Evaluation of a 5-year Programme to Prevent Mother-to-child Transmission of HIV Infection in Northern Uganda

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Summary

Prevention of mother-to-child transmission (PMTCT) is essential in HIV/AIDS control. We analysed 2000-05 data from mother-infant pairs in our PMTCT programme in rural Uganda, examining programme utilization and outcomes, HIV transmission rates and predictors of death or loss to follow-up (LFU). Out of 19 017 women, 1 037 (5.5%) attending antenatal care services tested HIV positive. Of these, 517 (50%) enrolled in the PMTCT programme and gave birth to 567 infants. Before tracing, 303 (53%) mother–infant pairs were LFU. Reasons for dropout were infant death and lack of understanding of importance of follow-up. Risk of death or LFU was higher among infants with no or incomplete intrapartum prophylaxis (OR = 1.90, 95% CI 1.07–3.36) and of weaning age <6 months (OR 2.55, 95% CI 1.42–4.58), and lower in infants with diagnosed acute illness (OR 0.30, 95% CI 0.16–0.55). Mother-to-child HIV cumulative transmission rate was 8.3%, and 15.5% when HIV-related deaths were considered. Improved tracking of HIV-exposed infants is needed in PMTCT programmes where access to early infant diagnosis is still limited.

Introduction

By the end of 2007, 480 000 women and 130 000 children were living with HIV/AIDS in Uganda [1]. In the absence of appropriate interventions to prevent mother-to-child transmission (MTCT) of HIV, at least 25% of HIV-exposed children acquire vertical HIV infection [2].

Guidelines to implement programmes for prevention of mother-to-child transmission (PMTCT) of HIV are available, but few evaluations of their effectiveness have been conducted in resource-limited settings [3–5]. Beyond the difficulties related to ensuring follow-up and HIV testing of infants in such settings, little is known about the proportion of mother–infant pairs that are lost to follow-up (LFU) after enrolment and the reasons for dropouts [6]. Furthermore, the effectiveness of reducing perinatal HIV transmission under routine field conditions has been overestimated, as the substantial numbers of early dropouts are rarely considered in the evaluations.

The international medical aid organization Médecins Sans Frontières (MSF), in collaboration with the Ministry of Health, provides HIV/AIDS care in Arua, a rural region in northwestern Uganda. Arua district has a total population of about 2 million and is near the borders of the Democratic Republic of Congo and Sudan. MSF also treats HIV-TB coinfection and supports 10 decentralized health centres in surrounding areas. The main objectives of

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this study were to quantify the utilization of PMTCT services in Arua over a 5-year period, describe the outcomes of mother–infant pairs enrolled in the programme, determine reasons for programme drop-outs and identify the predictors of programme losses after tracing of mother–infant pairs LFU.

Materials and Methodology

Arua PMTCT programme

In 2000, a PMTCT pilot project was initiated by the Uganda Ministry of Health with the support of MSF in the Arua Regional Referral Hospital (ARRH) in northwestern Uganda. Voluntary counselling and testing (VCT) was offered to all women attending their first antenatal care (ANC) visit. HIV-infected women were invited to enrol in the PMTCT programme and were referred to the HIV/AIDS clinic for WHO staging and CD4 testing.

The anti-retroviral (ARV) prophylaxis protocol included the administration of either short-course zidovudine (sc-AZT) from the 36th week of pregnancy to the mothers and in the first week of life to their newborns, or single-dose nevirapine (sd-NVP) at the onset of labour or at least 2 h before delivery to the mothers and within 72 h after birth to their newborns. For women in need of ARV therapy (ART), an NVP-containing regimen was administered following international recommendations [7]. At antenatal care, mothers were encouraged to deliver at the hospital, but also received NVP prophylaxis for them and their babies in the event of home delivery.

After delivery, clinical examination and feeding counselling were provided at weeks 1, 6, 10 and 14, then every 3 months up to 18 months post-partum. Infant formula was provided free of charge up to June 2004, but exclusive breastfeeding was advised thereafter because most of the mothers who received infant formula had been practicing mixed feeding even though it had always been counselled against. The HIV serostatus of the infants was determined at 18 months of age using two serological rapid tests.

Study design and procedures

We retrospectively analysed the information of all mother–infant pairs enrolled in the PMTCT programme in Arua between July 2000 and July 2005. LFU pairs were those with unknown infant HIV status at 18 months of age and who had missed their last scheduled appointment for $\geq$2 months before the start of the study. After active tracing of the mother–infant pairs who had been LFU, we conducted a cross-sectional survey to determine the clinical–immunological and HIV status of the children alive, and investigated the reasons for care discontinuation. The tracing took place in all neighbouring health facilities and at the patients' home. To preserve patient confidentiality, the study team members introduced themselves as hospital nurses who were providing routine health care to mothers and their babies. The mothers were invited to attend the nearest health facility where the study objectives and procedures were explained. They were free to accept or decline the invitation. For those who agreed to participate, a written informed consent was obtained and study procedures were initiated.

For children not yet tested, VCT and HIV testing were proposed. HIV infection was diagnosed by two positive rapid serological HIV 1/2 tests for the children aged $\geq$18 months (Determine®, Abbott Diagnostic Division, Hoofddorp, the Netherlands; and Statpack®, Chembio Diagnostic Systems, Medford, NY, USA) or by DNA PCR tests if aged <18 months (Amplicor HIV-1 Monitor® Test, v1.5, Roche Diagnostic Systems, Indianapolis, IN, USA).

Data collection and analysis

Data on HIV diagnosis, ART history, PMTCT enrolment, delivery and follow-up outcomes were extracted from medical records. A standardized pre-tested questionnaire, which had been back-translated into the local languages Lugbara, Kiswahili, Kakwa and Alur, was administered during the cross-sectional survey to complete missing PMTCT follow-up information and collect reasons for LFU. Compliance to the PMTCT protocol was evaluated only among mother–infant pairs who received NVP prophylaxis [8, 9] or ART (information on adherence related to sc-AZT had not been recorded). Mothers' compliance to the PMTCT protocol was defined as follows: 'fully' (on ART at the time of delivery, or sd-NVP taken at the onset of contractions and at least 2 h before delivery); 'moderately' (sd-NVP taken before the onset of contractions and 2–7 h before delivery); 'non compliant' (no ART and no sd-NVP prophylaxis taken at the time of delivery or sd-NVP taken either within 2 h of delivery or $\geq$7 h before delivery). Infants' compliance was defined as follows: 'fully' (received NVP within 72 h of birth); 'moderately' (received NVP between 72 h and 7 days after birth); and 'non compliant' (did not receive ARV prophylaxis or received NVP >7 days after birth). Standard WHO definitions were used to define breastfeeding, replacement feeding or mixed feeding [10, 11]. For children who died before testing, probable HIV infection was assessed through verbal autopsy using the definition proposed by the Ghent International Working Group [12].

We used Kaplan–Meier methods to estimate the probabilities of completing follow-up in the PMTCT programme by 18 months post-partum, after excluding stillbirths. The follow-up time was right-censored at the date of the confirmatory HIV test for infants tested before or at 18 months of age, of death for those who died before HIV testing, of the last

follow-up visit for those LFU before 18 months of age and at 18 months for other infants. We used multiple logistic regression, allowing for clustering by mother–infant pairs to assess risk of LFU or death. All variables associated with the outcome in univariate analyses (Wald p-value <0.25) were included in the multivariable model. A backward-stepwise strategy was then applied to obtain the final model. Statistical analyses were performed using Stata 9.2 (Stata Corp., College Station, TX, USA).

The study was approved by the Ugandan National Council for Science and Technology, the Ugandan AIDS Research Committee and the Ethics Committee of Saint-Germain-en-Laye (France).

Results

Study population

Of the 30 536 women who attended their first ANC visit between July 2000 and July 2005, 19 017 (62%) underwent counselling and HIV testing (Fig. 1). Five per cent (1037/19 017) of these women were HIV positive, and 517 (50%) of the 1037 agreed to enrol in the PMTCT programme. A total of 567 infants were born from the women enrolled. Before tracing, 303/567 (53.4%) mother–infant pairs had been LFU, 89 (15.7%) were followed, 97 (17.1%) children had died and 78 (13.8%) had completed their follow-up and the child had been tested for HIV. After active tracing, outcome data from 327 women and 368 babies were available and analysed.

Mother characteristics

Of the 327 HIV-positive women analysed, 71.3% (233/327) enrolled during their third trimester of pregnancy, and their median age was 28 years (IQR 25–32). A total of 164 (50.2%) women were in clinical Stage 1 or 2, and the median CD4 cell count was 368 cells/mm^3 ($n=201$; IQR 200–535) (Table 1). Of the 100 (30.6%) women eligible for ART at enrolment but not yet on therapy, 19 started ART before delivery, 47 after delivery and 34 never received ART.

A total of 242 (74.0%) women delivered at the hospital and 68 (20.8%) at home or on the way to the hospital. At delivery, 227 (69.4%) women received intrapartum sd-NVP, 17 (5.2%) sc-AZT, 23 (7%) did not take any prophylaxis and 52 (15.9%) had been on ART for a median time of 6.7 months (IQR 2.0–15.4) prior to delivery (Table 1). Of those receiving ART or intrapartum sd-NVP ($n=302$), 205 (67.9%) were fully, 5 (1.6%) moderately and 92 (30.5%) not compliant with the PMTCT protocol.

At discharge from the PMTCT programme or at the last recorded visit, 91% of the women had disclosed their HIV status to their partner. Furthermore, 74% reported that their partners were aware of their attendance to the PMTCT programme and that this had not caused any family conflict.

Infant characteristics

Of the 368 infants, 8 (2.2%) were stillborn and 7 (1.9%) died within 24 h of birth. Of the 353 infants alive, 288 (81.6%) received sd-NVP, 12 (3.4%) sc-AZT and 50 (14.2%) did not receive post-partum ARV prophylaxis (Table 2). Among those receiving sd-NVP or no ARV prophylaxis ($n=338$), 282 (83.4%) were fully, 3 (0.9%) moderately and 53 (15.7%) non-compliant with the PMTCT protocol. Of the 353 babies alive, 47 (13.3%) were exclusively breastfed, 96 (27.2%) received replacement feeding and 210 (59.5%) were mixed fed. Median age at start of weaning was 6 months (IQR 4–6), irrespective of the type of feeding ($p=0.15$). At least one serious acute illness, namely acute respiratory tract infection (RTI), malaria or diarrhoea, was reported during the follow-up in 70% of infants.

Of the 72 children who died during follow-up (excluding stillborn), 33 (45.8%) died of HIV-related causes. The most frequently reported HIV-related events were diarrhoea (34.7%), RTI (20.8%), candidiasis (13.9%) and bacterial infection or septicaemia (11.1%).

Overall, 367 children had been tested for HIV. Cumulative HIV transmission rate was 8.3% (24/288, 95% CI 5.6–12.2) among infants tested, and 15.5% (57/367, 95% CI 12.2–19.6) when probable HIV-related deaths were included. Transmission rates did not differ by type of feeding (19.2, 10.5 and 18.1% for exclusive breastfeeding, replacement feeding and mixed feeding, respectively; Pearson χ^2 test, $p=0.20$).

Lost to follow-up mother–infant pair outcomes

Overall, 303/567 (53.4%) mother–infant pairs had been LFU after a median time of 1 month (IQR 0–5). Of the 197 pairs successfully traced, 45 (22.8%) had been LFU after PMTCT enrolment, 2 (1%) between enrolment and delivery, 42 (21.3%) after delivery and 108 (54.8%) during follow-up. Main reasons for dropping out were the mothers' lack of understanding of the importance of follow-up (29.9%) and infant death (27.4%) (Table 3). Probability of completing PMTCT follow-up by 18 months post-partum was 0.50 (95% CI 0.44–0.55) (Fig. 2).

Risk of LFU or death was decreased in children with recorded episodes of acute infection during their follow-up (OR 0.30; 95% CI 0.16–0.55). In contrast, risk was higher in infants who started weaning before the age of 6 months than in those who started later (OR 2.55; 95% CI 1.42–4.58), and in infants who breastfed for >6 months than in those who breastfed for <6 months (OR 4.40; 95% CI 2.00–9.65) (Table 4).

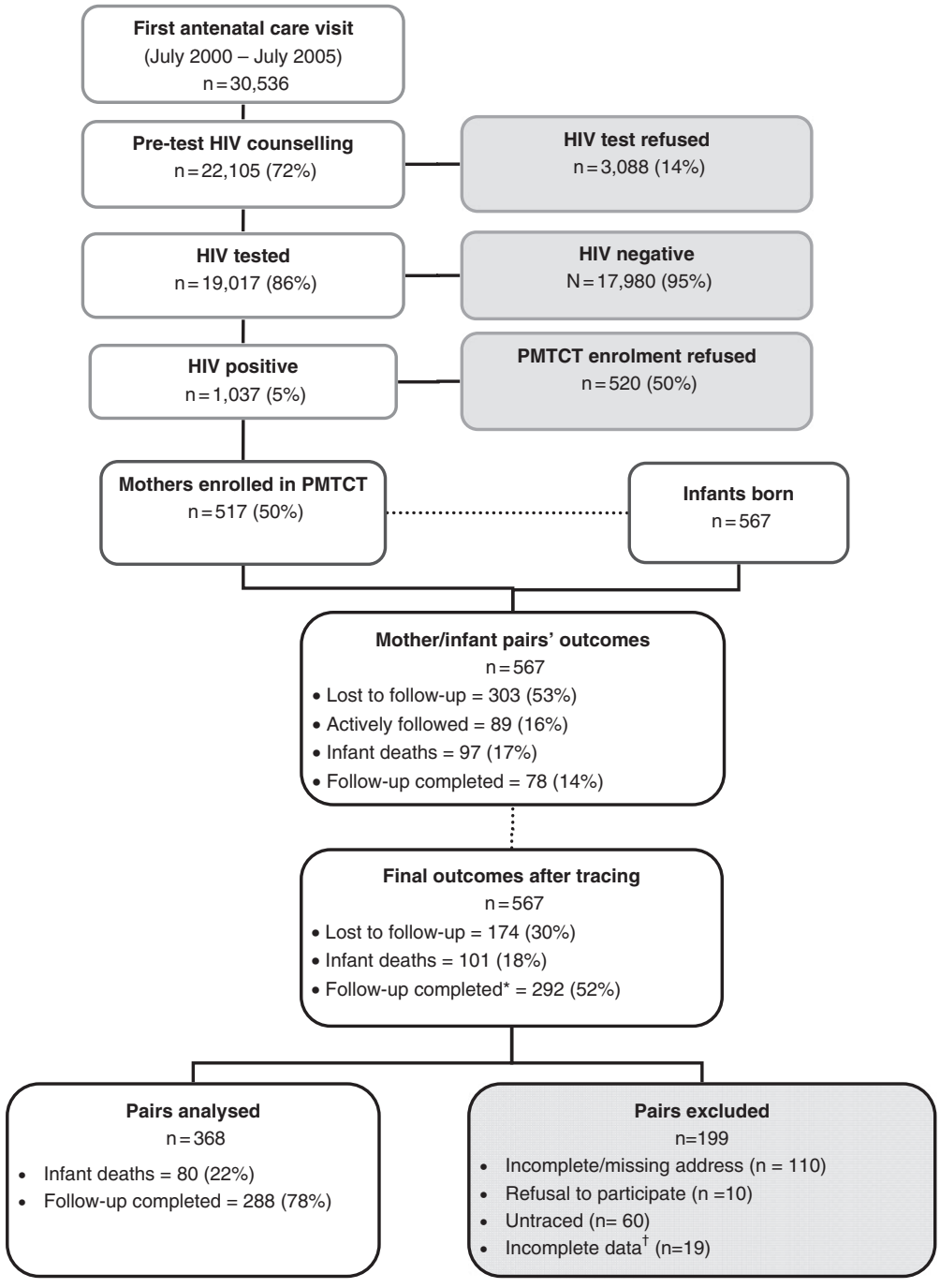


FIG. 1. Diagram of mother–infant pairs included in the study, Arua, March 2006.

TABLE 1
Characteristics of mothers at PMTCT enrolment and delivery, Arua, March 2006

	Total ($n=327$)
Mother characteristics at enrolment	
Age (years), median (IQR)	28 (25–32)
Number of gestations, median (IQR)	4 (2–6)
Trimester of pregnancy, *n* (%)	
First	4 (1.2)
Second	72 (22.0)
Third	233 (71.3)
At/after birth	18 (5.5)
ARV history, *n* (%)	
ARV naive	294 (89.9)
ARV non-naive	33 (10.1)
On ART	32
Other	1
WHO stage ($n=326$), *n* (%)	
Asymptomatic	5 (1.5)
Stage 1/2	164 (50.2)
Stage 3	144 (44.0)
Stage 4	13 (4.0)
CD4 cells/mm^3 ($n=201$), median (IQR)	368 (200–535)
Count *n* (%)	
<200	50 (24.9)
200–349	43 (21.4)
350–499	52 (25.9)
≥500	56 (27.8)
Perception of counselling received, *n* (%)	
Clear and supportive	314 (96.0)
Not clear and/or supportive	13 (4.0)
Mother characteristics at delivery	
Place of delivery, *n* (%)	
Arua Regional Referral Hospital	242 (74.0)
Home/on the way to hospital	68 (20.8)
Health centre/other hospital	16 (4.9)
Other	1 (0.3)
Type of delivery, *n* (%)	
Normal/assisted vaginal	292 (89.3)
Caesarean section	30 (9.2)
Other	3 (0.9)
Unknown	2 (0.6)
Delivery complications, *n* (%)	40 (12.2)
Premature labour, *n* (%)	12 (3.7)
Type of intrapartum ARV received, *n* (%)	
Not taken	23 (7.0)
Single dose NVP	227 (69.4)
Short-course AZT	17 (5.2)
ART	52 (15.9)
Other	1 (0.3)
Unknown	7 (2.1)

ARV, anti-retroviral; AZT, zidovudine; IQR, interquartile range; NVP, nevirapine.

TABLE 2
Characteristics of infants at birth and last PMTCT follow-up, Arua, March 2006

Infant characteristics	Total ($n=368$)
Females, *n* (%)	182 (49.5)
Weight at birth (kg) ($n=334$), median (IQR)	3 (2.7–3.4)
Vital status at birth, *n* (%)	
Alive	360 (97.8)
Stillborn	8 (2.2)
Prematurity at birth, *n* (%)	15 (4.1)
Death within 24 h after birth, *n* (%)	7 (1.9)
Vital status at hospital discharge, *n* (%)	
Alive and well	351 (95.4)
Alive with problems	2 (0.5)
Dead	15 (4.1)
Timing of mother ARV use, *n* (%)	
ART initiated ≥3 months before birth	44 (12.0)
ART initiated <3 months before birth	21 (5.7)
ARV intrapartum prophylaxis	272 (73.9)
No intrapartum medication taken	24 (6.5)
Unknown	7 (1.9)
Type of infant ARV prophylaxis after birth[a] ($n=353$) *n* (%)	
NVP	288 (81.6)
AZT	12 (3.4)
Not given	50 (14.2)
Unknown	3 (0.8)
Number of PMTCT visits, median (IQR)	7 (3–12)
Pre-natal visits	3 (1–4)
Post-natal visits	4 (0–8.5)
Number of immunization visits, *n* (%)	
No visits	16 (4.3)
1–3 visits	30 (8.1)
4–6 visits	285 (77.5)
≥7 visits	30 (8.2)
Unknown	7 (1.9)
Occurrence of ≥1 acute illness during follow-up[a], *n* (%)	257 (69.8)
Type of care giver at last visit, *n* (%)	
Mother	361 (98.1)
Father/other family member	7 (1.9)
Type of feeding received during follow-up ($n=353$), *n* (%)	
Exclusive breastfeeding	47 (13.3)
Replacement feeding	96 (27.2)
Mixed feeding	210 (59.5)
Duration of breastfeeding[a,b] (months) ($n=353$), median (IQR)	3 (0–6)
Age at start of weaning[a] (months) ($n=353$), median (IQR)	6 (4–6)
Infant follow-up outcome, *n* (%)	
Death[c]	80 (21.7)
HIV tested before survey	75 (20.4)
HIV tested during survey	213 (57.9)

[a]Among babies born alive only.
[b]Regardless of the type of feeding (i.e. exclusive or mixed feeding).
[c]Including 8 stillborns, 7 deaths <24 h after birth and 65 deaths during post-partum follow-up.
ARV, anti-retroviral; AZT, zidovudine; IQR, interquartile range; NVP, nevirapine.

TABLE 3
Timing and reasons for PMTCT dropout of mother–infant pairs lost to follow-up, Arua, March 2006

Mother–infant pairs	Included, $n = 197$	Excluded, $n = 175$	p-value
Geographical residence, *n* (%)			
Arua Municipality Council	89 (45.2)	86 (49.1)	<0.0001
Ayivu county	72 (36.6)	40 (22.9)	
Other Arua counties	24 (12.2)	13 (7.4)	
Other	12 (6.0)	36 (20.6)	
Year of PMTCT enrolment, *n* (%)			
≤2002	27 (13.7)	51 (29.1)	0.001
2003	41 (20.8)	43 (24.6)	
2004	67 (34.0)	42 (24.0)	
2005	62 (31.5)	39 (22.3)	
Duration of follow-up, median (IQR)	2.9 (0.1–7.7)	0.5 (0–3.4)	<0.0001
Time of LFU, *n* (%)			
At enrolment in PMTCT programme	45 (22.8)	60 (34.3)	0.08
Between enrolment and birth	2 (1.0)	1 (0.6)	
At the time of birth	42 (21.3)	38 (21.7)	
During follow-up	108 (54.8)	76 (43.4)	
Reasons for LFU, *n* (%)			
Maternal illness/death	6 (3.1)	N/A	N/A
Infant death	54 (27.4)		
Lack of partner involvement	26 (13.2)		
Moved away	24 (12.2)		
Lack of understanding of follow-up benefit	59 (29.9)		
Fear of stigma	12 (6.1)		
Other	16 (8.1)		

LFU, lost to follow-up; IQR, interquartile range.

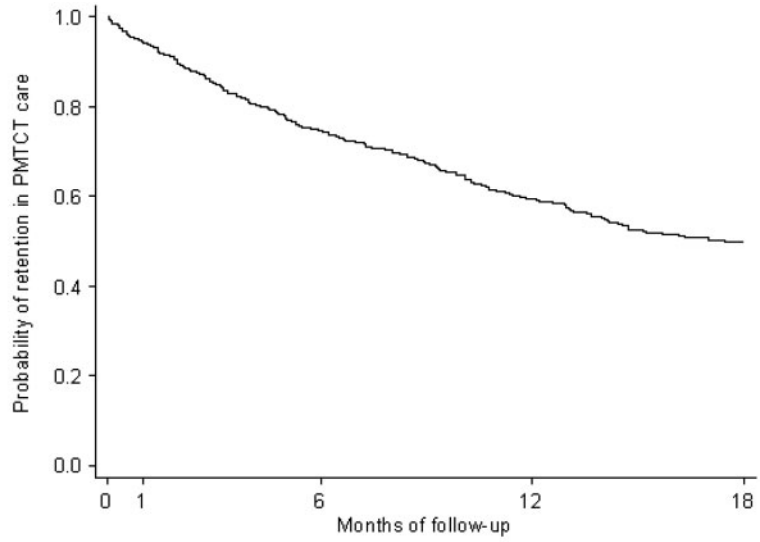
Discussion

In this evaluation of a PMTCT programme in rural Uganda, only half of the women tested HIV-positive agreed to attend PMTCT services and more than 5 in 10 mother–infant pairs were lost to follow-up. The low PMTCT uptake observed in our study is similar to that previously reported in Ethiopia (57%) and Zimbabwe (59%), but higher than in Kenya (17%) [13]. It is, therefore, essential to intensify efforts to improve programme uptake to ensure optimal access to ARV prophylaxis for women who are in need.

Women's characteristics at enrolment were similar to those described in other resource-limited settings [14, 15]. Thus, 7 in 10 women were enrolled during their third trimester of pregnancy and 5 in 10 at early stage of HIV disease. The proportion of hospital deliveries was high, probably because the maternity ward was rehabilitated in 1999 and improved access to health care for deliveries. Still, 20% of women delivered at home. Half of the women who entered the programme were eligible for ART. Yet, only 16% were on ART at time of delivery, and 7% did not receive any prophylaxis or treatment.

These results highlight the importance of identifying women eligible for ART early in their pregnancy in order to initiate treatment, as high maternal viraemia is the most important risk factor for perinatal HIV transmission [16]. They also show the existence of missed opportunities for the timely provision of health care to HIV-infected patients and stress the need to strengthen the links between the PMTCT and HIV care services. Despite the simplicity of the protocols used, 30% of women and 16% of newborns did not comply with the protocol. The effectiveness of the PMTCT prophylaxis to prevent perinatal HIV transmission requires that both mother and infant correctly take the drugs. Maternal dosing alone would fail to achieve prolonged infant prophylactic drug concentrations, especially if the time between ingestion and delivery is short [17]; and infant dosing alone has modest, if any, prophylactic efficacy [18].

In our cohort, women were given the choice between using exclusive free infant formula or exclusive breastfeeding, but our assessment showed that ~60% of children were mixed fed, reflecting the difficulties that HIV-positive mothers find to adhere to their initial feeding choice in rural Uganda as well as the confusing nature of the counselling messages related to infant feeding given at that time. The most appropriate infant-feeding practice for PMTCT in resource-limited settings is still highly debated [19]. Exclusive breastfeeding offers the best possible nutritional option during the first months of life, protecting children against diarrhoea and lower RTI, which are the leading causes of infant mortality [20, 21]. Nevertheless, the cumulative probability of late



Time (months)	**1**	**6**	**12**	**18**
Children at risk	307	244	181	107
Deaths or lost to follow-up	19	63	49	27
Probability to complete 18 months follow-up (95% CI)	0.94 (0.90-0.96)	0.75 (0.70-0.79)	0.59 (0.54-0.64)	0.50 (0.44-0.55)

FIG. 2. Probabilities of mother–infant pairs completing follow-up by 18 months postpartum, Arua, March 2006 ($n = 360$).

postnatal HIV transmission at 18 months is 9% in breastfed children [22]. In certain settings, opting for formula feeding has been shown to be feasible when individual and environmental criteria are used [23]. Infant formula in combination with a single oral dose cabergoline, a long-lasting dopaminergic drug with prolactin inhibitory properties, can be effectively used to avoid mixed feeding [24, 25]. However, in most rural African settings, replacement feeding might not be feasible due to social and cultural pressure and to poor hygiene [26, 27], and mixed feeding is in practice the most prevalent mode of feeding among those opting for infant formula. Given that mixed feeding increases the likelihood of HIV transmission, a large proportion of the infants in our cohort were exposed to HIV infection during the postnatal period despite good compliance with PMTCT protocols. Effective interventions to reduce postnatal HIV transmission during breastfeeding, such as providing ART to the mother during the first 6 months after delivery, are some of the strategies that have been evaluated [28].

Twenty-two per cent of the children died before HIV testing, and diarrhoea accounted for more than a third of the deaths. Similar figures were reported in a study in Côte d'Ivoire, where 18% of the infant deaths were attributed to diarrhoea [29]. In this study, the cumulative HIV transmission rate was 8% among children tested up to 18-months of age and increased to 16% when probable HIV-related deaths were considered. In the absence of tracing, we would have estimated an HIV transmission rate of 4%, knowing that 53% of mother–infant pairs had been LFU. This illustrates how high LFU rates can bias programme estimates of HIV transmission and corroborates previous reports showing how HIV transmission can be seriously underestimated when routine data are used [6, 30].

Most women defined the counselling provided at enrolment as clear and supportive. However, half of the mother–infant pairs were LFU before determination of the child's HIV status. Previous studies have also reported high LFU rates in routine PMTCT services. In rural Malawi, the LFU rate was 81% by 6 months of postnatal follow-up [6]. In South Africa, despite reported high rates of NVP administration and good acceptance of infant formula, >70% of infants were LFU by 4 months of age [5]. Also, in our study, nearly 37% of mothers traced could not be found. This finding highlights the difficulties with tracing in retrospect instead of using active defaulter tracing, since many women might have moved to

TABLE 4
Associations between lost to follow-up or death and maternal and infant factors, Arua, March 2006

			OR					
	n (%)	*N*	Crude	95% CI	*p*-value	Adjusted[a]	95% CI	*p*-value
Maternal factors								
Trimester of pregnancy at enrolment								
Third or after delivery	150 (54.3)	276	1		0.95	1		0.09
First or second	46 (54.7)	84	1.02	0.62–1.66		1.81	0.91–3.60	
Enrolment in Arua hospital								
Yes	159 (51.3)	310	1		0.005	1		0.20
No	37 (74.0)	50	2.70	1.35–5.41		1.90	0.72–5.06	
Number of previous gestations								
<4	91 (60.7)	150	1		0.08	1		0.20
≥4	104 (51.0)	204	0.67	0.43–1.05		0.67	0.36–1.23	
Clinical stage at enrolment								
1 or 2	108 (60.0)	180	1	0.43–0.98	0.04	1	0.39–1.15	0.15
3 or 4	88 (49.2)	179	0.64			0.67		
Partner disclosure of PMTCT attendance								
No	57 (57.6)	99	1		0.47	1		0.91
Yes	139 (53.3)	261	0.84	0.52–1.35		0.96	0.51–1.83	
Paternal factors								
Occupation of the father								
None/farmer	24 (61.5)	39	1		0.04	1		0.39
Businessman	46 (69.7)	66	1.44	0.61–3.40		1.67	0.56–4.99	
Employee	48 (49.0)	98	0.60	0.27–1.33		1.04	0.39–2.79	
Unemployed/other	77 (51.0)	151	0.65	0.31–1.38		0.80	0.33–1.97	
Infant factors								
RV intrapartum prophylaxis								
Complete (mother and child)	62 (82.7)	75	1		0.08	1		**0.03**
None or incomplete	134 (47.0)	285	1.56	0.95–2.55		**1.90**	**1.07–3.36**	
Type of feeding								
Exclusive breastfeeding	26 (55.3)	47	1		0.02	1		0.83
Replacement feeding	40 (41.7)	96	0.58	0.28–1.18		0.89	0.30–2.60	
Mixed feeding	123 (58.6)	210	1.14	0.61–2.15		0.76	0.28–2.07	
Duration of breastfeeding								
0–5.9 months	129 (46.2)	279	1		<0.0001	1		**0.0002**
≥6 months	60 (81.1)	74	4.98	2.65–9.37		**4.40**	**2.00–9.65**	
Age at start of weaning								
≥6 months	91 (42.5)	214	1		<0.0001	1		**0.002**
<6 months	98 (70.5)	139	3.23	2.06–5.07		**2.55**	**1.42–4.58**	
Recorded acute illness[b]								
No	168 (62.7)	268	1		<0.0001	1		**0.0001**
Yes	28 (30.4)	92	0.25	0.16–0.41		**0.30**	**0.16–0.55**	

[a]Ratios from multiple logistic regression allowing for clustering by mother–infant pairs and adjusted for all other variables except partner disclosure.
[b]Includes episodes of malaria, lower respiratory tract infections and diarrhoea.
CI, confidence interval; OR, odds ratio.

other locations, such as the Sudan or Democratic Republic of Congo.

In our cohort, the main reasons for dropping out were the lack of understanding of the importance of follow-up and infant death. Absence of partner involvement and stigma were the reasons that were less frequently reported. Reasons for dropout are likely to differ by the type of PMTCT service provided and by the sociocultural context. In Botswana, the main reasons reported were poor acceptability of infant formula and the fear of HIV disclosure [31]. Others have reported negative experience with the health staff or negative perception of the PMTCT programme [32]. In our setting, earlier age of weaning, prolonged breastfeeding and incomplete/absent ARV prophylaxis were associated with an increased risk of LFU or death, while the occurrence of infant acute illness decreased this risk. This suggests that in the absence of infant illness, mothers do not perceive the need to seek medical care and stresses the necessity of improving the quality of the information provided to the mothers

about the early weaning and the importance of the follow-up.

Due to logistic and financial constraints, we focused our tracing on mother–infant pairs living in the Arua district, and we cannot generalize the findings to those residing outside this area. Pairs not traced were more frequently LFU shortly after PMTCT enrolment and in the early years of the programme. Although ensuring patient confidentiality was challenging, women were free to participate or not in the study. Most of them accepted (10 patients declined participation). They also expressed their appreciation to have the opportunity to discuss freely their experience with the study team. Because the exact age of infection was unknown for most infants, we could not estimate the infants' HIV-free survival. Nevertheless, our estimates can be reported as a proportion of the total number of infants tested [33]. Finally, we corrected HIV transmission rates by including probable HIV-related deaths in the calculation. The cause of death was ascertained through verbal autopsy [12] and, therefore, it is possible that some have been misclassified as being related or not to HIV infection, resulting in underestimation or overestimation of the transmission rates.

Our results reflect the day-to-day difficulties faced by PMTCT programmes in rural, resource-limited settings, which are far more challenging than those observed in the context of clinical trials or 'model programme' settings. The effectiveness of PMTCT programmes depends on a cascade of interventions, the adequate provision of an effective ARV prophylaxis being only one of them. Increasing ART coverage for women in need, better tracking and follow-up of HIV-exposed infants and an enhanced quality of infant feeding counselling are all essential to improve PMTCT effectiveness in rural Africa. Current recommended strategies include short-course AZT + 3TC + NVP in pregnant women with HIV (from 28 weeks of pregnancy or as soon as possible thereafter), ART for life in all mothers with CD4 count <350 cells/mm^3 at time of programme entry, and immediate ART start in HIV-positive newborns [34–36]. Such strategies will help achieve the goals for paediatric AIDS control to reduce vertical transmission by 50% and provide PMTCT services to 80% of those in need by 2010 [37].

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