ANRS CO1 EPF – Information for research participants

Title: National prospective study on mother-to-child transmission of HIV-1 and/or HIV-2 and its prevention

In brief	Principal Investigator: Dr Josiane WARSZAWSKI
	Organisation/teams: INSERM-Université Paris-Saclay Joint Unit – CESP-INSERM U1018 – Clinical Epidemiology and Pharmacoepidemiology Team / AP-HP Public Health Department
	Date: The first participant was enrolled on 24 September 1984 End of mother enrolment: 28 June 2022 End of follow-up for newborns: 29 March 2023
	Average number of mother-child pairs expected: 900 to 1,000 annually, totalling 26,976 women living with HIV enrolled during pregnancy or at childbirth (9,988 before 2005, 11,291 in CO1 and 5,687 in CO11).
	Research status: Completed
	Condition: HIV-1 and HIV-2
	Funding body: Inserm – ANRS MIE
	Funded by ANRS MIE
The project	The ANRS CO1 EPF study is a national prospective cohort study, launched in late 1984, aimed at estimating the rate of mother-to-child transmission of HIV-1 and/or HIV-2 (MTCT), assessing its trends, and subsequently evaluating the tolerability and efficacy of strategies to prevent this transmission (PMTCT), as well as identifying situations of vulnerability. From 2004 onwards, it comprised a detailed arm (CO1) and a simplified arm (CO11), drawing on a network of maternity units in France and the French overseas departments, including approximately 900 HIV-positive women each year who wished to carry their pregnancies to term, as well as their newborns. Newborns born to these mothers who were diagnosed as HIV-positive were included in the CO10 cohort for long-term follow-up until they reached the age of majority. The main objective, initially focused on assessing the effectiveness of PMTCT strategies, shifted from the 2000s onwards towards identifying the impact of antiretroviral treatments on the health of mothers and uninfected children in the short, medium and long term. Specific objectives include the study of PMTCT practices, risk factors for non-adherence to recommendations, the role of precarious living conditions, disclosure of HIV status, and co-infections. The study also examines the effects of treatment on pregnancy, preterm birth, congenital malformations and infant morbidity. Follow-up is based on clinical and biological data collected for up to 24 months in the child, with the period extended in the event of illness. Samples for biobanks were collected with the mothers' consent. Inclusion in the cohort is based on the collection of a 'no objection' statement, except in the case of biobanking, for which explicit consent was sought. Since Amendment 15, no further samples have been collected for biobanks. The study has contributed to public health surveillance, to improving clinical guidelines and the implementation of therapeutic trials.
References List of Publications	List of CO1/CO11 publications in the appendix
Study type	National, prospective, multicentre cohort study

Main objectives	Launched in 1985 (with a single enrolment at the end of 1984), the objectives of this cohort have evolved in line with advances in the prevention of mother-to-child transmission of HIV. From 2005 onwards, the main objective focused on assessing the tolerability of strategies for the prevention of mother-to-child transmission of HIV (PMTCT) whose efficacy had been demonstrated, both for the mother during pregnancy and the postpartum period and for the child in the short, medium and, where possible, long term. This observational assessment, conducted within the largest and longest-running national cohort, primarily involved describing the combined evolution of PMTCT strategies and the maintenance of their effectiveness in preventing transmission, alongside their impact on the course and outcome of pregnancy and their toxicity/tolerability in children not infected with HIV.
Secondary objectives	• To investigate the frequency and risk factors associated with PMTCT strategies that do not comply with expert group recommendations, taking into account how these have evolved over time. • To assess the impact of changes in clinical management over time on transmission rates, particularly in terms of the timing of cART initiation and the type of antiretroviral drugs used, mode of delivery, perinatal and postnatal prophylaxis, as well as practices that are becoming more common (assisted reproductive technology, amniocentesis, etc.). • Analyse the role of precarious living conditions and the disclosure of HIV status on care provision. • To assess trends in the prevalence of breastfeeding amongst women living with HIV, which is not currently recommended in France. • To study the immunovirological response during pregnancy according to the duration and type of antiretroviral treatment received. • To investigate the relationships between preterm birth, modes of delivery and therapeutic strategies, and the associated morbidity. • To estimate the incidence of conditions occurring during and following pregnancy, their association with preterm birth and their links to the antiretroviral treatments received. • To investigate the prevalence, management and risk of transmission of maternal co-infections (HBV, HCV, CMV). • To assess the potential role of maternal HIV, social vulnerability, perinatal exposures or obstetric management with antiretrovirals on growth, perinatal and infant mortality, the occurrence of congenital malformations, haematological and biochemical abnormalities, serious infectious diseases, serious neurological disorders, cancers, endocrine disorders or conditions related to mitochondrial toxicity, and unexpected conditions in uninfected children. • To assess the medium- and long-term health risks for children not infected with HIV.

<u>Overall research findings</u>

EPF has contributed to the dissemination and evaluation of strategies to prevent mother-to-child transmission of HIV, with spectacular progress over the past 20 years:

• The prescription of potent combination antiretroviral treatments during pregnancy began in 1997 and, by 2014, covered 98 per cent of pregnant women.

- Thanks to these treatments, almost all women now give birth with a very low viral load in their blood, which is the main factor in preventing transmission.
- Whilst the mother-to-child transmission rate was over 20 per cent before 1990, it fell below 1 per cent in the mid-2000s, then below 0.2 per cent from 2011 onwards, with no mother-to-child transmission among women treated throughout their pregnancy who maintained an undetectable viral load.
- The effectiveness of antiretroviral treatment has made it possible to relax the guidelines for other prevention strategies, particularly with regard to transmission, thereby reducing the need for caesarean sections

Publication references

	EPF-CO1/CO11 PUBLICATIONS (>2005)
2023	Sibiude J, Le Chenadec J, Mandelbrot L, Hoctin A, Dollfus C, Faye A, Bui E, Pannier E, Ghosn J, Garrait V, Avettand-Fenoel V, Frange P, Warszawski J, Tubiana R. Update on perinatal human immunodeficiency virus type 1 transmission in France: zero transmission among 5,482 mothers on continuous antiretroviral therapy from conception and with an undetectable viral load at delivery. Clin Infect Dis. 8 February 2023;76(3)
2022	Dollfus C, Le Chenadec J, Mandelbrot L, Tubiana R, Faye A, Brossard M, Frange P, Blanche S, Warszawski J; ANRS CO1/CO11 study group. Improved haematological outcomes in HIV-1-exposed infants receiving nevirapine compared with zidovudine for postnatal prophylaxis in a high-resource setting. Pediatr Infect Dis J. 1 May 2022;41(5):420–423.
2022	Saint-Lary L, Diallo A, de Monteynard LA, Paul C, Marchand L, Tubiana R, Warszawski J, Mandelbrot L, Rekacewicz C, Petrov-Sanchez V, Faye A, Sibiude J, Dabis F, Sommet A, Leroy V. In utero exposure to antiretroviral drugs and pregnancy outcomes: Analysis of the French ANRS pharmacovigilance database. Br J Clin Pharmacol. 2022 Mar;88(3):942–964
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