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‘Wamepotea’ (They have become lost): Outcomes of HIV-positive and HIV-exposed children lost to follow-up from a large HIV treatment program in western Kenya

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Abstract

Objective—The objective of this study was to identify the vital status and reasons for children becoming LTFU from a large program in western Kenya.

Methods—This was a prospective evaluation of a random sample of 30% of HIV-exposed and positive children LTFU from either an urban or rural HIV (AMPATH) clinic. LTFU is defined as absence from clinic for >6 months if on cART, and >12 months if not. Experienced Community Health Workers were engaged to locate them.

Results—There were 97 children sampled (78 urban, 19 rural). Of these, 82% were located (78% urban, 100% rural). Among the HIV-positive, 16% of the children were deceased, and 16% had not returned to clinic because of disclosure issues/discrimination in the family or community. Among the HIV-exposed, 30% never returned to care because their guardians either had not disclosed their own HIV status or were afraid of family/community stigma related to their HIV status or that of the child. Among children whose HIV status was unknown, 29% of those found had actually died, and disclosure/discrimination accounted for 14% of the reasons for becoming LTFU. Other reasons included believing the child was healed by faith or through the use of traditional medicine (7%), transport costs (6%), and transferring care to other programs or clinics (8%).

Conclusion—After locating > 80% of the children in our sample, we identified that mortality and disclosure issues including fear of family or community discrimination were the most important reasons why these children became LTFU.

Keywords

pediatrics; HIV; Africa; retention; losses-to-follow-up; mortality

Introduction

The Joint United Nations Program on HIV/AIDS (UNAIDS) has estimated that as of the end of 2008, there were approximately 2.1 million children living with HIV/AIDS¹. Also in 2008, 430,000 children became newly HIV-positive, while another 280,000 died of AIDS¹. Despite the well-documented fact that combination antiretroviral therapy (cART) in HIV-positive children improves survival, physical growth and other important clinical outcomes^{2–10}, only 38% of children in urgent need of cART are actually receiving therapy¹¹. Unfortunately not only do pediatric HIV care programs face significant challenges with regard to expanding access for new children, maintaining care for already enrolled children can be difficult.

Losses to follow-up (LTFU) specifically have emerged as a clinical and epidemiologic challenge, with approximately 10–14% of those receiving cART becoming LTFU^{2, 3, 5, 6, 12}. LTFU among HIV-positive children not on cART and among HIV-exposed children are even higher (20%–40%)^{12–15}. Risk factors for becoming LTFU include advanced disease stage, severe malnutrition, and other negative clinical indicators¹². These risk factors suggest a high probability that these lost children are in fact deceased. Unidentified mortality within this population has important implications for our understanding of the true mortality rates of both HIV-positive and HIV-exposed children, as well as for accurate HIV transmission rates from mother to child. Moreover, understanding the reasons for LTFU among children and families is the first step toward implementing programs that retain participants and achieve their goals for prevention, treatment, or research. We therefore prospectively sought the outcomes of a random sample of children who became lost to follow-up from our HIV care and treatment program in western Kenya with the ultimate aim of revising mortality estimates among them. Here, we present the methods and outcomes of these investigations.

Methods

The Program

The Academic Model Providing Access to Healthcare (AMPATH) was initiated in 2001 as a joint partnership between Moi University School of Medicine (Eldoret, Kenya), the Indiana University School of Medicine (Indianapolis, USA), and the Moi Teaching and Referral Hospital (Eldoret, Kenya). The USAID-AMPATH Partnership was initiated in 2004 when AMPATH received ongoing funding through USAID and the United States Presidential Emergency Plan for AIDS Relief (PEPFAR). Details of the development of this program have been described elsewhere¹⁶. In brief, the first urban and rural HIV clinics were opened in November 2001. Since then, the program has enrolled more than 120,000 HIV-positive patients, including approximately 18,000 children, in 25 Ministry of Health facilities and numerous satellite clinics in western Kenya. All HIV and tuberculosis-related care and treatment are provided free at the point of care.

Since late 2005, AMPATH has had an outreach program that utilizes trained HIV-positive adults to obtain detailed *locator information* at each new and returning patient visit. This information is then used to contact patients when they do not return for their scheduled appointments. Per protocol, when an HIV-positive pediatric patient receiving cART does not return for a scheduled visit, an outreach attempt is made within 24 hours through a telephone call or home visit. For HIV-positive patients not on cART and for HIV-exposed children, the outreach attempt is made within 1 week of the missed visit. A patient is only considered LTFU after the outreach program has tried to reengage a patient with the program.

Study Population

Inclusion criteria—We identified all children who at their last visit were known to be HIV-positive, HIV-exposed, or whose HIV-status was missing in the database, who were attending the clinic at the central AMPATH centre located at the urban Moi Teaching and Referral Hospital (MTRH) in Eldoret, or the rural sub-District Hospital in Burnt Forest, and who were documented as LTFU during September and October, 2009. A child was documented as being LTFU if they met one of the following criteria: 1) HIV-positive and last known to be receiving cART, and absent from the clinic for at least 6months; 2) HIV-positive child not on cART at last visit, and absent from the clinic for at least 12months; 3) HIV-exposed child absent from the clinic for at least 6 months; 4) HIV-status missing for a child who has been absent from the clinic for at least 6 months. There were no exclusion criteria.

Sampling—We randomly sampled 30% of the eligible population, stratified by clinic and HIV-status. A sample of 30% was chosen because based on previous related work, sampling more than 30% does not yield any more precise mortality estimates when using outreach data to revise mortality estimates^{17, 18}.

The random sample was generated using Excel (Vista OS) Data Analysis – Random Number Generation. We generated random numbers between 0 and 1 and randomly assigned them to eligible patients. We then sorted from lowest to highest and selected participants from lowest to highest according to our target sample size.

Study Design and Implementation

This was a prospective observational study. The study was approved by the Moi University School of Medicine Institutional Research and Ethics Committee and the Indiana University School of Medicine Institutional Review Board.

We recruited 45 Community Health Workers (CHW's) with extensive experience working with the AMPATH Orphans and Vulnerable Children program in the community, to ensure they had knowledge of and sensitivity to issues surrounding HIV-affected children and their families, including disclosure, stigma, and clinical protocols. All of the CHW's were already working with either MTRH or Burnt Forest clinics. The investigations took place between January and July, 2010.

Using the locator information (previously described in the program description) of the child or the parent (where available), the CHW's were each assigned at least 2 children to locate. They were reimbursed for all transportation-related costs (using local means), accommodation when necessary, and given a per diem if they were required to travel a significant distance in order to locate a child. CHW's were sensitized that the tracing was like detective work and encouraged them if they couldn't locate a child to ask around with neighbors and community leaders identifying themselves only as coming from Moi Teaching and Referral Hospital. To confirm the location of a child, the CHWs were to provide one of the following: a signed letter from the local Chief or Assistant Chief, Village Elder, Pastor, or other community leader attesting to the whereabouts or death of a child; a photocopy of the child's death or burial certificate; a photocopy of the mother's identification; or, if all else failed, a telephone conversation between the child's parent/guardian (caregiver) and the project coordinator (e.g. if a photocopy machine or a community leader was not available). During interviews with the caregiver, the project coordinator asked a series of questions to ensure the authenticity of the information provided and documented these responses in detailed field notes, such as the full names and birth date of the child, when they last attended clinic, etc. Several meetings with the CHW's were held

during the 6 months to identify challenges and obstacles and strategize about over-coming them. Other resources required for this study included telephone credit, a project coordinator, office space and equipment.

Data Collection

Clinicians complete standardized forms capturing demographic, clinical, and pharmacologic information at each patient visit. These data are manually entered into the AMPATH Medical Record System (AMRS), a secure computerized database designed to support clinical management. Data entry is validated by a random review of 5% of the entered forms¹⁹. At the time of registration, patients are provided with a unique identification number.

CHW's were provided with a standardized data collection form to be used in the field for LTFU assessment. This form collected basic sociodemographic information, and the child's AMPATH ID. If the child was deceased, the form captured the date of death, whether the date was estimated or exact, and the general cause of death (illness, accident, suicide, murder). If the child was found alive, the form collected information on the date and location where the child was found, as well as the reasons for LTFU. Possible reasons for LTFU included the following: transport costs, family commitments, work commitments of the child or the caregiver, either the child or the caregiver was too ill to come to clinic, school commitments, disclosure issues, insecurity (afraid to travel), having travelled, having been displaced (from post-election violence), they forgot about the appointments, they did not actually miss the appointment(s), the caregiver or the child refused care (family discrimination, community discrimination, healed by faith, using traditional or herbal medicines), or 'other' reasons.

This standardized form was supplemented with narratives from the CHW's, both about the process of locating the child (also used for the reimbursement process), and the story of the child and his/her family and how the child came to be LTFU from the clinic. Frequently there were multiple reasons listed on the form. To identify the primary reason for becoming LTFU, we had 3 independent reviewers evaluate all documentation that was available for located children in order to make a determination as to the primary underlying cause. Where there was disagreement amongst them, the Principal Investigator reviewed the documentation and made the final determination.

Results

There were 308 children who met the inclusion criteria, including 254 from the urban clinic and 54 from the rural clinic. Table 1 summarizes general performance characteristics of the two clinics selected for the study. From this population, a sample of 97 children was randomly selected, 78 from the urban clinic and 19 from the rural. Table 2 compares the population who met the inclusion criteria and the random sample. The average age at enrolment of children in the sample was 0.6 years, 43% were female, 45% were HIV-positive, 21% were either single or double orphans at enrolment, and 25% were WHO Stage III/IV at their last visit.

We were able to locate 82% of children (Table 3): 19/19 (100%) of children lost from the rural clinic, and 61/78 (78%) lost from the urban clinic. Children were located in an average of 5 attempts, including telephone calls and home visits. The majority of children were located in the first 3 months.

The reasons for failure to return to clinic varied greatly by the HIV status of the child (Table 4). Among HIV-positive children, 16% were found to be deceased. Another 16% of HIV-

positive children failed to return to clinic because of disclosure issues or fear of family or community discrimination. There were two cases where the HIV-positive child's caregiver moved and changed their names because of the HIV status of the child. There were another two cases where the mother of the child had died and had not informed the child's new caregiver of the child's HIV status. There were two cases where the guardian reported that the child was HIV-negative but where the patient's clinic chart documented that the child was in fact HIV-positive; although it may have been a legitimate misunderstanding on the part of the caregiver we had no documentation to support this and we therefore classified both of these cases' primary reasons for LTFU as disclosure/discrimination (i.e. denial of the child's HIV status). Other reasons for LTFU among the HIV-positive children included having travelled or been displaced (14%), transport costs (14%), having transferred to another clinic (11%), believing the child was healed by faith or from the use of traditional medicine (7%), family or work commitments (2%), and family conflict (2%).

Among the HIV-exposed children, the most common reason for not returning to clinic was disclosure issues or fear of community or family discrimination (30%). Either the mother had not disclosed her own HIV status, or the family/caregiver was afraid of family or community stigma related to their or the child's HIV status. The next most frequent primary reason for LTFU was that the caregiver or guardian believed the child was no longer required to attend clinic (13%). Chart review was used to confirm the report of a negative HIV status in each of the six instances in which this was reported. Other reasons for not returning to clinic included a belief that the child had been healed by faith or through the use of traditional medicine (9%), refusing care because of family conflict or other reasons (8%), the child had died (4%), travelled or been displaced (4%), transferred to another clinic (4%), family or work commitments (4%), and in two cases the child hadn't actually missed their appointments. There was only 1 case (2%) of an HIV-exposed child not returning to clinic because of transport costs.

Among the 7 children whose HIV status was unknown, 5 were located (71%). Of those found, 29% were deceased, while disclosure issues (14%), having transferred care (14%), and refusal of care because of family conflict or other reasons (14%) were the common causes of LTFU for those found alive in this group.

Of the 17 children who could not be found, eight had either no or insufficient locator information. Reviewing the charts of those children who could not be located revealed that most of the HIV-positive children who were untraceable had been extremely ill at their last visit (e.g. CD4% of 2%, constant unexplained vomiting, etc.); one HIV-positive child was an orphan and had only one visit before becoming LTFU. Although one of the HIV-exposed children who was not located was ill at the last visit and another had a history of non-adherence to clinic visits prior to becoming LTFU, the majority of the HIV-exposed children were healthy at their last visit.

Discussion

This is among the first attempts to document the outcomes of HIV-positive and HIV-exposed children who have become LTFU from an HIV care program in sub-Saharan Africa^{20, 21}. We were able to locate and determine the vital status of 82% of the children overall, including 100% of those children who had been attending the rural clinic. We found similar proportions of the HIV-exposed and the HIV-positive children, but a smaller proportion of the children whose HIV status was unknown. Of the children we found, 11% had died, including 16% of the HIV-positive, 29% of the HIV status unknown, and 4% of the HIV-exposed. Disclosure and the fear of discrimination accounted for one-third of all the LTFU among the HIV-exposed. This is consistent with the work of others in our group who

have identified disclosure and fear of discrimination as leading barriers to pediatric adherence to antiretroviral medication among families^{22, 23}.

Our efforts to trace a random sample of patients who have become LTFU are based on the formative work of others^{24, 25}. Our ability to locate lost patients appears to be at least as successful as others who have traced adults: specifically, a meta-analysis examining the proportion of lost HIV-positive patients who were able to traced found an average of 63%²⁰. Our success rate may in part be due to our deliberate attempt to locate patients who had been defined as LTFU in the months just prior to the initiation of this project. Because we did not attempt to trace children who had been LTFU for an extensive amount of time, the chances of actually finding patients in this study was likely increased, even though they had been missing from clinic for 6–12 months. We had a much higher rate of success in locating patients who were lost from the rural clinic (100%). This is consistent with other studies which have located higher proportions of individuals lost from a rural setting²⁵. We postulate this is because the social networks in rural communities are much stronger, so that even without good locator information, households can be traced because the Chiefs, village elders, and other community leaders have extensive knowledge about each household in their respective communities. What decreased our overall average of locating patients were the children whose HIV status was missing, of whom we were only able to locate 71%. These children, in general, had only presented for one to two clinic visits prior to becoming lost, and did not have testing for HIV prior to becoming LTFU. It may be presumed that all 7 of these children were at least HIV-exposed since they had all presented for HIV-related care. Although 29% of those found were deceased, only 1 was documented as being WHO Stage III/IV at their last visit, 3 were WHO Stage I/II at their last visit, and 3 had no information on WHO Stage.

Mortality estimates among HIV-positive children on cART in sub-Saharan Africa have previously been described as approximately 7%^{2, 8}, with LTFU rates reported to be approximately 15%, and no real difference whether they are receiving cART or not^{2, 12}. If at least 16% of the HIV-positive children who are LTFU are actually dead, these mortality estimates are likely to be low and requiring revision based on our findings. We had anticipated, based on retrospective epidemiologic analyses of rates and risk factors of pediatric LTFU¹² that a higher proportion of the children LTFU would have been found to have died. Indeed, work from Malawi suggests that HIV-positive children who have defaulted may be at much higher risk of death than our population²¹. We were, however, unable to locate 18% of the HIV-positive sample, many of whom, based on the records from their last visit date, appear to have been quite ill. Therefore, the 16% deceased among our traced HIV-positive population is likely to be the lowest bound for mortality among those LTFU and revisions to mortality estimates should employ sensitivity analyses to more accurately describe the probability of mortality in this population.

Children have unique vulnerabilities because of their dependency on their parents or other caregivers. More specifically, this work supports other findings that children's health outcomes and retention in care are deeply embedded within the family unit and the accompanying social context^{22, 23, 26}. For example, disclosure of the child's or family members (e.g. mother) HIV status was a major issue, affecting particularly the HIV-exposed children. Although we didn't specify on the data collection form whose HIV disclosure and to whom was being referenced, in each case, the CHW's narratives were specific. There was no case in which the issue was disclosure of the child's HIV status to the child. Each case was about the fear of having the HIV status of the child and/or mother disclosed to other family members (including the father of the child), or the HIV status of the child and/or mother disclosed to the community. Disclosing a child's HIV status usually means having to disclose the mother's HIV status, and this may threaten the entire family with community

discrimination²³. Even as a result of disclosing the child's diagnosis to family members, the mother-child pair may experience intra-family discrimination, or even violence or expulsion from the home²³. In contrast, not disclosing the child's HIV status is a tremendous threat to the health of the child because of their need for care, treatment, and support. HIV stigma, manifested in non-disclosure and fear of discrimination, is clearly an enormous issue, particularly for the children who are HIV-exposed. We postulate that these issues were more important reasons for not returning to clinic for HIV-exposed children because they were likely in better health and not in immediate need for clinical care. In short, whether it is disclosure issues, family conflicts, poverty, or a preference for traditional or faith healers, the child's challenges in being retained in care are essentially the caregivers'. Substantially more effort is required to decrease the stigma associated with HIV infection and AIDS, improve disclosure counseling for children and their caregivers, and implement child protection measures so that the care of the child is more independent of the issues of the caregiver.

There are several important strengths and also some limitations to this study. First, by including children who at their last visit were HIV-positive, HIV-exposed, or whose HIV-status was missing, we adequately represented the pediatric clinic population attending our care program. By not restricting our study to HIV-positive patients receiving cART, we have been able to overcome the limitations of some other studies in adults whose sole focus is on cART outcomes. Moreover, these findings offer information on issues related to retention in care for preventative programs such as PMTCT efforts. Further, by randomly sampling from both an urban and a rural clinic we are able to better generalize our findings to other settings.

Limitations of our study include that because we sampled from children LTFU more recently, we may not be able to extend our interpretation to children who have been LTFU for a greater length of time. As HIV care programs scale-up, both the rates and risk factors for becoming LTFU can be expected to change^{12, 27}. We deliberately chose to sample from more recently lost children to increase our ascertainment of subjects' vital status, as low ascertainment would prevent us from being able to accurately revise mortality estimates (in a forthcoming analysis). Another factor limiting generalizability of our findings is that because AMPATH is decentralized throughout western Kenya, the outcomes of children who have become LTFU may be quite different from those in single-centre programs, where the majority of patients may have become LTFU because of transfers-out to other care systems²⁵. This may be why transfers-out accounted for a relatively small proportion (8%) of the LTFU in this population. Our numbers of subjects in different HIV status categories are relatively small and therefore comparisons between them may be due to chance alone. Finally, although we obtained a random sample and the sample was reflective of the sampling frame on most indicators, our sampled HIV-positive children were proportionately less likely to have been receiving cART at their last visit. The rest of the indicators were generally representative, and we can only conclude that it was the result of relatively small numbers in both the sampling frame and sample that caused reduced precision in the random assignments during the sampling process. Importantly, while in adults LTFU are higher pre-cART than on-cART²⁷, there is data to suggest that this does not appear to be the case with children¹², although there are conflicting findings²⁸ perhaps related to program structure. We believe therefore that the impact of this limitation on our ability to generalize from these results is reduced.

In conclusion, we were able to successfully locate a majority of this sample of children lost from our HIV care program in western Kenya. A major cause of the LTFU in the HIV-positive and HIV status unknown population was mortality. However, disclosure issues and fear of discrimination were other important reasons why many HIV-exposed children failed

to return to clinic. The findings from this study point to a significant need for improved data quality and reporting; however, they also demonstrate the substantial need to better address the pernicious stigma that still surrounds HIV infection and people living with HIV/AIDS.

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Table 1

General indicators of clinic performance for clinics selected for study

Clinic Indicators	MTRH (Urban)	Burnt Forest (Rural)
Number of children ever enrolled	4230	606
Number of children currently enrolled	4083	579
Cumulative number of children deceased	170	23
Number of children transferred out in September 2009	3	2

Table 2

Summary of Random Sample of Children Lost to Follow-up (LTFU) Sought by Community Health Workers

	All children defined LTFU from 2 clinics in Sept-Oct 2009 N=308	Random Sample N=97
Clinic		
Urban	254 (82%)	78 (80%)
Rural	54 (18%)	19 (20%)
Sex		
Male	162 (53%)	55 (57%)
Female	146 (47%)	42 (43%)
Median age at enrolment (interquartile range)	0.6 yrs (0.1–3.7)	0.6 yrs (0.1–2.7)
HIV status at last visit		
HIV-positive	149 (49%)	44 (45%)
HIV-exposed	152 (49%)	46 (47%)
HIV status missing	7 (2%)	7 (7%)
Median days from enrolment to last visit	364 (91–668)	244 (62–568)
Orphan status at enrolment		
Orphaned	53 (17%)	20 (21%)
Not Orphaned	185 (60%)	63 (65%)
Missing	70 (23%)	14 (14%)
Median CD4 at last visit (interquartile range)	697 (356–1062)	752 (452–1107)
WHO Stage at last visit		
WHO Stage I/II	198 (64%)	64 (66%)
WHO Stage III/IV	86 (28%)	25 (25%)
Missing	24 (8%)	8 (9%)
On cART at last visit		
Yes	70 (23%)	1 (1%)
No	238 (77%)	96 (99%)

Table 3
Summary of Children Located and Not Located by Community Health Workers

	Moi Teaching & Referral Hospital (Urban)		Burnt Forest Sub-District Hospital (Rural)		Total
	Located	Not Located	Located	Not Located	
HIV-positive	27	8	9	0	44 (82% found)
HIV-exposed	32	7	7	0	46 (85% found)
HIV status unknown	2	2	3	0	7 (71% found)
Sub-totals	61 (78%)	17 (22%)	19 (100%)	0 (0%)	97 (82% found)
Total	78		19		97

Table 4

Primary reasons given for losses to follow-up (LTFU)

Primary Cause	HIV-Positive N=44	HIV-Exposed N=46	HIV-status Missing N=7	Total N=97
Disclosure Issues/ Fear of Family or Community Discrimination	7 (16%)	14 (30%)	1 (14%)	23 (24%)
Died	7 (16%)	2 (4%)	2 (29%)	11 (11%)
Child HIV-negative and discontinued from clinic	0 (0%)*	6 (13%)	0 (0%)	6 (6%)
Travelled or displaced	6 (14%)	2 (4%)	0 (0%)	8 (8%)
Believed child healed by faith or use of traditional/herbal medicine	3 (7%)	4 (9%)	0 (0%)	7 (7%)
Transport costs	6 (14%)	1 (2%)	0 (0%)	6 (6%)
Transferred to another clinic	5 (11%)	2 (4%)	1 (14%)	8 (8%)
Refused care for other reasons including family conflicts	1 (2%)	4 (8%)	1 (14%)	6 (6%)
Family or work commitments	1 (2%)	2 (4%)	0 (0%)	3 (3%)
Did not miss appointment	0 (0%)	2 (4%)	0 (0%)	2 (2%)
Not found	8 (18%)	7 (15%)	2 (29%)	17(18%)

* Although 2 cases of HIV-positive children were reported being LTFU because they were HIV-negative, both were confirmed through chart reviews to be HIV-positive. These cases were subsequently classified as disclosure/discrimination as the primary reason.