Current HIV/AIDS Reports (2023) 20:121–130
https://doi.org/10.1007/s11904-023-00655-z

The End Is in Sight: Current Strategies for the Elimination of HIV Vertical Transmission

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Accepted: 8 March 2023 / Published online: 27 March 2023

Abstract

Purpose of Review The goal of this review is to highlight and interpret recent trends and developments in the diagnosis, treatment, and prevention of HIV vertical transmission from a clinical perspective.

Recent Findings Universal third-trimester retesting and partner testing may better identify incident HIV among pregnant patients and result in early initiation of antiretroviral therapy to prevent vertical transmission. The proven safety and efficacy of integrase inhibitors such as dolutegravir may be particularly useful in suppressing viremia in pregnant persons who present late for ART treatment. Pre-exposure prophylaxis (PrEP) during pregnancy may play a role in preventing HIV acquisition; however, its role in preventing vertical transmission is difficult to elucidate.

Summary Substantial progress has been made in recent years to eliminate HIV perinatal transmission. Future research hinges upon a multipronged approach to improving HIV detection, risk-stratified treatment strategies, and prevention of primary HIV infection among pregnant persons.

Keywords Sexually transmitted infections · Human immunodeficiency virus · Mother-to-child transmission · Vertical transmission · Congenital infections

Introduction

Despite advances in HIV care, pregnant people worldwide remain vulnerable to HIV acquisition. Elimination of vertical transmission, defined as < 1 per 100,000 live births, remains elusive and a pressing global health priority. In the era of combination antiretroviral therapy (ART), HIV transmission rates of less than 1% are achievable. Globally, around 85% of pregnant people living with HIV receive ART to prevent mother-to-child transmission (MTCT), which remains the leading cause of pediatric HIV worldwide [1]. However, an estimated 1.3 million pregnant people living with HIV per year still do not have access to ART. Less than a third of pregnant people living with HIV have been treated in countries such as Indonesia, the Democratic Republic of Congo, and Mali, leaving tens of thousands of infants at risk of perinatal HIV infection [2]. Conversely, Cuba, Thailand, and Malaysia have reported complete eradication of HIV vertical transmission countrywide [3]. Global elimination of HIV vertical transmission is attainable in the imminent future and has been prioritized as a goal for the twenty-first century [4, 5].

Effective elimination of HIV vertical transmission entails a multipronged approach. The first strategy is to stop people of childbearing potential from acquiring HIV in the first place. This is done through voluntary counseling and testing [6], prevention strategies such as pre-exposure antiretroviral prophylaxis (PrEP) [3], and testing of partners with prompt initiation of treatment [7]. Increased access to contraceptives, particularly in areas of the world where they are not readily available, can also lead to fewer vertical transmission events through the prevention of unintended pregnancies in people living with HIV [8]. Another strategy, since vertical HIV transmission is generally virus load dependent, entails the reduction of virus load through the implementation of

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maternal ART throughout pregnancy, labor, and delivery and throughout the course of breastfeeding, as recommended by guidelines and the WHO's B + approach [6]. Topical microbicides during labor have also been investigated as a potential approach in the reduction of viruses in the genital tract. Another strategy is to reduce infant exposure to the virus. This is also achieved through maternal treatment with antiretrovirals, which enables infant pre-exposure prophylaxis through the placental transfer of ART, peri-exposure prophylaxis during labor through continued maternal ART use, and neonatal post-exposure prophylaxis. Elective C-section also prevents ascending HIV infection from the maternal genital tract, thus reducing neonatal viral exposure. Finally, establishment of HIV infection can also be prevented through infant post-exposure prophylaxis or early preemptive neonatal antiretroviral treatment with three antiretrovirals in the case of high-risk infants (i.e., born to mothers with detectable viremia) [9, 10]. If infants are not found to be HIV infected, preemptive treatment may be discontinued. This review discusses recent developments within this multifactorial framework to achieving global elimination of HIV vertical transmission in this century: improved detection of incident HIV infection in pregnancy, optimization of ART regimen to reduce viral load prior to delivery, and the possible role of pre-exposure prophylaxis (PrEP) in pregnancy.

HIV Vertical Transmission

Perinatal HIV transmission is a complex process and can occur at several time points: in utero, intrapartum, or postpartum via breastfeeding. In utero HIV transmission accounts for 5 to 10% of perinatal HIV infections; intrapartum transmission accounts for 10 to 15% and postpartum transmission via breastfeeding for approximately 15% [11–13]. Therefore, the cumulative risk of HIV vertical transmission up to 12 months of age in an HIV-exposed child born to and breastfed by an untreated person living with HIV approaches 40%. For the determination of an HIV diagnosis, infants exposed to maternal HIV should be tested by molecular tests until 3 to 4 months of age [10]. The timing of HIV transmission is determined based on whether HIV is identified in infant blood by a molecular test in the first 48 h of life; in the case of a positive PCR result at birth, transmission is assumed to have occurred prior to delivery (in utero transmission) [14]. If an infant perinatally exposed to HIV has a negative PCR result for HIV in the first 48 h of life and a positive result is identified 7 days to 3 months later, in the absence of breastfeeding, this infant is assumed to have acquired HIV during labor and delivery (intrapartum transmission).

There are multiple risk factors for HIV perinatal transmission, but maternal virus load is recognized as a critical risk factor in transmission [15•, 16]. In utero HIV transmission is more likely with a high maternal virus load, chorioamnionitis, and co-infections that increase the expression of CCR5 receptors in the placenta [17–19]. Most in utero transmissions tend to occur after 20 weeks of gestation and increase further as pregnancy progresses; the length of ART use in pregnancy is associated with favorable pregnancy/infant outcomes and less vertical transmission events in women with a longer duration of ART throughout pregnancy [20]. Studies suggest that HIV transmission to the fetus in the first trimester tends to result in miscarriage and that this miscarriage risk may also extend to the second trimester [21–23•]. Antiretrovirals during pregnancy successfully reduced HIV in utero and intrapartum transmission from 25 to 8% in the landmark Pediatric AIDS Clinical Trials Group (PACTG) 076 study which only used zidovudine [24], and later in PACTG 316 which used cART and demonstrated MTCT rates lower than 2% [25]. Subsequent studies demonstrated progressively lower HIV transmission rates up to less than 1% when cART was used throughout pregnancy and even throughout the postpartum period by breastfeeding mothers [20, 26]. Although interventions solely focused on reducing intrapartum transmission had some historical success [27], they ultimately failed at eliminating HIV vertical transmission because they did not encompass all time points where transmission may occur (in utero and postpartum), nor effectively treated pregnant people living with HIV. Antenatal ART, ART during delivery, and ART to the infant for the first 4 weeks of life as peri-exposure prophylaxis are critical elements for complete elimination of HIV vertical transmission [28, 29].

For pregnant people who present to medical care very late in pregnancy where prevention of in utero HIV transmission can no longer be achieved, strategies for prevention of intrapartum transmission include the performance of elective cesarean section, which have been shown to reduce transmission rates to 10% in pregnant people not on therapy, and less than 2% in pregnant persons on zidovudine monotherapy throughout pregnancy [30–32]. Double or triple ART prophylaxis to the infant when the mother received no ART prior to delivery has been shown to effectively reduce intrapartum HIV transmission to 2.2 and 2.4% respectively, versus 4.8% among infants receiving only zidovudine (ZDV) as neonatal prophylaxis [9]. However, this transmission rate only considers intrapartum transmission, if the in utero time point is included, the overall transmission rate in the study was 11% in the infant ZDV arm, 7.1% in the double infant ART arm, and 7.4% in the triple ART infant arm [9]. The results of these studies inform today's HIV prenatal management guidelines, which recommend elective C-sections for women with a viral load higher than 1000 copies/mL close to delivery, and presumptive HIV therapy for infants at higher risk of HIV acquisition [10].

In the USA, breastfeeding guidelines for people living with HIV have recently changed [33]. Although breastfeeding was previously contraindicated, the current recommendation is for people with HIV to receive evidence-based, patient-centered counseling, and engage in shared decision-making with providers about infant feeding. This counseling would ideally begin prior to conception or as early as possible in pregnancy; information about and plans for infant feeding should be continuously reviewed later in pregnancy and after delivery. During counseling, information should be provided that replacement feeding with properly prepared formula or pasteurized donor human milk from a milk bank entirely eliminates the risk of postnatal HIV transmission to the infant and that achieving and maintaining viral suppression through antiretroviral (ARV) therapy during pregnancy and postpartum does decrease breastfeeding transmission risk to less than 1%, but not to zero. In people with HIV who are not treated and/or do not have a suppressed viral load during pregnancy (at a minimum throughout the third trimester) and at delivery, the use of replacement feeding with formula or banked pasteurized donor milk is recommended. Both individuals with HIV who are on ART and have an undetectable viral load who choose to breastfeed and people with HIV who choose to formula feed should both be supported in their decisions. The guidelines do not provide details regarding post-exposure prophylaxis for infants, the frequency of maternal viral load monitoring, and the role of local infection (e.g., mastitis) during breastfeeding, with management decisions being up to the discretion of individual HIV providers. These remain unanswered questions and should be further studied in order to ensure the safety and efficacy of preventing postnatal HIV transmission.

Diagnosis and Testing Strategies in Pregnancy

Pregnancy is a time period of increased risk for HIV acquisition [34]. HIV testing at the first or earliest prenatal visit is universally recommended. In addition, the WHO recommends retesting in the third trimester, postpartum, and/or during labor in high prevalence settings [35]. Previous studies have demonstrated that the HIV test positivity rate is higher late in pregnancy as compared to early pregnancy and the risk of vertical transmission is thus higher in patients who seroconvert after their first prenatal visit and are unaware of incident HIV infection with likely unsuppressed viremia [36, 37]. While the importance of universal retesting in high-prevalence settings has been established, the utility of universal retesting in settings of low HIV prevalence is currently being explored. Previous research has also shown that universal HIV testing is also cost-effective, even in low prevalence settings [38]. A recent cost-effective analysis of dual HIV and syphilis retesting late in pregnancy in both countries with high or low HIV burden was shown to be cost-effective even in countries with low HIV prevalence such as Colombia [39].

Another strategy to better identify HIV infection in pregnancy is to test the partner, although the utility of this approach as a strategy to curb vertical transmission is unclear. Uptake of partner HIV testing is generally low [40–43]; qualitative studies have reported barriers including poor communication, gendered perceptions, fear of intimate partner violence, and social stigma [44–46]. In southern Brazil, at the epicenter of a regional maternal HIV epidemic in the country, two large prospective cohort studies totaling more than 1000 cisgender and transgender male partners showed that encouragement and invitation by pregnant women to attend prenatal care and receive testing was successful in recruiting male partners for testing [47, 48]. Implementation of partner testing in southern Brazil proved to be such a promising intervention that the model was incorporated into the Brazilian standard of care. Some studies have suggested HIV self-testing (HIVST) kits as a promising strategy because it is preferred by partners; however, linkage to care after a positive result remains an obstacle [49–54]. The addition of HIVST to partner notification services in current HIV prevention programs could be considered, as this dual approach greatly improved HIV testing in Zambia [55]. Affordable and fixed financial incentives, in conjunction with HIVST kits, may also bolster linkage to care [56]. A recent randomized controlled trial demonstrated that the integration of HIVST kit distribution into routine antenatal care increased HIV testing among partners [57]. Another approach would be for both partners to receive HIV results together which entails a "couples sexual agreement," (mutual agreement about sexual behaviors within and outside of the relationship) and has only been studied in the USA [58]. To scale up partner testing, a holistic and gender-transformative approach may be crucial to address power differentials, impart novel communication strategies, and adapt to cultural attitudes and contexts to assuage fears of social stigmatization and isolation [59].

Recent Developments in ART in Pregnancy

For many years, recommendations for cART initiation for pregnant persons living with HIV lagged behind treatment guidelines developed for non-pregnant adults. Even though the use of antiretroviral monotherapy had been long abandoned for the treatment of non-pregnant adults, the use of zidovudine monotherapy in pregnancy, as well as short course delivery of other ARTs alone or in combination, continued to be used for the prevention of HIV vertical transmission in women who per treatment guidelines of those times, did not yet qualify for treatment of their own illness. Even when cART became the standard of care for pregnant women, depending on their CD4

cell count numbers, treatment would be interrupted in the postpartum period, only to restart again during the next pregnancy. Many of these strategies were later considered suboptimal, fostering the development of viral resistance. A major change occurred when WHO guidelines recommended widespread implementation of test and treat strategies, with treatment for life of all individuals identified with HIV, regardless of CD4 cell count values, i.e., the B + approach [6]. These guidelines have remained the standard of care today where high rates of viral suppression have been achieved to circumvent vertical transmission, which is generally less than 2% when there is access to cART, even in areas of high prevalence [60, 61].

In recent years, potent integrase strand inhibitors joined the HIV therapeutic arsenal. In 2021, the results of the IMPAACT 2010/VESTED trial demonstrated that dolutegravir-containing cART regimens were superior to efavirenz-containing regimens in achieving virologic suppression at delivery [62••]. The IMPAACT 2010/VESTED trial was a randomized controlled trial conducted in nine countries across North and South America, Asia, and Africa designed to compare the perinatal safety and virologic efficacy of three ART regimens in pregnancy: dolutegravir, emtricitabine, tenofovir alafenamide fumarate (DTG/FTC/TAF); dolutegravir, emtricitabine, tenofovir disoproxil fumarate (DTG/FTC/TDF); or efavirenz, emtricitabine, tenofovir disoproxil fumarate (EFV/FTC/TDF). The dosing regimen was as follows: DTG 50 mg once daily with either once daily FTC 200 mg/TAF 25 mg or FTC 200 mg/TFD 300 mg; and efavirenz 600 mg once daily. Pregnant women living with HIV were recruited between 14 and 28 weeks of gestation with the primary outcome as virologic suppression at delivery defined as < 200 copies/mL and a composite adverse pregnancy outcome defined as any pregnancy resulting in preterm birth, an infant small for gestational age, stillbirth, or spontaneous abortion. Among 605 women in the intention-to-treat analysis, the rate of viral suppression was 98% in the combined DTG-containing groups (DTG/FTC/TAF or DTG/FTC/TDF) compared to 91% in the EFV/FTC/TDF group ($p = 0.0052$). This difference in virologic efficacy remained significant even if viral suppression at delivery was defined as < 50 copies/mL with 95% in the DTG-containing groups virally undetectable at delivery compared to 90% in the EFV/FTC/TDF group ($p < 0.0001$). Both DTG/FTC/TAF and DTG/FTC/TDF have similar virologic efficacy. In terms of safety, the DTG/FTC/TAF had significantly fewer composite adverse pregnancy outcomes (24%) than the DTG/FTC/TDF (33%) and EFV/FTC/TDF (33%) groups ($p = 0.043$). Although a higher rate of stillbirth was observed in the combined DTG-containing groups (4% in DTG/FTC/TAF group and 5% in DTG/FTC/TDF group) than the EFV/FTC/TDF group (2%), this difference was not statistically significant ($p = 0.064$).

Concurrently, the IMPAACT P1081 trial demonstrated that raltegravir could be used as an alternative to dolutegravir and was more effective than efavirenz in ensuring viral suppression at or near delivery [63•]. The IMPAACT P1081 trial, conducted in five countries, was designed to compare the safety and efficacy of two triple backbone regimens, one with raltegravir and the other with efavirenz, and enrolled pregnant women living with HIV at 20 to 37 weeks of gestation. The dosing regimen was as follows: raltegravir 400 mg twice a day, efavirenz 600 mg once at night in addition to lamivudine 150 mg, and zidovudine 300 mg twice daily. The main outcome, viral suppression at/or near delivery (within 21 days before), was defined as < 200 copies/mL. Among 408 women, the proportion of women with suppressed viremia at delivery in the raltegravir group was 94% compared to 84% in the efavirenz group ($p = 0.0015$). This treatment effect was especially prominent among women who presented late to HIV care and were enrolled at 28 to 37 weeks of gestation, where 93% achieved virologic suppression by delivery in the raltegravir group compared to 71% in the efavirenz group. When the outcome measure was defined as < 50 copies/mL, raltegravir remained superior in virologic efficacy with 86% virally undetectable at or near delivery in the raltegravir group compared to 58% in the efavirenz group ($p = < 0.0001$). There were no significant differences in stillbirth and adverse infant outcomes. All vertical transmission events occurred among women who presented late for HIV care (enrolled 28–37 weeks or gestation) and differed significantly between the raltegravir group (0.5%) and the efavirenz group (3.3%, $p = 0.064$), highlighting the urgency for rapid initiation and effective treatment in this high-risk subpopulation of pregnant persons living with HIV. A longitudinal study conducted simultaneously in Brazil where 390 women living with HIV received either protease inhibitor-based regimens, efavirenz-based regimens, or raltegravir-based regimens demonstrated that among women receiving cART for 2 to 7 weeks during pregnancy, the virus load decline was significantly greater for raltegravir than for efavirenz or protease inhibitors [64•]. At the time of delivery, viral load suppression was achieved among 87% of women on raltegravir versus 73% on efavirenz and 70% on protease inhibitors ($p = 0.01$) [64•]. Clinically, the use of integrase strand inhibitors, given their potency, is particularly useful among patients who face social and structural barriers to accessing HIV care and initiate cART late in pregnancy (after 28 weeks of gestation).

Late presenting women generally have high viremia and increased risk of vertical transmission and benefit from more rapid virologic suppression strategies before delivery. Given that dolutegravir was found to reduce viral load to less than 50 copies/mL after a median day of 28 days compared to 84 days with efavirenz in non-pregnant people living with HIV [65], the DolPHIN-2 trial, which was conducted

in South Africa and Uganda, was designed to evaluate if dolutegravir led to faster virologic decline than efavirenz and improved virologic suppression, defined as < 50 copies/mL, prior to delivery in pregnant women who presented late for HIV care [66•]. Participants were enrolled after presenting for obstetric and HIV care after at least 28 weeks of gestational age with confirmed but untreated HIV infection. The dosing regimen was dolutegravir 50 mg or efavirenz 600 mg once daily co-formulated with either FTC 200 mg/TDF 300 mg (South Africa) or lamivudine 300 mg/TDF 300 mg (Uganda). In the intention-to-treat analysis of 268 women, 74% of participants in the dolutegravir group were virally undetectable prior to delivery compared to 43% in the efavirenz group with an estimated relative risk viral suppression with dolutegravir of 1.64 (95%CI: 1.31–2.06, $p < 0.0001$). Dolutegravir also led to more rapid viral decline and replicated results previously reported in non-pregnant adults: the median time to achieve viral copies < 50 copies/mL was 28 days for dolutegravir and 82 days for efavirenz. In the dolutegravir group, the median time to achieve a viral load of < 1000 copies/mL was 7 days compared to 23 days for efavirenz. Since late initiation of cART in pregnancy is associated with increased infant mortality, this trial also explored postpartum and long-term infant outcomes between the late use of dolutegravir and efavirenz and demonstrated that dolutegravir was beneficial in this setting [67].

Research in this area is ongoing with a focus on maternal side effects and long-term infant sequelae of DTG-based regimens. In the randomized clinical trials in non-pregnant adults which demonstrated that DTG with either TAF or TDF displayed non-inferior efficacy to EFV-based regimens, significant differences in weight gain were observed in cisgender women after 96 weeks of treatment initiation [68, 69]. These women gained an average of 8.1 kg in the DTF/FTC/TAF group, 4.8 kg in the DTF/FTC/TDF group, and 3.2 kg in the EFV/FTC/TDF group. The long-term metabolic postpartum changes and effects on weight gain of dolutegravir-containing regimens remain to be explored. Although there was concern that dolutegravir was associated with adverse maternal outcomes such as stillbirth, preterm birth, or small for gestational age (SGA) as well as congenital anomalies, these concerns were dispelled by subsequent studies [70, 71]. Early population-based studies suggested a potential association between neutral tube defects and dolutegravir use at or early in pregnancy [71–73]. In the large Tsepampo birth-surveillance study, dolutegravir was initiated at conception. Subsequent studies did not confirm an association [55–57]; a subsequent analysis of the data from the Tsepampo birth-surveillance study suggested that, given the rare occurrence of neural tube defects in the general population and the small number of cases identified, the magnitude of the risk of dolutegravir-associated neural tube defects remains less than 1%. Other studies include reports from Botswana with one case of neural tube defect in 152 pregnancies where dolutegravir was taken since conception and 2 cases in 2328 HIV-negative women [55]. In 2019, the WHO recommended dolutegravir as the preferred HIV treatment option for all populations including pregnant women [74]. The US perinatal HIV guidelines recommend dolutegravir + TAF/XTC as the preferred ART of choice for pregnant people who are drug naïve, for people on a continuing regimen who become pregnant, for people who are not drug naïve and are restarting ART in pregnancy, for people who are not suppressed on the current ART regimen, and for non-pregnant people who are trying to conceive. A raltegravir-based regimen is an acceptable alternative when dolutegravir is not available [10].

Prevention of Primary HIV Infection among Pregnant Persons

The feasibility and safety of pre-exposure prophylaxis (PrEP) in reproductive-age and pregnant people have yet to be elucidated and its role in eliminating vertical transmission is unclear. As one of the few HIV prevention methods which do not depend on the partner, PrEP may be an underutilized tool in eliminating primary maternal infection and subsequent perinatal transmission before conception or during pregnancy, a period of heightened risk for HIV acquisition. Obstetrician-gynecologists may play a role in bolstering PrEP acceptability [75]; last year, the American College of Obstetricians and Gynecologists updated their guidance to recommend PrEP to all sexually active adolescents and adults [76]. The introduction of PrEP as a part of routine prenatal care at the first antenatal visit has demonstrated high acceptability and uptake among cisgender pregnant persons [77].

Regardless of an expansion and access of PrEP to a wider cache of adolescents and adults, adherence is key to achieving and maintaining drug concentrations in vaginal and cervical tissues to prevent HIV acquisition. Additionally, physiologic changes of pregnancy may affect the pharmacokinetics of PrEP: during the second and third trimesters in pregnancy, increased plasma volume and increased renal clearance may lead to lower local drug concentrations. Generally, it is acknowledged that it takes 20 days to achieve optimal concentrations of tenofovir and/or emtricitabine in vaginal and cervical tissues [78, 79]. Currently, it is recommended that people who start PrEP who are planning to conceive or who are pregnant use another form of protection for at least 20 days to prevent primary HIV infection.

Current clinical trials are underway to examine the safety and efficacy of PrEP in pregnancy. Currently, FTC/TDF is the PrEP regimen recommended for people without HIV who are planning to have a child or who are pregnant or breastfeeding [10]. The HIV Prevention Trials Network (HPTN) 084 trial

demonstrated that intramuscular cabotegravir every 8 weeks [80] was effective in the prevention of HIV in cisgender non-pregnant women [81]. However, data on the use of cabotegravir as HIV prevention during pregnancy is sparse: a case series of 25 pregnancies of cisgender women who participated in the long-acting cabotegravir and rilpivirine clinical trials resulted in 10 live births, one of whom had a congenital anomaly [82]. Studies are planned to investigate the safety and efficacy of long-acting ART as a form of PrEP in pregnancy.

However, data on the safety and efficacy of oral FTC/TDF in pregnancy have been reported and is emerging. Retrospective analyses from clinical trials which suggested first trimester exposure to PrEP, demonstrate that oral PrEP is safe in pregnancy and is mostly not associated with significant fetal or maternal outcomes [83–85]. This month, the results of the CAP016 trial were published [86]; the CAP016 trial was a single-site, randomized, non-inferiority trial in South Africa which was designed to evaluate the maternal and perinatal safety of FTC/TDF in pregnancy were recently reported. Among 540 cisgender pregnant women not living with HIV enrolled at 14 to 28 weeks of gestation, preterm birth and small for gestational age were not associated with PrEP, supporting the safety of FTC/TDF in pregnancy. Aside from oral and long-acting PrEP regimens, monthly dapivirine vaginal ring also shows promise as a safe and effective method to prevent HIV seroconversion among people capable of pregnancy not living with HIV. In two clinical trials involving non-pregnant adults, the dapivirine vaginal ring lowered the risk of HIV acquisition and was not associated with any safety concerns [87, 88]. Several studies from these clinical trials found that there was a low incidence rate of HIV infection and improved adherence to treatment with the use of the dapivirine ring [89, 90]. The DELIVER study is an ongoing open label, phase 3b randomized controlled trial in Malawi, South Africa, Uganda, and Zimbabwe which seeks to determine maternal and fetal safety of dapivirine and oral FTC/TDF in pregnancy (#NCT03965923). The trial is set to be completed in 2024 and has already enrolled 859 participants. These studies, both previous and current, point to the potential of PrEP for preventing primary HIV infection in pregnant persons while diminishing the social stigma and need for daily pill-taking with current PrEP regimens. However, the true effect of PrEP during pregnancy on eliminating vertical transmission may better be explored through predictive modeling and are thus outside the scope of this review.

Conclusions

In the past decade, significant strides have been made in the diagnosis, treatment, and prevention of HIV vertical transmission. Research efforts should be made to find the most optimal cost-effective, universal third-trimester retesting strategy as well as increasing male partner involvement, and testing uptake leveraging community and socio-behavioral interventions. In terms of treatment during pregnancy, further investigation into the safety profile and long-term infant outcomes of integrase inhibitor-based regimens used in pregnancy should be explored. Lastly, the safety and efficacy of PrEP as an emerging strategy to prevent vertical transmission by preventing primary HIV acquisition in all who desire and are capable of pregnancy may become an integral part of family planning services for this population worldwide. With a holistic and multipronged approach, the elimination of HIV vertical transmission is possible and achievable in the current generation.

Funding Lanbo Yang was supported by the UCLA South American Program in HIV Prevention Program (PI: Clark), NIMH grant R25MH08722. The funders had no role in contributing to this review.

Declarations

Conflict of Interest The authors declare no competing interests.

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• Of importance
•• Of major importance

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