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Effectiveness of a project to prevent HIV vertical transmission in the Republic of Congo

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Objectives: To evaluate the effectiveness of a prevention programme against the vertical transmission of HIV in a resource-limited setting and to investigate variables associated with compliance.

Patients and methods: The Kento-Mwana project (2005–2008) provided counselling, serological and biomolecular testing and prophylaxis/therapy to HIV-positive pregnant women and their children attending four antenatal clinics in Pointe Noire, Republic of Congo. Expected and actual rates of vertical transmission of HIV were compared. Univariate and multivariate analyses were performed in order to identify variables associated with non-compliance.

Results: The observed transmission rate in the group who completed follow-up was 5/290 (1.7%, 95% CI 0.6%–4.1%). The overall estimated transmission rate in the target population, computed taking into account the expected vertical transmission of HIV among drop-outs, was 67–115/638 (10.5%–18.0%). A comparison between this rate and the expected transmission rate in the absence of intervention (25%–40%) showed that the programme was able to prevent approximately 50% of vertical transmissions. Older age (OR 0.33, 95% CI 0.16–0.66, $P = 0.002$), telephone availability (OR 0.42, 95% CI 0.24–0.72, $P = 0.002$) and occupation (OR 0.57, 95% CI 0.29–1.10, $P = 0.092$) were associated with better compliance.

Conclusions: Despite the vast majority of women accepting counselling and testing, many of them refused prophylaxis or dropped out, thus reducing the effectiveness of the intervention from an ideal 2% to a still important but less impressive median transmission rate of 15% (range 10.5%–18%). Promoting participation and compliance, rather than increasing the potency of antiretroviral regimens, is crucial for preventing the vertical transmission of HIV in Africa.

Keywords: PMTCT, mother-to-child transmission, drop-out, attrition, lost to follow-up

Introduction

Several strategies have been developed in resource-limited settings in order to prevent HIV mother-to-child transmission (PMTCT). Different approaches can be applied, among which are availability of antiretroviral (ARV) drugs, interventions related to the social and environmental context and stability of financial support. In recent years, the widespread use of a triple antiretroviral regimen has allowed more effective PMTCT interventions.[1,2] Several studies have shown a transmission rate of ~2% in women who adhered to a complete clinical protocol, including maternal ARV regimens, vaginal delivery and an appropriate feeding choice.[3,4] However, in these studies, women who did not accept the PMTCT protocol or were lost to follow-up were often excluded from the analyses;[1,3–5] as a result, it is often difficult to appreciate the overall effectiveness of these prevention programmes when deployed in the real world.

In this article, we present the results of a programme to prevent the vertical transmission of HIV based on a triple antiretroviral regimen in a resource-limited setting in the Republic of Congo, Africa, in terms of feasibility and effectiveness. The primary objective was to evaluate the impact of the clinical intervention on the overall target population, defined as all pregnant women who attended the healthcare units involved in the Kento-Mwana PMTCT project during the study period. Secondary objectives were to evaluate the clinical, demographic, social

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and behavioural factors associated with the risk of being lost to follow-up.

Patients and methods

Study design, participants and setting

We enrolled in a prospective uncontrolled interventional study (the Kento-Mwana project) all pregnant women who were attending four antenatal care units located at the Army Hospital in Pointe Noire, Republic of Congo, and in the districts of Ndaka Susu, Mbota and Ngoyo on the outskirts of the city, between September 2005 and December 2008. Follow-up of the mother and child pairs was terminated on 31 December 2010. The entire programme was carried out at the peripheral local care units. Voluntary counselling and testing for HIV infection was suggested to each pregnant woman at the first visit. If this was refused or omitted, the counselling was repeatedly offered by the midwife during the following visits. Those who accepted the offer received serological screening for HIV, as previously described.[6] If an HIV-positive status was identified, a global intervention for the prevention of vertical transmission of HIV was offered. The delivery and follow-up of the children were also carried out in local reference hospitals (the Army Hospital and Tie Tie Hospital).

Ethical approval and data collection

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Congolese Ministry of Health and the Congolese Council against AIDS, who regularly supervised the project's activities. All participants provided written informed consent or an equivalent. With women who were illiterate, the text of the consent was read by the physician or by the counsellor and translated into local idioms if needed. Confidentiality was maintained throughout all phases of the study. A code was assigned to each woman at the counselling step. The code included two letters referring to the local health structure (e.g. NS for Ndaka Susu care unit), a progressive number (e.g. 0001) and a letter (F for women and E for newborns). This code was universal and was used throughout the intervention, including for the laboratory tests. The name of the patient (woman or infant) was written only in the clinical record and was known only by the counsellor and the physician. Clinical records were securely stored behind a locked door, in the counsellor's office. Clinical data were collected by the Italian physicians using an Excel database. Only the code was reported.

Intervention protocol

The prophylactic intervention included a maternal ARV regimen, perinatal prophylaxis for the mother and child and postnatal support according to feeding choice. Women received triple zidovudine/lamivudine/nevirapine therapy. If anaemia (haemoglobin <8 g/dL) was present, zidovudine was replaced by stavudine. If toxicity with nevirapine or drug interactions occurred, a double-ARV regimen with two nucleoside reverse transcriptase inhibitors (NRTIs) was offered. If the maternal T lymphocyte CD4+ (CD4) cell count at the first visit was <350 cells/mm^3, the ARV regimen was started immediately and continued after delivery and weaning. If the CD4 cell count at the first visit was >350 cells/mm^3, the ARV regimen was started at the 28th week of gestation and stopped after delivery or after complete weaning in the case of formula or breast feeding, respectively; nevirapine was discontinued first, followed by the two NRTIs 2 weeks later.

Vaginal delivery was routinely performed, unless obstetric conditions required caesarean section. Vaginal washing with chlorhexidine (once, before fetal expulsion) was used, and all invasive procedures such as vacuum extraction, forceps or induced amniorrhexis were avoided whenever possible. All the mothers at the onset of the labour and their newborn infants at birth received a single dose of oral nevirapine. In addition, all the mothers received one tablet of zidovudine 300 mg every 3 h from the onset of labour until umbilical cord clamping while continuing the ARV regimen started during pregnancy. All the infants also received zidovudine (4 mg/kg) twice daily from birth to the age of 4 weeks.

All the women were counselled on infant feeding options (exclusive formula feeding or exclusive breast feeding). If chosen, formula milk and clean water were provided. With exclusive breast feeding, the maternal ARV regimen was continued regardless of the maternal CD4 cell count, and weaning was performed at 6 months.

At the first visit, demographic, social and behavioural characteristics, including age, nationality, housing conditions, telephone connection, occupation, marital status, number of children, number of people living in the house, disclosure of HIV-positive status to somebody else, use of condoms, number of sexual partners, previous HIV tests and known HIV-positive status, were collected in individual clinical records. All women were seen every 2 weeks for the delivery of ARV drugs and physical examination for possible signs of disease or toxicity. Adherence to the drug regimen was monitored by maternal self-report and pill count and was defined as follows: A, ARVs were never stopped; B, ARVs were stopped for fewer than 15 days; C, ARVs were stopped for more than 15 days. Women were defined as being lost to follow-up during pregnancy or after delivery if they did not return before the expected delivery date or before the end of follow-up, respectively.

Laboratory methods

Haematological and biochemical assays were performed at the central laboratory of the Army Hospital. Blood specimens were conveyed daily from the peripheral healthcare units to the project's central laboratory at the Army Hospital in Pointe Noire.

A complete blood count, CD4+, CD8+ and CD3+ cell count (FACSCount, BD) and chemical analysis including alanine aminotransferase, aspartate aminotransferase and blood glucose level were obtained at baseline, 6 weeks after starting the ARV regimen, at the baby's birth and 3 months after delivery. Alanine aminotransferase and aspartate aminotransferase were also checked 2 weeks after starting nevirapine (before increasing the dose of nevirapine) and if clinical signs of hepatic or skin toxicity appeared.

Infants born to HIV-infected women were followed at birth and at 1, 3, 4, 6, 8, 12, 14, 24, 26, 48 and 72 weeks after birth to be clinically examined for possible signs of disease or toxicity. A complete blood cell count was performed at birth and at 4, 8, 12, and 24 weeks.

Infants were tested for HIV-1 infection at birth and at 4, 12 and 24 weeks (as well as at 8 weeks after complete weaning if applicable) using DNA proviral PCR, as previously described.[7] Positive specimens were confirmed by testing a new blood specimen at the next visit. The child was defined as being HIV infected if two positive specimens were obtained. A further confirmation of HIV status was performed at 12 and 18 months by serological methods (Genscreen Plus HIV Ag/Ab EIA by BIO-RAD, Marne la Coquette, France; Vironostika HIV Ag/Ab Uni-Form EIA, bioMérieux Laboratories, Boxtel, NL, USA).

Formula-fed infants were defined as not being infected with HIV if they tested negative on two PCR tests, both performed after 4 weeks of life. With breast feeding, an additional PCR 8 weeks after completion of weaning was required to assess the HIV-negative status.

Statistical analysis

The effectiveness of the intervention in terms of a reduction in the incidence of vertical transmission of HIV was evaluated by comparing the overall transmission rate expected in the target population without the intervention with the actual vertical transmission rate of HIV observed with the intervention. The target population was defined as all pregnant

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women who attended the four antenatal clinics during the study period. The total number of HIV-positive pregnant women was estimated by assuming that the seroprevalence of HIV among the women who refused counselling and testing was identical to that observed in the women who were tested. Based on previous reports, with reference to the cultural and social attitudes concerning feeding choice in the intervention area, the transmission rate in HIV-positive women in the absence of any intervention was estimated to be 25%–40%, according to the rates of transmission in the placebo arms of the major published studies.[1,8,9] The same rate of vertical transmission was assumed to exist in the HIV-positive women who refused counselling and testing or prophylaxis, and in the women lost to follow-up during pregnancy before starting ARV. In the women lost to follow-up after the start of the ARV protocol, during pregnancy or after delivery, the transmission rates of HIV were assumed to be 15%–35% and 6%–20%, respectively.[8,10]

In order to minimize bias, two authors (F. B. and A. C.) worked independently in performing the literature search in order to estimate the transmission rates in the different subgroups. Once each author had made his estimations, we consulted as a team (F. B., A. C. and P. B.) to achieve a consensus regarding the assumptions. In particular, in relation to the transmission rate among the women lost to follow-up, the estimates took into account the wide range of behaviours observed in these women, ranging from a few weeks of prophylaxis during early pregnancy to an almost complete compliance with the protocol except for assessment of the infant's HIV status.[8,10] The range of estimated and assumed transmission rates was used in sensitivity analyses to evaluate the potential impact of the uncertainties related to the rates of transmission on the overall estimates of the programme's effectiveness. The total number of potentially HIV-positive children in the study population was estimated by adding up the number of cases actually observed among the women who completed the follow-up and the estimated number for the different groups of women who dropped out. The number of children in whom HIV-positivity was potentially averted by the intervention delivered to the total target population was calculated as the difference between this number and the expected number of cases in the absence of any intervention.

Among the HIV-positive women, factors evaluated for their association with compliance with follow-up were age, nationality, gestational age, housing conditions (building material, availability of running water and electricity), telephone connection, occupation (housewife, student or worker), marital status, number of children (dead and still alive), number of people living in the house, disclosure of HIV-positive status to somebody else, use of condoms, number of sexual partners, previous HIV tests, known HIV-positive status, HIV-related conditions and clinical conditions, according to the classification of the United States Centers for Disease Control and Prevention (CDC). Univariate statistical analysis was performed using the Mann–Whitney non-parametric test, χ^2 test and χ^2 for trend. Stepwise multivariate logistic regression analysis was performed, with loss to follow-up as the dependent variable, and all variables with a univariate $P < 0.1$ as covariates. The final model was arrived at by means of a step-down procedure, based on the likelihood ratio test.

Results

Participants

Patient flow and results are summarized in Figure 1. A total of 13 309 pregnant women attended the four antenatal clinics for a scheduled visit during the study period. Of these, 98.9% (13 164/13 309) agreed to be counselled, and 97.5% (12 830/13 164) of these women agreed to be screened for HIV. Of these, 4.8% (615/12 830, 95% CI 4.4%–5.2%) were seropositive for HIV-1. Of the seropositive women, 75.5% (464) agreed to be included in the prophylactic intervention programme. In this group, the median gestational age at the first visit was 23 weeks (IQR 19–28 weeks), the median CD4 cell count was 290 cells/mm^3 (IQR 167–452 cells/mm^3) and the median haemoglobin level was 9.5 g/dL (IQR 8.5–10.5 g/dL). An HIV-related disease was detected in 29.1% of the women (135/464), and 12.9% (60/464) had an AIDS-defining condition; 18.1% (84/464) said they had had an HIV test in the past, and 10.8% (50/464) declared themselves as being aware that the result of that had been positive.

ARV regimens, adherence to protocol, adverse events and pregnancy outcome

From the first visit to the day of delivery, 8.8% (41/464) of the women enrolled did not start prophylaxis (and were therefore considered to have been lost to follow-up), and 1.7% (8/464) had a stillbirth before beginning the ARV regimen. Of the remaining 415 women who actually started the ARV drugs, 88.7% (368/415) were naive to any therapy. ARV drugs were given as prophylaxis (32.1%; 133/415) or as therapy (56.6%; 235/415). Of the 11.3% (47/415) women not naive to treatment, 6.8% (28/415) were already on an ARV therapy when they came to their first visit, whereas 4.6% (19/415) declared having started ARV drugs in the past but then discontinuing them. Of these women, 1.2% (5/415) had started ARV prophylaxis and 3.4% (14/415) ARV therapy.

Among the 415 women taking ARVs during pregnancy, 86.5% (359/415) received zidovudine/lamivudine/nevirapine and 10.8% (45/415) stavudine/lamivudine/nevirapine, whereas 2.7% (11/415) received a regimen of two NRTIs. The median duration of the ARV regimen during pregnancy was 77 days (IQR 50–112 days). A modification of the ARV regimen was deemed necessary in 16.1% (67/415) of the women: 43.3% (29/67) and 13.4% (9/67) for nevirapine- or zidovudine-related toxicity, respectively, and 43.3% (29/67) for other reasons. Adherence to ARV therapy or prophylaxis was classified as A (ARVs were never stopped), B (ARVs were stopped for fewer than 15 days), C (ARVs were stopped for more than 15 days) or not assessable in 58.6% (243/415), 13.0% (54/415), 26.7% (111/415) and 1.7% (7/415) of women, respectively. No death was associated with a drug-related adverse event. Pregnancy was complicated by confirmed malaria in 26.3% of the women (109/415). As shown in Figure 1, of the 415 women taking ARV drugs during pregnancy, 9.4% (39/415) were lost to follow-up before delivery, 4.8% (20/415) had a stillbirth, 0.5% (2/415) died and 85.3% (354/415) delivered a live-born infant.

Delivery and birth outcomes

Among women who received ARV during pregnancy, a total of 354 gave birth to 365 live-born infants (11 sets of twins). The prophylactic protocol at delivery was correctly performed in 76.0% (269/354) of the cases. Premature rupture of membranes was observed in 15.5% (55/354) of the women and obstetric complications in 8.2% (29/354). The mean CD4 cell count at delivery was 452 cells/mm^3 (IQR 273–587 cells/mm^3) and the mean haemoglobin value was 11.2 g/dL (IQR 10.1–12.4 g/dL). The clinical characteristics of the 354 newborns evaluated are described in Table 1. Exclusive formula feeding was chosen in 89.0% (315/354) of cases, exclusive breast feeding in 5.7% (20/354) and a combination of the two options in 2.5% (9/354). For 10 infants, the modality of feeding was not assessable. As shown in Figure 1, among all the 354 children evaluated,

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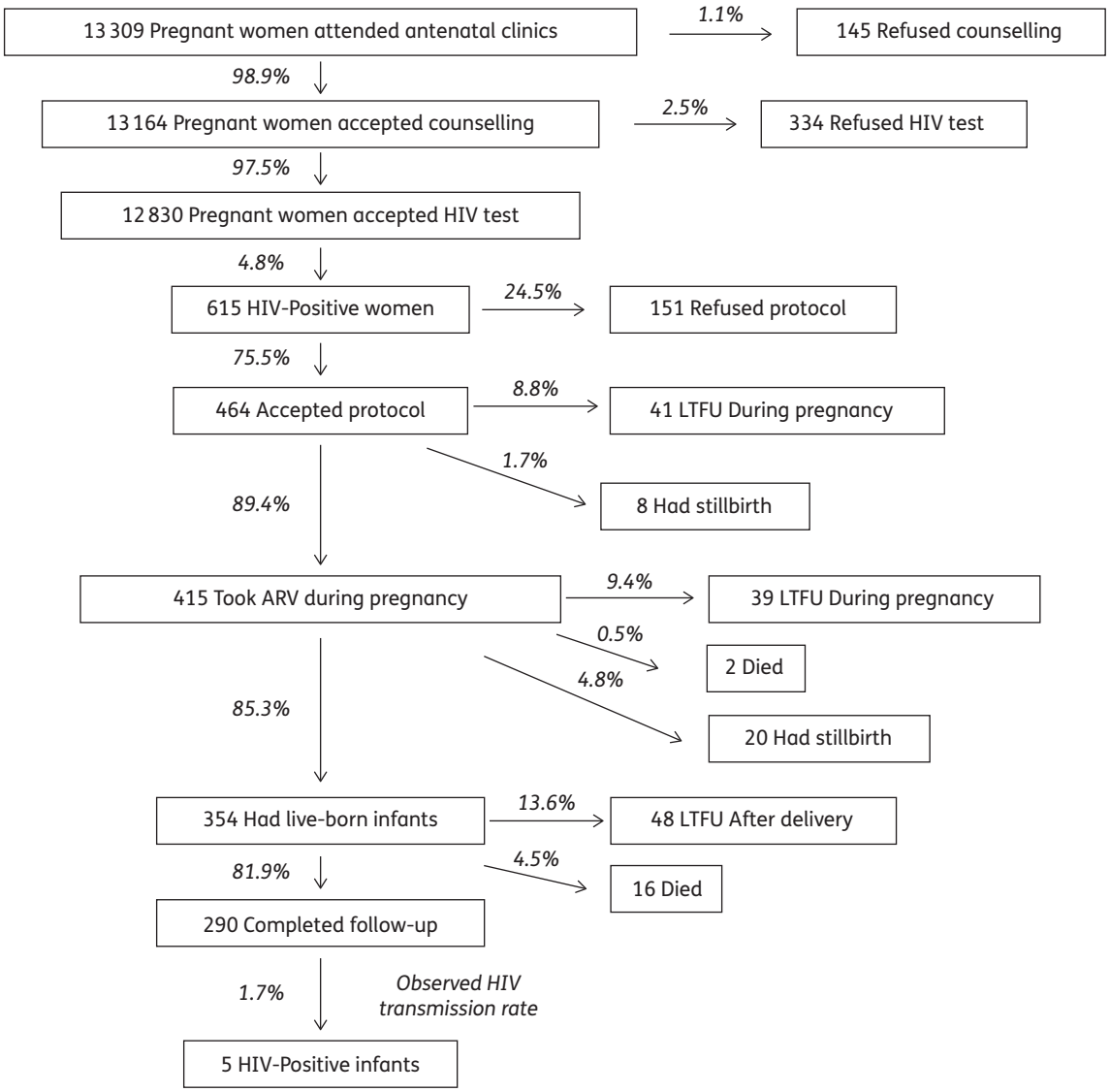

Figure 1. Flow diagram reporting the number of women who were taking part in or had dropped out of the programme at each stage of the study, from the target population to the group who completed the follow-up. The percentages refer to the number of women who had reached the preceding stage. The final observed transmission rate of HIV refers to the 290 mother and child pairs who completed the follow-up and should not be interpreted as an estimate of the overall transmission rate in the study population (see Figure 2). LTFU, lost to follow-up.

81.9% (290/354) completed the follow-up, while 13.6% (48/354) were lost to follow-up after delivery and 4.5% (16/354) died before a final conclusion about their HIV status could be obtained. The mean age at death was 21 days (IQR 2–98 days), and 56.3% (9/16) of the newborns who died did so during the first 3 days of life.

HIV transmission and global performance of the intervention

Five out of 290 children who completed the follow-up were diagnosed as being HIV positive, giving an observed transmission rate of 1.7% (95% CI 0.6%–4.1%). None of the second twins excluded from the analysis was diagnosed as being HIV infected. The characteristics of mother and child pairs in which vertical transmission of HIV occurred are described in Table 2. According to our estimates (Figure 2), approximately 62–110 additional infected children should have been born to women who eventually dropped out. This means that the overall estimated transmission rate in the target population was 67–115 cases out of 638 children, i.e. 10.5%–18.0%. This number can be compared with an expected transmission rate in the absence of the intervention of 25%–40%, i.e. 160–255 cases. As a result, it can be estimated that the intervention was able to prevent more than one-half of the expected cases of vertical transmission.

Factors associated with the risk of being lost to follow-up

Table 3 reports univariate and multivariate analyses of the probability of not completing the programme (being lost to follow-up). In the univariate analyses, declaring more than one sexual

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partner appeared to be associated with a higher risk of being lost to follow-up, while older age, better housing conditions (defined as the availability of at least one of the following: running water, electricity or a generator), telephone availability, occupation, having disclosed the status of HIV seropositivity to somebody else other than the partner, having been tested for HIV serology in the past, being aware of seropositivity, co-habitation with more than three people and a more severe CDC stage were all associated with a lower risk of being lost to follow-up. When analysed in a multivariate model, only older age (group 26–30 years: OR 0.33, 95% CI 0.16–0.66; group >30 years: 0.40, 95% CI 0.21–0.75; $P = 0.002$ for heterogeneity), telephone availability (OR 0.42, 95% CI 0.24–0.72; $P = 0.002$) and occupation (OR 0.57, 95% CI 0.29–1.10; $P = 0.092$), albeit with a lower statistical strength, remained significantly associated with the outcome.

Discussion

In agreement with other reports,[2–4,10] these data confirm that an exhaustive prophylactic protocol is effective in PMTCT in a resource-constrained setting, with an observed vertical transmission rate of less than 2% among women who fully comply with the prevention programme.

In our study, the acceptance of voluntary counselling and testing was satisfactory, and an optimal HIV vertical transmission rate was obtained in the mother and child pairs who completed the follow-up, when compared with other studies.[11–13]

However, the overall impact of this intervention was strongly affected by the large number of women who refused to enter the prophylactic protocol or dropped out, with an estimated transmission rate for the whole target population of pregnant women of 10.5%–18.0%. As a consequence, the programme was able to prevent approximately 50% of cases of vertical transmission. This is a noteworthy result, but it is much less impressive than the 10–20-fold reduction that was observed in the population who completed follow-up. Although the rates of refusal and premature drop-out from the programme were satisfactory when compared with other studies,[14–19] their impact on the overall effectiveness of the intervention was critical. Indeed, according to our estimates, a large majority of mother-to-child transmission of HIV occurs in these two groups, and any intervention aimed at increasing the overall effectiveness of a prevention programme should be focused on promoting participation in and compliance with the prevention programme, rather than on increasing its efficacy among compliers (e.g. with more effective drugs or caesarean section).

No previous study has used assumptions on the unobserved proportions of infected women and the rates of transmission in different subgroup to estimate the overall number of cases of PMTCT occurring in the cohort and to compare them with the number expected without the intervention, using sensitivity analyses. The most important source of potential error in our estimates is the choice of expected HIV transmission rates in the different groups of women. Notably, the estimated HIV transmission rate in women who refused the protocol or were lost to follow-up accounts for the majority of the estimated HIV-infected children. However, the impact of this potential bias is balanced by the same uncertainty in estimating the vertical transmission of HIV in the overall target population in the absence of any intervention. The assumption related to the seroprevalence of women refusing counselling and testing, thought to be arbitrary, is not critical due to the low refusal rate (<5%). In fact, even if the seroprevalence in women refusing counselling

Table 1. Clinical characteristics of the 354 live-born infants included in the analysis

Characteristic	Value [number (%) or median (IQR)]
Male sex	176 (49.7)
Gestational age (weeks)	39 (38–40)
Premature (<37 weeks of gestation)	59 (16.6)
Very premature (<32 weeks of gestation)	11 (3.1)
Haemoglobin level (g/dL)	14.4 (12.6–15.9)
Birth weight (g)	2900 (2580–3200)
Very low birth weight (<2.5 kg)	54 (15.2)
Body length (cm)	49 (47–50)
Head circumference (cm)	33 (31–34)

Numbers and percentage or median value and interquartile range (IQR) are shown for non-continuous and continuous variables, respectively.

Table 2. Characteristics of mother-and-child pairs in which HIV vertical transmission occurred

Code	Maternal ARV regimen	Duration of ARV during pregnancy, days	Adherence to ARV regimen	Maternal CD4 at baseline, cell/mm^3 (%)	Maternal CD4 at delivery, cell/mm^3 (%)	Gestational age at delivery	Infant weight at birth, g	Infant age at first positive DNA PCR, days	Infant status at 6 months
HM 0349 F	AZT+3TC+NVP	33	C	370 (47)	ND	41	3100	85	alive
NS 0479 F	d4T+3TC+NVP	28	B	95 (17)	193 (19)	40	2790	48	dead
NS 1406 F	AZT+3TC+NVP	8	A	137 (11)	136 (18)	40	3500	51	dead
NS 2013 F	AZT+3TC+NVP	135	A	163 (12)	169 (23)	37	ND	192	alive
NS 2748 F	AZT+3TC+NVP	243	A	233 (19)	ND	34	1000	96	alive

All women were naive to the ARV regimen and all infants were exclusively formula fed.
AZT, zidovudine; 3TC, lamivudine; NVP, nevirapine; ND, not determined.

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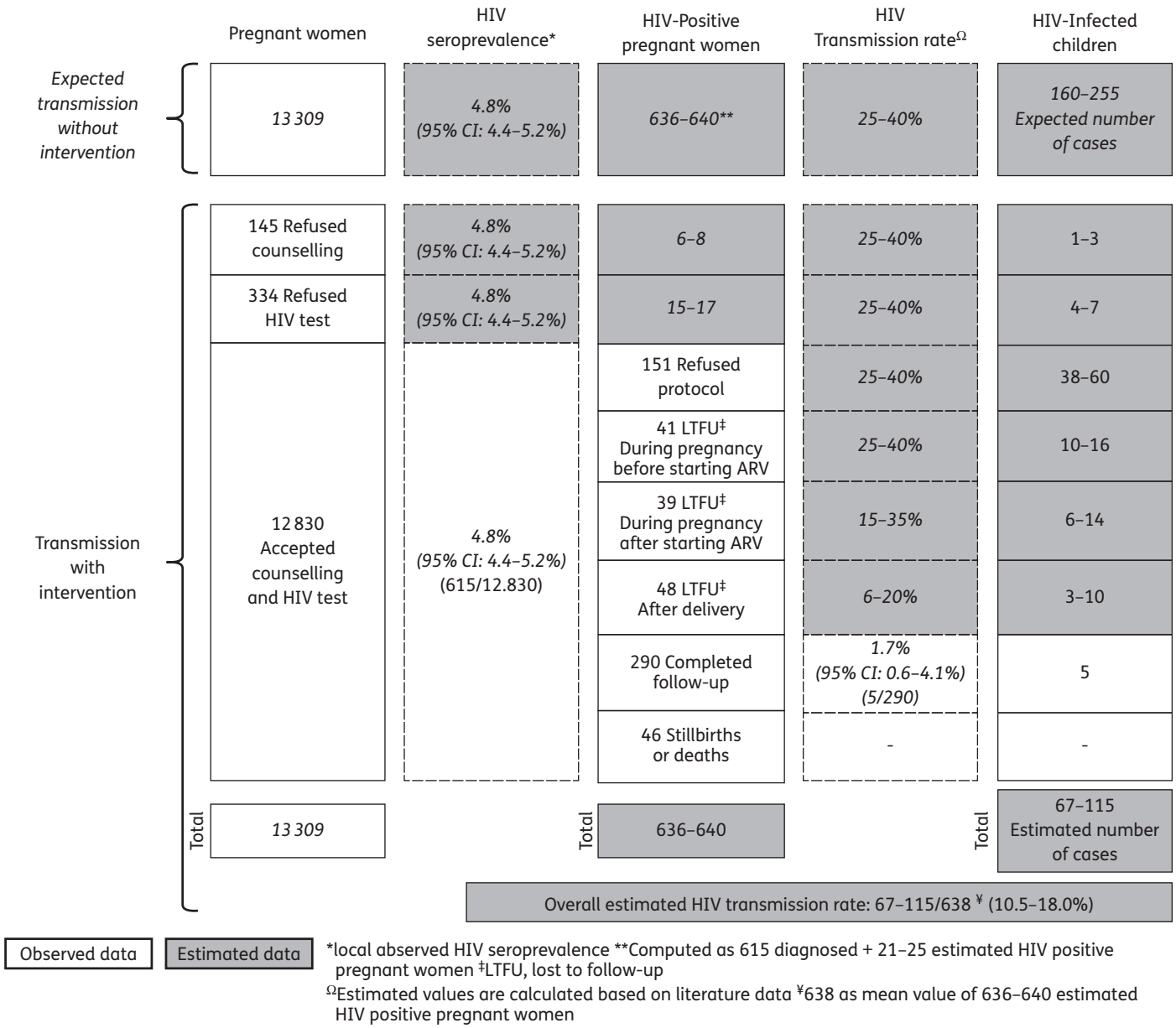

Figure 2. Total number of cases of vertical transmission of HIV expected in the target population in the absence of any intervention, and the estimated number of cases that actually occurred, based on observed data (white boxes) and on estimated (grey boxes) vertical transmission rates of HIV at each stage of drop-out. See the text for underlying assumptions.

and testing is assumed to be three times the upper limit of that observed among participating women, i.e. 15.6%, the overall estimates of the efficacy of the intervention in terms of the fraction of infants in whom HIV infection was prevented should be only marginally affected (51% instead of 55%). In addition, our assumption exactly overlaps with previous local estimates.[20]

An ancillary source of bias is that a second test at the end of pregnancy was not routinely offered in this programme and information on women who seroconverted during pregnancy is not available. Owing to this limitation, the overall impact of the programme could be overestimated in our study.

The representativeness of the study population is another important issue in this study. The whole population of pregnant women expected to attend the 28 antenatal clinics of Pointe Noire during the study period was approximately 110 000 (unpublished data provided by the Congolese Ministry of Health). As a consequence, the proportion of pregnant women attending the four public antenatal clinics involved in the project should be ~12% (13 309/110 000) of the total number of pregnant women in the economic capital of the Republic of Congo, roughly equivalent to the proportion of clinics (4/28 = 14%) participating in the study. This suggests, albeit indirectly, an acceptable representativeness of the study population.

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Table 3. Univariate and multivariate analyses for loss to follow-up (LTFU)

Variable	LTFU group, *n* (%) (*n*=128)	Not LTFU group, *n* (%) (*n*=336)	*P* value univariate	OR (95% CI) univariate	OR (95% CI) multivariate
Age (years)			0.002*		
mean	27.8	29.7			
median	27.4	29.7			
Age (categories)			0.001**		
≤25 years	47 (37)	69 (20)		Ref.	Ref.
26–30 years	31 (24)	117 (35)		0.39 (0.22–0.69)	0.33 (0.16–0.66)
>30 years	46 (36)	148 (44)			0.40 (0.21–0.75)
total	124 (97)	334 (99)			
missing	4 (3)	2 (1)			
Nationality			0.587**		
Congolese	126 (98)	328 (98)			
other	2 (2)	8 (2)			
total	128 (100)	336 (100)			
Gestational age (weeks)			0.119*		
mean	24.4	23.4			
median	24.0	23.0			
Housing conditions[a]			0.003**		
none	58 (47)	103 (32)		Ref.	
at least one	66 (53)	220 (68)		0.53 (0.34–0.83)	
total	124 (100)	323 (100)			
Telephone			<0.001**		
no	74 (58)	106 (31)		Ref.	Ref.
yes	54 (42)	230 (69)		0.34 (0.22–0.52)	0.42 (0.24–0.72)
total	128 (100)	336 (100)			
missing	0 (0)	0 (0)			
Occupation			0.006**		
unemployed[b]	97 (76)	213 (63)		Ref.	Ref.
worker	24 (19)	106 (32)		0.50 (0.29–0.85)	0.57 (0.29–1.10)
total	121 (95)	319 (95)			
missing	7 (5)	17 (5)			
Marital status			0.296**		
single	12 (9)	35 (10)		Ref.	
partner	82 (64)	185 (55)		0.50 (0.29–0.85)	
husband	30 (23)	98 (29)		0.89 (0.39–2.08)	
total	124 (96)	318 (94)			
Number of children			0.445**		
0–2	98 (76)	238 (71)			
>2	28 (22)	93 (27)			
total	126 (98)	331 (98)			
missing	2 (2)	5 (2)			
Number of people in the house			0.029**		
0–2	59 (46)	181 (54)		Ref.	
>2	50 (39)	93 (27)		0.61 (0.38–0.98)	
total	109 (85)	274 (81)			
missing	19 (15)	62 (19)			
Disclosed HIV-positivity to somebody			0.080**		
none	87 (68)	205 (61)		Ref.	
partner	30 (23)	78 (23)		0.91 (0.54–1.52)	
other	7 (5)	42 (12)		0.39 (0.15–0.96)	
total	124 (96)	325 (96)			
missing	4 (4)	11 (4)			

Continued

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Table 3. *Continued*

Variable	LTFU group, *n* (%) (*n*=128)	Not LTFU group, *n* (%) (*n*=336)	*P* value univariate	OR (95% CI) univariate	OR (95% CI) multivariate
Use of condoms			0.163**		
no	59 (46)	178 (53)		Ref.	
yes	60 (47)	134 (40)		1.35 (0.87–2.11)	
total	119 (93)	312 (93)			
missing	9 (7)	24 (7)			
More than one sexual partner			0.060**		
no	12 (9)	15 (4)		Ref.	
yes	82 (64)	218 (65)		2.13 (0.89–5.06)	
total	94 (73)	233 (69)			
missing	34 (27)	103 (31)			
Previous HIV test			0.053**		
no	16 (12)	68 (20)		Ref.	
yes	112 (88)	268 (80)		0.56 (0.30–1.05)	
total	128 (100)	336 (100)			
missing	0 (0)	0 (0)			
Known HIV-positive status			0.001**		
no	3 (23)	47 (71)		Ref.	
yes	10 (77)	19 (29)		0.12 (0.02–0.56)	
total	13 (100)	66 (100)			
HIV-related conditions			0.483**		
no	34 (26)	101 (30)		Ref.	
yes	92 (73)	232 (69)		0.85 (0.52–1.37)	
total	126 (99)	333 (99)			
missing	2 (1)	3 (1)			
CDC classification[c]			0.067***		
A	98 (76)	233 (69)		Ref.	
B	19 (15)	53 (16)		0.85	
C	11 (9)	50 (15)		0.52	

*, Mann–Whitney test; **, χ^2 test; ***, χ^2 test for trend.
Only maternal variables in which the univariate $P<0.1$ were included as covariates in the stepwise multivariate logistic regression.
Ref., reference.
[a] Availability of running water, electricity and generator.
[b] Housewife or student.
[c] Clinical classification of US CDC.

The above considerations underline the relevance of factors associated with an increased probability of successfully completing the intervention, as these factors might help in focusing future preventive programmes. In multivariate analyses, older age, telephone availability and occupation (with a lower statistical strength in multivariate analysis but significant in univariate analysis, as shown in Table 3) were found to be predictors of compliance with the programme. This is in agreement with others' experiences showing that young maternal age and a lack of income-generating activity are significant risk factors for declining ARV prophylaxis.[21–24] Telephone availability has been found to be associated with better compliance,[25–28] both making women easily reachable and reflecting a higher independence. A limitation of this multivariate model is that many of the variables are probably highly intercorrelated, and the sample size is limited. For this reason, variables significant only in the univariate analysis should also be discussed.

We found it particularly interesting that sharing information on the HIV-positive status with the partner is not crucial in women being lost to follow-up, while sharing this information with a third party can be helpful for adhering to the clinical protocol. Discordant data are reported on this topic.[29–31] In many African countries, women known to be HIV infected are rejected by their partner. For this reason, only a small percentage decide to inform their partner. Another interesting finding was that the gestational age at baseline was not significant in the loss to follow-up, in contrast with recent experience[21] and WHO recommendations.[32] This might be explained by the fact that the gap between enrolment and starting ARV prophylaxis was filled, in our intervention, by monthly clinical consultations with the administration of ferrous sulphate and folic acid. In the context of a PMTCT programme, all the identified risk factors should be taken into consideration when scoring all women at the first visit. Attention should be focused on women classified as being

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at higher risk of giving up the programme, providing them with stronger psychosocial support.

Unfortunately, no analysis could be carried out for women who tested HIV positive but refused the protocol; these women could have provided useful information,[33,34] but the collection of personal data in clinical records was performed only after acceptance of the study intervention and the provision of informed consent. However, qualitative information on the attitudes of the women who refused the intervention was collected during the study period by the counsellors and the physicians. These attitudes can be summarized as follows: fear of disclosure to the partner, distrust in European health science and an unwillingness to believe that an HIV-infected individual could be apparently in good health. In addition, other factors that were neither collected nor analysed may have played a role in determining the loss to follow-up.

In conclusion, two strategies to improve the effectiveness of a PMTCT programme can be recommended. First, improving women's awareness of the importance of a PMTCT intervention in order to preserve their health and to give birth to an HIV-negative baby should be the focus of the initial contacts, in order to improve compliance in the subsequent phases. In fact, a high acceptance rate of voluntary counselling and testing may conceal a low awareness among women when making this choice, creating the premise for a subsequent refusal or drop-out. Second, clinical, social and environmental conditions associated with an increased probability of premature termination of the programme need to be identified, in order to focus and possibly tailor the intervention to women at increased risk of not completing it.

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