Project Brief: MIP Longitudinal Study (OPPTIM)

Full Title of Study/Programme	Optimising maternal viral load testing and infant HIV testing to improve postnatal PMTCT outcomes in HIV-infected women and their children **NEW title: OPPTIM** (Optimised Postpartum PMTCT Testing for Infants and their Mothers)
Technical Focus Area/Key Words	Maternal and Child Health
Rationale	The prevention of mother-to-child transmission of HIV (PMTCT) is the most successful HIV prevention intervention globally. In 2015 South Africa adopted the WHO's "Option B+" PMTCT strategy: lifelong antiretroviral therapy (ART) for all HIV-positive pregnant and breastfeeding women, regardless of CD4 count. However the early effectiveness of PMTCT, especially in low resource settings, is largely centered on pregnant women and early infant diagnosis with less emphasis on preventing transmission to infants born to HIV-positive women further along the PMTCT cascade. For example, in the City of Johannesburg (CoJ), despite the recommendation in the South African National Department of Health (SANDoH) guidelines for an integrated approach to maternal and child health, maternal HIV re-testing postpartum, infant testing beyond 10 weeks and maternal viral load testing are currently not well integrated into the Expanded Programme for Immunisation (EPI). These interventions are intended to reduce postpartum HIV transmission, as the postpartum period is a recognised high risk period for poor maternal adherence to ART and subsequent transmission of HIV to infants. There are few studies that have evaluated this integrated approach, mainly reporting on EPI coverage rates and maternal and infant testing rates, but not evaluating additional maternal care such as adherence to ART and viral load testing. Current programme indicators on infant HIV testing, beyond early infant testing, are difficult to interpret because of difficulties with data quality and accurate denominators. It is important to note that there are currently no postpartum programme indicators on maternal re-testing or maternal viral load monitoring. Poor implementation of postpartum HIV testing and monitoring of HIV-infected women and/or recording of these activities has resulted in a void of information on the maternal and infant HIV incidence in the postpartum period in this high maternal HIV prevalence setting.
Primary Objectives	To compare viral load suppression rates (viral load<1000 copies/ml) between HIV-positive postpartum women on first line ART, receiving a package of enhanced viral load monitoring with viral load point of care testing to those receiving standard of care lab-based viral load monitoring

Secondary Objectives	To determine the proportion of HIV-exposed children who test positive at 6, 9, 12, 18, 21 an 24 months using HIV rapid tests and an EID point of care test
Primary Endpoint/Outcome	Identify an appropriate package of services for viral load monitoring for HIV positive women during the postnatal period, incorporating the use of point of care viral load testing
Secondary Endpoint/Outcome	Identify an appropriate testing algorithm for HIV exposed infants in the PMTCT era, incorporating point of care PCR testing and HIV rapid testing.
Study Design	This study is a non-blinded randomized controlled trial with longitudinal follow-up of HIV-positive women and their children up to 24 months postpartum. At enrolment (infant age of 6-14 weeks), participants will be randomized to either the Standard of Care (SOC) viral load monitoring arm (Arm 1) or the Enhanced Care viral load monitoring arm (Arm 2). In arm 1, standard of care laboratory-based viral load testing will be done in HIV-positive mothers. In arm 2, 3 monthly viral load testing using POCT will be done in HIV-positive mothers. All enrolled infants will be tested for HIV with EID POCT and HRT at study entry, 6, 9, 12, 18, 21 & 24 months. Socio-demographic, PMTCT, sexual and reproductive health and adherence information will be collected through interviewer-administered questionnaires for women. Feasibility and acceptability of POCT questionnaires will be completed by both women and health care workers at the study clinics.
Study population	The study population will comprise of consenting mother-infant pairs from three urban primary health care clinics, Hillbrow Community Health Centre, Malvern clinic and Esselen clinic in sub-district F, City of Johannesburg, an HIV burden among the highest in South Africa. For the primary objective, all HIV-positive postpartum women (aged ≥14 years) on first line ART, who have given birth to a live infant and who are attending an EPI clinic for a 6-, 10- or 14-week immunization visit with their infant at one of the three study sites will be considered for inclusion. For the secondary objective, all HEU infants of the mothers enrolled for the primary objective, attending an EPI clinic at 6-, 10- or 14-weeks at the study sites. Women may be enrolled independently, even if their infant is not enrolled on the study for whatever reason; including refusal of consent for infant participation or death of an infant after study enrolment.
Study sample size	This study will recruit a minimum of 476 HIV-positive mothers and their HEU infants over a 4-month period at the 3 health facilities. Of the estimated 595 eligible women anticipated at these facilities, we anticipate recruiting at least 80% (N=476). Of these, based on previous studies, we anticipate a maximum loss-to-follow-up proportion of 20%. Power calculations are based on the primary objective only. In a study conducted in South Africa, where

	breastfeeding cessation is recommended at 12 months for HIV positive women, Hoffman et al (2016) reported 70% viral suppression 12 months postpartum among 103 women. We believe that a similar rate of suppression will be found in routine public health clinics in South Africa (i.e., Arm 1 (Standard of Care Arm) at our study sites). Using PoC viral load monitoring and doing viral load monitoring more frequently in Arm 2 (Enhanced viral load monitoring arm), we anticipate achieving at least 85% viral suppression in HIV-positive women at 18 months postpartum.
Follow up/duration	The study will be conducted for 24 months with participant follow-up of up to 18 months. The study conduct has been extended for a further 12 months with an addition 6 months of participant follow-up of up to 24 months (OPPTIM+ Extension)
Study/Programme sites	This study will be conducted in two primary care clinics, Malvern and Hillbrow in Region F, a densely populated, highly mobile population in inner city Johannesburg, South Africa.
Study/Programme duration	24 months; extended to 36 months in March 2020.
Investigators	Dr Lee Fairlie, Prof Gayle Sherman, Ms. Shobna Sawry, Dr Candice Fick & CDC colleagues.
Sponsors/Donors	Centers for Disease Control and Prevention (CDC) & UNICEF
Progress Update	Study commenced with recruitment in July 2018. Enrolment was concluded in April 2019. Follow-up till 18 months has been completed. Currently conducting 21- and 24-months visits for participants. Final visits to be concluded by April 2021.
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