, 22 (28%) transferred to another facility and 18 (23%) never returned to care. Two patients were unable to be located and were thus assumed to be out of care. The cumulative incidence of re-engagement in clinical care at a new clinic was 14% (95% CI 7–23%) at three months and 24% (95% CI 16–34%) at six months following the last attended appointment. The cumulative incidence of return to the Sena Health Center was 0% at three months and 36% (95% CI 26–47%) at six months. (Figure 2) The cumulative incidence of reengaging in care overall, to either a new clinic or the original clinic) was 14% (95% CI 7–23%) at three months and 60% (95% CI 48–69%) at six months after the most recent attended clinic appointment at the Sena Health Center. (Figures 1 & 2)

From the last attended appointment, the median return date for the LTFU group was scheduled 56 days later (range 14–84). This corresponds to the quantity of drugs given to patients upon their last visit at the Sena Health Center before missing a clinic visit and becoming LTFU. The missed visit marks the time point when patients likely ran out of cART, assuming that they were previously taking medications consistently and did not first transfer to another facility or obtain medications from other non-clinic sources. Of those who were LTFU, 71 of 78 (91%) experienced a treatment gap of greater than 14 days. Of the seven patients who did not experience a treatment gap, two patients died within 14 days of missing their appointment and the remaining 5 reengaged in care at another health facility within 14 days of their missed appointment.

In univariable Cox proportional hazards modeling, patients who left care with an official transfer letter re-linked to care at 5.5 times the rate of those who left without a transfer letter (HR 5.5, 95% CI 3.2–9.3). (Table 1) Each one-point increase in perceived stigma in the community, as measured by the 17-point Parallel Stigma Scale(Visser et al., 2008), was associated with an 8% relative decrease in the rate of re-linkage to care (HR 0.92, 95% CI 0.86–0.98). Having been on cART for a longer duration at the time of departure from the clinic was also associated with an increase in the rate of re-engagement (HR 1.16 per 1-year increase, 95% CI 1.04–1.3).

The final model yielded similar effect sizes for leaving with an official transfer, perceived stigma and time since cART initiation; however only leaving with an official transfer (aHR 6.1, 95% CI 3.4–11.0) and perceived stigma (aHR 0.90, 95% CI 0.84–0.96) remained statistically significant.

## Discussion

In our study, HIV-infected patients receiving cART who left their original clinic usually reconnected to care, though rates of reengagement differed based on the circumstances of departure. Those who left with an official transfer reengaged in care at six times the rate of patients who were LTFU. In both groups, however, treatment interruptions were frequent, suggesting vulnerability to poor health outcomes.(Kranzer et al., 2012) Work by Parenti et al suggests that 50% of patients who experience a 15 day treatment interruption on a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen subsequently experience virologic rebound.(Parienti et al., 2008) This suggests that a substantial proportion of patients in our study, where 96% of patients were on an NNRTI-based regimen, may also have experienced virologic rebound. Among patients making official transfers, approximately 40% experienced a treatment gap greater than 14 days, implying that 20% of those leaving with an official transfer could have experienced a treatment gap-related viral rebound. The situation among those who stopped without an official transfer was worse: 91% of these patients had a treatment gap >14 days, implying that nearly 50% of patients leaving clinic without an official transfer could have experienced viral rebound. Because many patients experienced gaps longer than 15 days, the proportion experiencing viral rebound may have been even higher. In short, though neither mode of clinic departure appears to facilitate complete transition of care without substantial risk of virologic rebound, many patients transfer care to other facilities through “unofficial” pathways that appear to confer additional risks over those associated with official transfers.

Another key finding was the association between higher degrees of perceived stigma in the community and subsequent decreased rate of reengagement in care following departure from the Sena clinic. This finding persisted in the multivariate model and is consistent with other reports suggesting that stigma is associated with reduced medication adherence.(Katz et al., 2013) Others have reported that patients may develop a ‘reluctance to return’ following gaps in care.(Ware et al., 2013) Our findings suggest that stigma may play a role in exacerbating this reluctance to return, resulting in delays in reconnection to care following a treatment interruption.

At face value, one way to interpret these data is to conclude that all patients should obtain official transfers and that health systems should be strict about this practice. However, we believe this oversimplified interpretation of these data would be unfortunate for both health systems and patients. In reality, many patients are engaged in livelihoods that require mobility. In communities surrounding Lake Victoria, one third of households are engaged in fishing,(Fiorella et al., 2014) requiring frequent travel to keep up with the migratory patterns of fish.(Camlin, Kwena, & Dworkin, 2013), Such mobility is not always predictable. As a result, “silent transfers”, or even missed visits with subsequent return to the same clinic, are not necessarily the result of patient failure to comply with administrative requirements, but rather a reflection of the fact that livelihoods compete with health care as a priority and patients have limited control over mobility and the proximity of new or temporary residences to clinical services.(Ware et al., 2013) We believe that health systems need to adapt to better accommodate patient needs regarding accessing care from new or multiple facilities. While transfer letters may improve the likelihood of successful “send-offs” to new

clinics, requiring them for intake at a “receiving” clinic would likely have serious deleterious effects for the majority of patients in our study who lacked letters, leading to longer treatment interruption or total disengagement from care.

Ideas for improving the coordination of transfers include both improving platforms for sharing clinical data and helping patients feel more comfortable moving between health facilities. Sharing clinical data between former and recipient health facilities can help ensure that the patient continues to receive the same cART regimen, without having to repeat staging or cART initiation procedures. Such sharing platforms could include shared electronic medical records, patient data cards that patients keep with them, or a structured phone call between recipient and former facilities to facilitate a patient handoff. National registries of clinic contact information would be inexpensive to implement and could facilitate inter-clinic communication. Procedures to help patients feel more comfortable transferring care to another facility include more overt advertising of the procedures by which patients can receive assistance with transfers, as well as more friendly procedures for receiving patients at the new facility. Clinician attitudes may represent both a source of patient transfers and a barrier to facilitation of transfers, thus interventions to train clinicians to be more patient-friendly may intervene on multiple pathways.(Ware et al., 2013)

Movement across clinic sites is fueled through three predominant mechanisms. (Figure 3) Some patients leave their original clinics after requesting an official “transfer letter” to facilitate transition of care to another site.(Nglazi et al., 2013) Other patients depart from their original site without notifying the clinic, and are thus labeled “lost to follow-up”. This group includes both patients who depart with the intention of moving their care to another site, and those who simply stop attending appointments, with or without the intention to later return or transfer.(Brinkhof et al., 2009; Geng et al., 2010; Ware et al., 2013) Regardless of the conditions of departure, the timing of re-engagement in care, at either the original clinic or a new clinic, has important implications for the safety and effectiveness of HIV treatment. (Bastard et al., 2012; Kranzer & Ford, 2011; Kranzer et al., 2012; Mugavero et al., 2012; Pinoges et al., 2015)

As decentralization of health facilities continues to expand delivery of HIV care to increasing numbers of rural sites, numbers of patients who officially transfer care and who are LTFU from their original clinic are increasing.(Fox & Rosen, 2010; Nglazi et al., 2013; Nglazi et al., 2011) Though outcomes among those who leave a particular clinic are largely unknown, some tracing studies have confirmed that substantial numbers of patients who are classified as LTFU actually made a silent transfer to another facility.(Brinkhof et al., 2009; Geng et al., 2011) To date, tracing studies of patients who are LTFU have not ascertained the timing of re-engagement in care following silent transfer. Two studies evaluating transfer outcomes following clinic-initiated ‘official’ transfer have concluded that nearly all patients actively referred for transfer reach their destination clinic, however timing of transfer linkage was not assessed.(Cloete et al., 2014; O’Connor, Osih, & Jaffer, 2011) Only one prior study has reported on the timeliness of linkage to the new clinic following transfer, concluding that nearly all patients making official transfers out of a large hospital-based clinic in Malawi reached their destination facilities, with a mediation duration between departure and re-engagement of 1.3 months.(Yu et al., 2008) All three of these studies, however, have focused

on official transfers from a central site to lower level health facilities. Our study expands on this literature by describing the timeliness of re-engagement in care following departure from a rural primary care HIV clinic. Patients making an official transfer in our cohort had similar success and rates of linkage to these prior studies in urban settings. In contrast, we observed that patients who become LTFU from their clinic, including those who self-transfer to another clinic, frequently sustain treatment interruptions prior to re-engaging in care.

## Limitations

Though this study was small, we believe the setting is emblematic of many rural settings in East Africa: the health facility is staffed by health workers from the Ministry of Health, it is supported by an academic partnership (FACES), and the patient population served is engaged in livelihoods that are typical of the region. Overall, we believe that findings from other clinic sites in the region are likely similar.

Second, we do not know whether patients who were LTFU intended to go to a different facility when they left their original facility, or whether they intended to stop care and only reengaged when they felt unwell (Figure 3). If the former is true, this suggests that access to care is a problem once patients leave their original clinic. If the latter is true, it implies that patients who are silent transfers may lack motivation or empowerment to play a more active role in their care. Although we found a strong association between having a transfer letter and more rapid re-engagement among patients who stopped attending the original clinic, we did not account for all unmeasured common causes of this relationship, thus precluding a clear causal interpretation. We did, however, measure and adjust for several plausible confounders, including measures of socioeconomic status and stigma, and the association remained large. We therefore believe that the process of obtaining a transfer has an important effect on re-engagement and that making transfers more administratively streamlined may help reduce gaps in care as patients move from one facility to another.

Further, among patients who did transfer, the reason for the transfer is not known. Reasons are likely multiple and may include migration, wanting to move to a more convenient facility, problems with the clinic staff at the old facility or concerns about confidentiality at the old clinic.(Geng et al., 2010; Ware et al., 2013) More definitive information about the patient perspective would allow stronger inferences, and also more clearly identify areas for intervention.

## Conclusion

In conclusion, this is the first study that we know of which explicitly assesses the timeliness and completeness of re-engagement in care among patients who transfer or are lost to follow-up. We found that official transfers nearly always connected to the new clinic. Yet for both official transfers and those who left without an official transfer, a substantial proportion experienced treatment gaps during the care transition. We believe that transfers – whether silent or official – are part of the natural history of treatment in resource-limited settings. Systems must be patient centered to optimize engagement and thereby overall effectiveness over time by making transfers easy and accessible. Assessing the safety of transfers, to date

rarely done, needs to be a core component of promoting high-quality HIV care in resource-limited settings.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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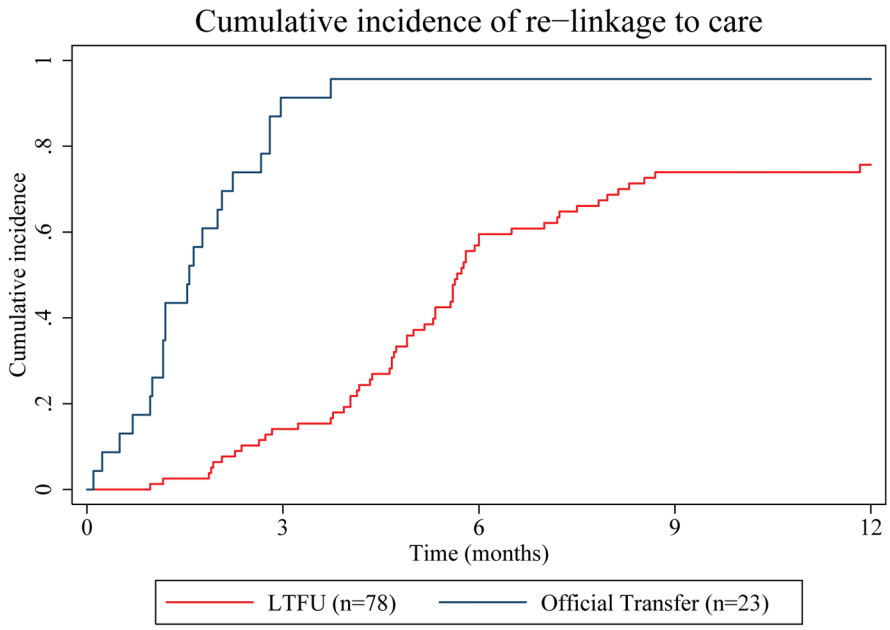


**Figure 1.**

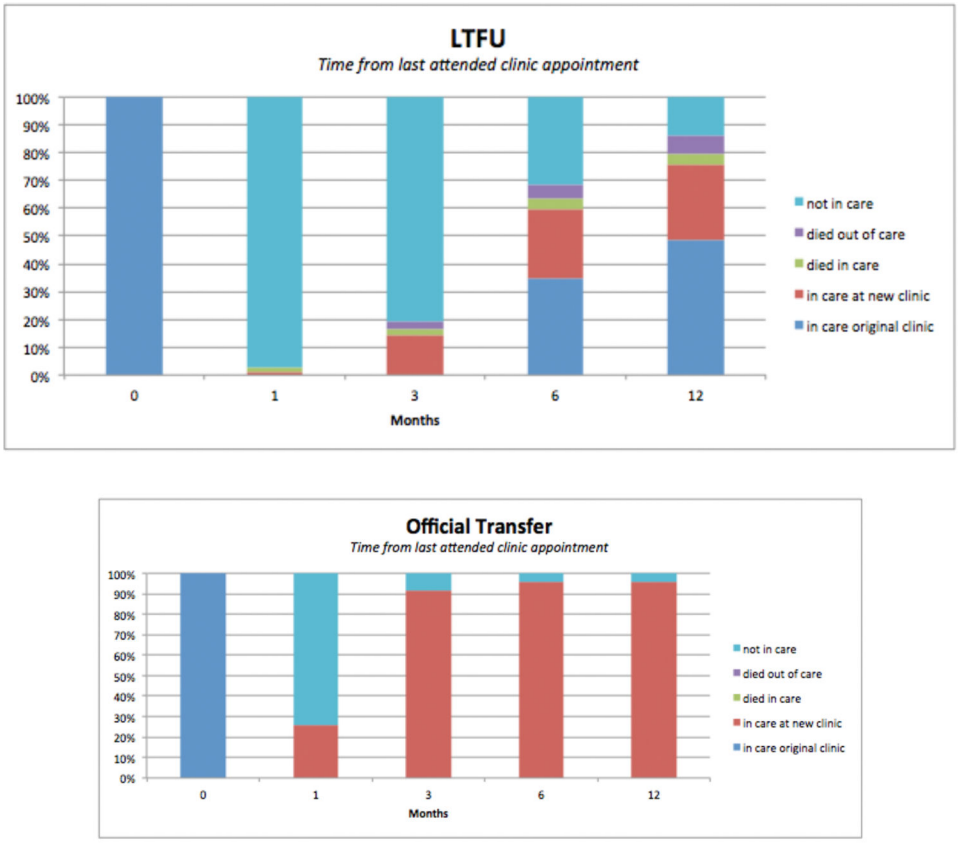


**Figure 2.**

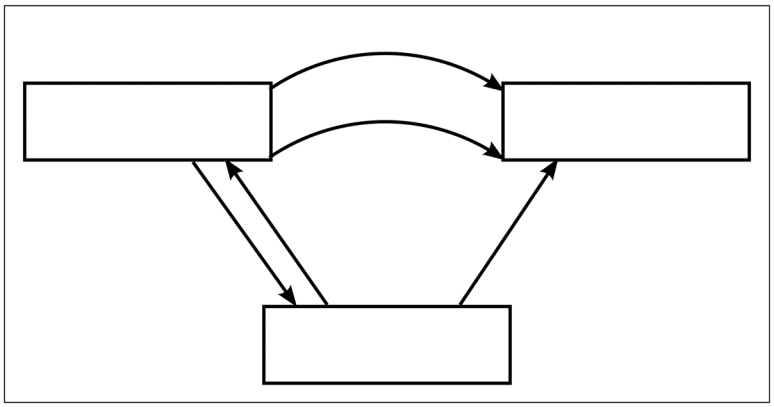

**Figure 3.**

## Table 1

Cox Proportional Hazards Model: hazard of re-linking to care

| | Unadjusted HR (95% CI) | P | Adjusted HR (95% CI) | P |
|---|---|---|---|---|
| **Official transfer** | **5.51 (3.25 to 9.34)** | **<0.0005** | **6.15 (3.44 to 11.0)** | **<0.0005** |
| Age at transfer (yrs), per 10 years | 1.0 (0.84 to 1.18) | 0.96 | | |
| Sex | | | | |
| Female | ref | | | |
| Male | 0.71 (0.43 to 1.17) | 0.18 | | |
| Monthly income in Kenyan Shillings | | 0.64 | | |
| <2,000 | ref | | | |
| 2,000 – 4,000 | 1.11 (0.63 to 1.94) | | | |
| 4,001 – 6,000 | 1.53 (0.79 to 2.99) | | | |
| >6,000 | 1.22 (0.68 to 2.19) | | | |
| HFIAS Food Insecurity Scale | 1.02 (0.98 to 1.06) | 0.29 | | |
| Education | | | | |
| Primary or less | ref | | | |
| Secondary or greater | 1.14 (0.70 to 1.86) | 0.60 | | |
| **Attributable stigma** | **0.92 (0.86 to 0.98)** | **0.01** | **0.90 (0.84 to 0.96)** | **0.003** |
| HIV knowledge | 1.02 (0.91 to 1.14) | 0.76 | | |
| Walking Distance from Sena | | 0.75 | | |
| ≤60 minutes | ref | | | |
| >60 minutes | 1.07 (0.69 to 1.66) | | | |
| **Time since ART initiation (yrs), per 1 year** | **1.16 (1.04 to 1.30)** | **0.01** | 1.08 (0.96 to 1.22) | 0.21 |
| CD4 count at transfer | | 0.54 | | |
| <200 | ref | | | |
| 200–350 | 1.40 (0.70 to 2.78) | | | |
| >350 | 1.08 (0.57 to 2.05) | | | |