Béninwendé Leticia Delphine Sakana et al.

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This online first version has been peer-reviewed, accepted and edited, but not formatted and finalized with corrections from authors and proofreaders

Prevention of mother-to-child transmission of HIV at the second immunization visit; a cross-sectional study, Burkina Faso

Béninwendé Leticia Delphine Sakana, a Anaïs Mennecier, b Paulin Fao, a Souleymane Tassembedo, a Jean-Pierre Moles, b Dramane Kania, a Ajani Ousmane Taofiki, a Frank Edgar Kadeba, a Ibrahim Diallo, a Sabrina Eymard-Duvernay, b Morgana D’Ottavi, b Nicolas Meda, c Beatriz Mosqueira, b Philippe Van de Perre b & Nicolas Nagot b on behalf of the ANRS 12388 PREVENIR-PEV Study Group

a Centre Muraz, Bobo-Dioulasso, Burkina Faso.
b INSERM, 60 rue de Navacelles, 34090 Montpellier, France.
c Département de Santé Publique, Université de Ouagadougou, Ouagadougou, Burkina Faso.

Correspondence to Anaïs Mennecier (email: anais.mennecier@inserm.fr).

(Submitted: 26 April 2022 – Revised version received: 3 October 2022 – Accepted: 3 October 2022 – Published online: 2 November 2022)

Abstract

Objective To evaluate the performance of the cascade of activities for prevention of mother-to-child transmission (PMTCT) of human immunodeficiency virus (HIV) at the second immunization visit in Burkina Faso.

Methods In a cross-sectional study, we recruited mothers attending the second immunization visit for their infant in 20 health centres of Bobo-Dioulasso city, Burkina Faso over 12 months (2019–2020). We administered a short questionnaire and HIV serological test to 14 176 mothers. All mothers were asked about their attendance for antenatal care and HIV rapid testing. HIV-infected mothers were also asked about the timing of their HIV diagnosis, antiretroviral therapy, pre-exposure prophylaxis initiation at birth and infant diagnosis of HIV.

Findings Of 14 136 respondents, 13 738 (97.2%) had at least one HIV serological test in their lifetime. Of 13 078 mothers who were never tested or were HIV-negative, 12 454 (95.2%) were tested during or after their last pregnancy. Among HIV-infected mothers already aware of their status, 110/111 (99.1%) women were on antiretroviral therapy. Among HIV-exposed infants, 84/101 (83.2%) babies received 6 weeks of antiretroviral prophylaxis at birth and 58/110 (52.7%) had a blood sample collected for early infant diagnosis. Only two mothers received their child’s test results at the time of the second immunization visit. Four mothers were newly diagnosed as HIV-positive during the study.

Conclusion Collecting data at the second immunization visit, a visit rarely missed by mothers, could be useful for identifying gaps in the PMTCT cascade in settings where mothers are difficult to reach, such as in low-income countries with intermediate or low HIV prevalence.
Introduction

Despite progress in preventing new paediatric human immunodeficiency virus (HIV) infections, the goal of eliminating mother-to-child transmission remains unattained.\textsuperscript{1} According to an estimate from the United Nations Children’s Fund, approximately 150 000 children worldwide were newly infected with HIV in 2020.\textsuperscript{2} Furthermore, children living with HIV are frequently underdiagnosed.\textsuperscript{3}

Successive international guidelines on the prevention of mother-to-child transmission (PMTCT) have been issued over the last decade, with the goal of eliminating mother-to-child transmission of HIV. HIV testing for pregnant women and all HIV-exposed infants within 6 weeks after birth has been recommended for over a decade.\textsuperscript{4,5} In 2013, the World Health Organization (WHO) recommended the test-and-treat strategy (called option B+). The strategy includes lifelong antiretroviral therapy for pregnant and breastfeeding mothers, and 4–6 weeks of single drug pre-exposure prophylaxis for HIV-exposed infants.\textsuperscript{6} In 2016, dual-drug pre-exposure prophylaxis was recommended for high-risk children during the first 6 weeks of life. The recommended duration of treatment was increased to 12 weeks for breastfed children at high risk of contracting HIV.\textsuperscript{7}

The PMTCT cascade is a succession of key activities and associated indicators for the overall period in which children are at risk of HIV infection: that is, from conception to the cessation of breastfeeding for HIV-exposed uninfected children. This series of steps facilitates the identification of the gaps that need to be addressed, and influences decision-making. Nevertheless, the lack of reliable data is often an obstacle to meaningful analysis and can impede health-care professionals from making decisions that are needed to decrease mother-to-child transmission of HIV.\textsuperscript{8} This lack of reliability occurs because data from mothers who are missed out of the PMTCT programme are not accounted for, and because the quality of the data collected depends on the performance of the facilities.

In Burkina Faso, the HIV prevalence among 11 627 tested pregnant women (aged between 15 and 49 years) was 1.3% (95% confidence interval, CI: 1.07–1.48) in 2018. In Bobo-Dioulasso, the second largest city in the country with an urban population of 900 000, the prevalence of HIV was 1.7% (95% CI: 1.10–2.75). Young women (5813 women aged 15–24 years old) were less affected, with a 0.8% (95% CI: 0.63–1.12) and 0.6% (95% CI: 0.18–1.7) prevalence of HIV in Burkina Faso and in Bobo-Dioulasso, respectively.\textsuperscript{9} According to the national guidelines, HIV testing is offered to pregnant women every 3 months.\textsuperscript{10} HIV-exposed infants should systematically receive 6 weeks of nevirapine for HIV prophylaxis.
from birth. Regardless of the mother’s HIV status, all mother–child pairs should attend the 42nd-day healthy baby visit, during which a blood sample is taken from HIV-exposed infants for early diagnosis of infection. The second immunization visit – a visit that is detached from the PMTCT programme but integrated into health and social promotion centres – is performed when the baby is 2 months old. In addition to visits to the centres, some health and social promotion centres organize mobile outreach immunization activities (in private health facilities or outdoor places). In 2020, these mobile visits represented 2336 (9.5%) of the 24 590 second immunization visits conducted by the health and social promotion centres involved in the study (data provided directly by the centres).

The objective of this study was to assess the effectiveness of the PMTCT cascade up to 2 months’ postpartum in Bobo-Dioulasso, Burkina Faso. To bypass recruitment bias in studies of the PMTCT cascade, we took advantage of the second infant immunization visit – a visit that is almost never missed by mothers and their infants outside the PMTCT programme.11

Methods

Study design
We conducted this cross-sectional study at 20 health and social promotion centres in the urban area of Bobo-Dioulasso from 4 December 2019 to 4 December 2020. Outreach visits were not included. The study comprised component 1 of the Elimination of Paediatric HIV-1 Infection: Evaluation of the Prevention Programme and Rescue Intervention Based on the Expanded Programme on Immunization (ANRS 12388 PREVENIR-PEV) study; trial registration number: NCT03869944. The ANRS 12388 PREVENIR-PEV study protocol was approved by the ethics committee for health research and the health authority of Burkina Faso.

Data collection
We enrolled mothers aged 15 years or older who attended the second immunization visit for immunization of their 5–16-week-old infants. The staff of the health and social promotion centres administered a short questionnaire to mothers after obtaining opt-out consent from mothers and before the infants were vaccinated (the questionnaire is available in the data repository).12 The questions collected only basic information to minimize bias associated with self-reporting, as well as to avoid discouraging mothers from participating in the study if the questionnaire were too cumbersome. The questionnaire concerned mothers’ activities related to PMTCT during the current pregnancy. All mothers were asked about their attendance for
antenatal care and HIV rapid testing. HIV-infected mothers were in addition asked about the timing of their HIV diagnosis, whether they were on antiretroviral therapy (ART), whether their infant had received pre-exposure prophylaxis at birth, and their infant’s diagnosis of HIV at birth.

Staff checked the newborns’ health record booklets for information about the mothers’ HIV status. This strategy avoided considering mothers as newly diagnosed with HIV when they were already aware of their status. Indeed, some mothers prefer not to reveal their positive status to health-care providers for fear of stigmatization, as observed in another study in Africa. An HIV rapid test was offered to all mothers with no relevant documented test results within the last 3 months. A mother was considered HIV-infected if she had two positive HIV rapid tests (Alere Determine HIV-1/2 SD, Abbott Laboratories, Chicago, United States of America), confirmed by Bioline HIV 1/2 (Abbott Laboratories, Chicago, USA) or OnSite HIV 1/2 Ab Plus Combo rapid test (CTK Biotech, Poway, USA), as per the national algorithm.

The mothers’ questionnaires were formatted as electronic case report forms using the REDCap software (Vanderbilt University, Nashville, USA) and recorded by site staff on electronic tablets. The data collected on the tablets were synchronized daily with the web server. We carried out on-site and centralized monitoring to increase data quality and prevent errors and possible oversights by staff.

In addition, we retrieved the data collected by the district regarding the monthly second immunization visit attendance in the 20 health and social promotion centres in the study.

**Data analysis**

We included all enrolled participants in the analysis. We present descriptive summary statistics for outcome variables of interest using percentages and 95% confidence intervals (CIs). We omitted missing data from the denominators for percentage calculations. Specific key indicators were stratified according to the maternal age. We calculated relative risks (RRs) with 95% CIs to evaluate if certain age groups were associated with lower rates of antenatal care attendance and missed opportunities for HIV rapid testing, using the over-24 year age group as the reference group. We performed statistical analyses using Stata version 16.1 (Stata Corp., College Station, USA).
Results

Study population
In 2020, 24,590 mother–child pairs participated in the second immunization visit at the 20 participating health and social promotion centres, according to district data. Between 4 December 2019 and 4 December 2020, a total of 14,191 mothers were screened, and 14,176 were enrolled in this study (Fig. 1). The median age of the enrolled mothers was 25.9 years (interquartile range, IQR: 21.3–31.0 years). Among the enrolled mothers, 14,140 (99.8%; 95% CI: 99.8–99.9; 12 missing answers) had attended at least one antenatal care visit during their last pregnancy and 10,355 (73.3%; 95% CI: 72.6–74.0; 53 missing answers) had attended four or more antenatal care visits.

HIV test status
Among the 14,176 mother–child pairs, 398 mothers declared they had never been tested (2.8%; 95% CI: 2.5–3.1) and 13,738 mothers had had at least one HIV rapid test in their lifetime (97.2%; 95% CI: 95%; 96.9–97.5; 40 missing answers). Of the participants who had not been tested, 235 mothers (1.7%) reported that they had never been offered HIV testing, 69 mothers had refused testing and 94 mothers had accepted testing but ultimately had not been tested.

Among the mothers who had been tested, the last documented result was HIV negative for 12,680 mothers (corresponding to 99.1% of 13,738 participants with a clear positive or negative HIV status) and HIV positive for 114 mothers (0.9%). Of the 398 mothers never tested for HIV, 391 mothers (98.7%; 2 missing answers) had attended at least one antenatal care visit during their last pregnancy and 206 mothers (52.4%; 5 missing answers) had attended four or more antenatal care visits.

A total of 12,454 mothers had been tested for HIV during or after the last pregnancy (up to the second immunization visit). This figure represents 98.3% (95% CI: 98.1–98.5; 9 missing answers) of the 12,680 HIV-negative mothers, or more broadly 95.2% of the 13,078 mothers never tested or with negative status. Among the mothers tested during or after the last pregnancy, 8263 mothers (65.7%; 95% CI: 64.9–66.5; 106 missing answers) had been tested in the last 3 months, in line with national recommendations.

Awareness of HIV status
Among the HIV-positive participants, 114 out of 118 mothers (96.6%) were already aware of their HIV infection. Of these 114 mothers, 76 (68.1%; 95% CI: 59.8–77.1; 4 missing answers)
were diagnosed before their last pregnancy and 35 (31.5%) were diagnosed during or after their last pregnancy (no information for 3 mothers).

Of the 111 mothers who provided information concerning ART, all women reported that they had been offered ART; we therefore considered them as linked to care. All but one of these mothers (110 mothers; 99.1%) were on ART at the time of the second immunization visit. Nevirapine prophylaxis was initiated at birth in 91 infants (90.1%; 95% CI: 84.3–95.9; 13 missing answers) and 84 of these HIV-exposed babies (83.2%; 95% CI: 75.9–90.5; 13 missing answers) received prophylaxis for the entire recommended 6-week period. According to mothers, blood samples were collected at the 42nd day visit for early infant diagnosis for 58 babies (52.7%; 95% CI: 43.4–62.1; 3 missing answers and one mother did not know if samples had been collected or not). However, only two mothers were aware of the test result at the time of second immunization visit (1.8%; 4 missing answers).

Overall, 5606 mothers did not have a documented HIV test performed in the last 3 months and were tested for HIV. These women included 379 mothers who had never been tested before (19 of 398 mothers never tested before did not receive a test during the study for various reasons). Four mothers were diagnosed as HIV positive. Among these, one mother had a negative HIV test result during the last pregnancy and two mothers had never been tested before (one mother with no information).

**HIV status by age**

When compared with the 8528 mothers over the age of 24 years, the 1277 adolescent mothers (younger than 19 years) were significantly more likely to have not attended any antenatal care visits (RR: 3.34; 95% CI: 1.35–8.26); not attended four or more antenatal care visits (RR: 1.33; 95% CI: 1.22–1.45); and never been tested for HIV (RR: 1.44; 95% CI: 1.06–1.96). Young mothers (4373 aged 20–24 years) also had a significantly higher risk of not having attended at least four antenatal care visits than had older mothers (RR: 1.16; 95% CI: 1.10–1.24; Table 1).

Of the 118 HIV-infected mothers, 108 (including three women who were newly diagnosed) were older than 24 years, eight women (including one woman newly diagnosed) were between 20 and 24 years of age, and two women were younger than 19 years.

**Discussion**

According to the data recorded in this survey, all the WHO process indicators for achieving elimination of mother-to-child transmission were reached. We found that 99.8% of women
had attended at least one antenatal care visit, 95.2% of mothers had been tested for HIV during pregnancy (or breastfeeding up to the second immunization visit), and 99.1% of HIV-positive mothers were on ART. Improvements in PMTCT facilities and organization in Burkina Faso and in pregnant women’s adherence to the PMTCT programme over the last decade have contributed to these impressive results.

The WHO impact indicators correspond to different rates of new paediatric HIV infections. These indicators are only relevant if the country’s health system allows for effective and exhaustive diagnosis of infants with HIV. The main gap identified during the study was the low proportion of HIV-exposed infants who had their sample collected for diagnosis before 2 months of age (52.7%) and the much lower proportion for those with results available at 2 months of age (1.8%). Our figure is far below 10% rate of early infant diagnosis for Burkina Faso reported by the Joint United Nations Programme on HIV/AIDS (UNAIDS). This difference may be explained by the choice of denominator (an estimate in the case of the UNAIDS data) and numerator (number of samples tested or results disclosed to mothers). Either result (1.8% or 10%) remains far from the UNAIDS interim target of 95% by 2025.

We identified two critical bottlenecks in testing infants for HIV in this study; first, samples were not always collected; and second, turnaround times for test results were prolonged. Our data show an improvement compared with figures in the 2017 annual report for Burkina Faso, in which only 902 (36%) of the 2476 HIV-exposed infants had a sample taken for early infant diagnosis of HIV. However, increasing the collection of dried blood samples in PMTCT settings is still needed. Long turnaround times can be attributed to the frequent shortages of reagents, as described some years ago in the central region of Burkina Faso, and to the complex system for polymerase chain reaction (PCR) testing. The transfer of samples and results between the health and social promotion centres, referral health centres and central laboratory could be optimized. Although infants may receive their results later, early infant diagnosis is defined as a test received within the first 2 months of life so that treatment can be started as soon as possible. However, with samples collected at 42 days of age for infants, and the organization of HIV PCR testing in a central laboratory, the 2-month date is easily missed. Point-of-care early infant diagnosis reduces the lag in delivery of the results and consequently promotes early initiation of ART.

Although most women participating in the study attended antenatal care visits, adolescents (15–19-year-olds) and young mothers (20–24-year-olds), according to the
UNAIDS definition,\textsuperscript{14} were significantly less compliant than older mothers. These findings are consistent with those of previous studies in Africa.\textsuperscript{24,25} This result may be attributed to fear of stigmatization in the context of illegitimate pregnancies and inadequate knowledge and misconceptions about antenatal care services.\textsuperscript{25} Low compliance with antenatal care visits has implications for obstetric outcomes as well as HIV prevention, with lower testing rates, as demonstrated for adolescent mothers in this study. Pregnancy is a frequent entry point for accessing HIV prevention, especially for adolescent girls and young women, who are considered priority target populations.\textsuperscript{14}

Over half of the mothers who attended the second immunization visit were asked to participate in the study (14 191 out of 24 590 mothers; 57.7%). Researchers were in close contact with the health centre staff and identified a variety of reasons for the low recruitment to the study. These challenges included: difficulty for staff in deploying electronic tablets for data collection; overburden of some staff in addition to their daily activities; staff turnover and difficulty in training new staff; and low pay or late payment of wages (as reported by some staff) reducing the incentive to work. We cannot evaluate the representativeness of the study population as sociodemographic or health data for the included mother–child pairs were not recorded. The HIV prevalence in our study (0.9%) was lower compared with that observed in the 2018 Burkina Faso serosurveillance report (1.7%, 18/1034 samples for the Bobo-Dioulasso urban area), although the population was similar (pregnant women with a median age of 25 years).\textsuperscript{9} The non-inclusion of mothers coming for the second immunization visit in our study was not related to the mother’s HIV status, but rather to the recruitment challenges described above.

This study has some limitations. Most of the questions concerned past events and were susceptible to recall bias, even though the time that had elapsed since the events in question was 6 months or less. The study was conducted in the urban area of a single city, Bobo-Dioulasso. PMTCT implementation is context-dependent, and challenges in other cities and rural areas may differ from those observed in the present study. Another study that is ongoing in a different city in Burkina Faso and in Zambia\textsuperscript{26} will help to validate the study methods in countries with high HIV prevalence. An additional limitation is that infants who died before reaching 2 months of life were not tracked. No data were collected on why the rate of early infant diagnosis was so low; however, an ongoing qualitative study will likely address this concern. Finally, the study assessed the PMTCT cascade up to 2 months’ postpartum and not
until the end of HIV exposure via breastfeeding (breastfeeding being prolonged well beyond 2 months for the majority of infants).

We acknowledge that no single method can fully measure the effectiveness of a programme. WHO considers statistical modelling, surveys and analysis of routine programmes to be complementary.\textsuperscript{27} Recommendations are focused on a group of priority countries in which high HIV prevalence may facilitate implementation, and Burkina Faso is not included.\textsuperscript{28} In the context of low or intermediate HIV prevalence, especially in a low-income country, routine prospective national programme monitoring can be difficult to set up.

Regular assessment of the PMTCT cascade, measured among the entire population, is necessary to analyse the improvements and gaps in a constantly changing scientific, political, economic and public health context.\textsuperscript{15,29} We propose that the second visit for infant immunization provides this opportunity and can be implemented by national programmes in low-income countries with low to intermediate HIV prevalence.

WHO recommends a shift from aggregate to individual-level data collection.\textsuperscript{30} The implementation of electronic medical records, as advocated by WHO, is not feasible for low-income countries with a low to intermediate HIV prevalence. Nevertheless, the integration of a short questionnaire for mothers during routine second immunization visit activities is highly feasible. In our study, this activity was well accepted by staff and patients. By replacing the aggregate data collected by facilities for annual activities with our strategy on a continuous basis, countries would obtain several benefits. First, they would benefit from a common data source for different uses: patient care, programme management and programme monitoring.\textsuperscript{30} Second, countries could benefit from obtaining denominators for all PMTCT indicators. Third, countries would avoid the risk of overestimating indicators. Although we conducted no cost analysis, the main costs are attributed to staff compensation and appear to be affordable for national programmes.

Although Burkina Faso is not a country with a high HIV prevalence, mother-to-child transmission is a concern, with UNAIDS estimating a final transmission rate of 15\% in 2020.\textsuperscript{18} Our strategy, a quick questionnaire among mothers during the second immunization visit, is simple to apply and centred on the people who benefit. We believe that routine implementation of the strategy is appropriate for assessing the effectiveness of the PMTCT cascade in low-income countries with low HIV prevalence, where mothers are difficult to reach.
Acknowledgements

BLDS and AM are joint first authors and PVdP and NN are joint senior authors.

Members of the ANRS 12388 PREVENIR PEV study group:

University of Montpellier (France): Philippe Van de Perre; Nicolas Nagot; Jean-Pierre Moles; Anais Mennecier; Beatriz Mosqueira; Morgana D’Ottavi; Sabrina Eymard-Duverny; Marianne Peries; and Vanessa Daoudi. Centre Muraz (Burkina Faso): Paulin Fao; Béninwende Leticia Delphine Sakana; Souleymane Tassembedo; Dramane Kania; Ajani Ousmane Taofiki; Edgar Franck Kadeba; Ibrahima Diallo; Abdramane Berthé; Lalla Sanou; Amélie Nikkiema; Emmanuel Coulibaly; Karim Savadogo; Sy Traore; Seydou Otoré; Moussa Sinare; Idrissa Ouedraogo; Alassane Ouattara; and Christine Kafando. Université de Ouagadougou (Burkina Faso): Nicolas Meda. Centre Hospitalier Universitaire Sourô Sanou, Bobo-Dioulasso: Makoura Traore/Barro; and Adama Dembele. Organisation Ouest Africaine de la Santé Bobo-Dioulasso, (Burkina Faso): Issiaka Sombie. World Health Organization: Nigel Rollins. School of Public Health, Harvard University (USA): Roger L Shapiro. London School of Hygiene and Tropical Medicine, London (England): Melissa Neuman. University of Toulouse III (France): Valeriane Leroy. Assistance Publique – Hôpitaux de Paris (France): Albert Faye. Centre Hospitalier Universitaire de St Etienne (France): Thomas Bourlet. South African Medical Research Council (South Africa): Ameena Goga. Kwame Nkrumah University (Zambia): Connie Osborne. ANRS-MIE (France): Laura Fernandez.

We thank Aaron Pontsler and Alison Martinez at Thrasher Research Fund as well as the women and their infants who agreed to participate in the trial.

Funding:

This study was funded by the Thrasher Research Fund (Thrasher Award Number 13501). INSERM-ANRS MIE (Agence Nationale de Recherches sur le Sida et les hépatites virales/ Maladies Infectieuses Emergentes) sponsored the PREVENIR-PEV study.

Competing interests:

None declared.

Acknowledgements:

References


| Variable | Age 15–19 years (n = 1277) | | Age 20–24 years (n = 4373) | | Age > 24 years (n = 8528)a |
|----------|--------------------------|--------------------------|--------------------------|--------------------------|
|          | Total no. of mothers responding | No. (%) of mothers | RR (95% CI) | Total no. of mothers responding | No. (%) of mothers | RR (95% CI) | Total no. of mothers responding | No. (%) of mothers |
| All mothers |                             |                          |                       |                           |                          |                       |                           |                          |
| Attended no antenatal care visits | 1274 | 7 (0.5) | 3.34 (1.35–8.26) | 4366 | 3 (0.1) | 0.42 (0.12–1.45) | 8512 | 14 (0.2) |
| Attended < 4 antenatal care visits | 1272 | 417 (32.7) | 1.33 (1.22–1.45) | 4352 | 1252 (28.8) | 1.16 (1.10–1.24) | 8487 | 2096 (24.7) |
| Never tested for HIV | 1270 | 48 (3.8) | 1.44 (1.06–1.96) | 4359 | 128 (2.9) | 1.12 (0.91–1.39) | 8495 | 222 (2.6) |
| HIV-negative mothers | Not tested for HIV during or after the last pregnancy | 1133 | 15 (1.3) | 0.70 (0.41–1.20) | 3923 | 60 (1.5) | 0.82 (0.61–1.10) | 7603 | 142 (1.9) |
| Not tested for HIV in the last 3 months | 1128 | 381 (33.8) | 0.98 (0.90–1.07) | 3899 | 1331 (34.1) | 0.99 (0.94–1.04) | 7535 | 2597 (34.5) |

CI: confidence interval; HIV: human immunodeficiency virus; RR: risk ratio.

a Reference group.

b Age was missing for 3 mothers who answered the questions.

c Age was missing for 2 mothers who answered the questions.

Notes: A total of 14,176 mother-child pairs were included in the study. n is total number of mothers enrolled in each age group. We compared mothers’ risk of deviation from the prevention of mother-to-child transmission of HIV programme between age groups using relative risk and their 95% CIs.
Fig. 1. Flowchart of the study of prevention of mother-to-child transmission of human immunodeficiency virus in Bobo-Dioulasso city, Burkina Faso, 2019–2020

24,590 mother–child pairs attended second immunization visit for infant

14,191 mothers selected

14 mothers not eligible
1 mother with incoherent data

14,176 mothers included in study:
– 14,140/14,164 (99.8%) mothers attended at least one antenatal care visit
– 10,355/14,123 (73.3%) mothers attended at least four antenatal care visits

14,136 mothers with information on HIV testing

398 (2.8%) mothers without HIV rapid test performed at least once in their lifetime

13,738 (97.2%) mothers with HIV rapid test performed at least once in their lifetime

12,680 mothers (99.1%) HIV negative (documented)

944 mothers with HIV status not documented:
– 815 HIV status unknown
– 129 self-declared HIV negative

114 mothers (0.9%) HIV infected (documented):
– 111 (100%) mothers linked to care; 110/111 (99.1%) mothers on ART at second immunization visit for infant
– 91/101 (90.1%) infants with pre-exposure prophylaxis initiated at birth; 84 (83.2%) of infants with 6 weeks of pre-exposure prophylaxis
– 58/110 (52.7%) infants with sample taken for early HIV diagnosis; 2/110 (1.8%) infants with early HIV diagnosis at 2 months

ART: antiretroviral treatment; HIV: human immunodeficiency virus.