Title
Eliminating perinatal HIV in the United States

Journal
AIDS, 33(3)

ISSN
0269-9370

Authors
Gnanashanmugam, Devasena
Rakhmanina, Natella
Crawford, Keith W
et al.

Publication Date
2019-03-01

DOI
10.1097/qad.0000000000002080

Peer reviewed

HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2020 March 01.

Published in final edited form as:

AIDS. 2019 March 01; 33(3): 377–385. doi:10.1097/QAD.0000000000002080.

Eliminating Perinatal HIV in the United States: Mission Possible?

Devasena Gnanashanmugam, MD[1,15,*], **Natella Rakhmanina, MD, PhD**[2a,2b,*], **Keith Crawford, PhD**[1], **Steven Nesheim, MD**[3], **Theodore Ruel, MD**[4], **Guthrie S. Birkhead, MD, MPH**[5], **Rana Chakraborty, MD, PhD**[6,16], **Robert Lawrence, MD**[7], **Patrick Jean-Philippe, MD**[1], **Lakshmi Jayashankar, PhD**[8], **Ashley Hoover**[9], **Anne Statton**[10], **Patricia D'Souza, PhD**[1], **Joseph Fitzgibbon, PhD**[1], **Rohan Hazra, MD**[11], **Barbara Warren, BSN, MPH, PNP**[12], **Somer Smith, PharmD**[6,14], and **Elaine J. Abrams, MD**[13]

[1]Division of AIDS, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD;

[2a]Children's National Medical Center, Washington, DC;

[2b]Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC

[3]Centers for Disease Control and Prevention (Division of HIV/AIDS Prevention), Atlanta, Georgia;

[4]University of California- San Francisco, San Francisco, CA;

[5]School of Public Health, University at Albany, Albany, NY;

[6]Emory University School of Medicine, Atlanta, Georgia;

[7]University of Florida, Gainesville, Florida;

[8]Columbus Technologies Inc., Contractor to National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD;

[9]Louisiana State Department of Health, Baton Rouge, Louisiana;

[10]Pediatric AIDS Chicago Prevention Initiative, Chicago, IL;

[11]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD;

[12]New York State Department of Health, Albany, NY;

[13]ICAP at Columbia University, Mailman School of Public Health and Vagelos College of Physicians & Surgeons, Columbia University, New York, NY

[14]Theratechnologies, Inc. Montreal, Canada

[15]Cepheid, Inc. Sunnyvale, CA.

[16]Mayo Clinic College of Medicine, Rochester, MN

Corresponding author & request for reprints: Elaine Abrams, ICAP at Columbia University, Mailman School of Public Health, 722 West 168th Street, New York, NY 10032, USA. eja1@columbia.edu; phone 212-342-054; fax 212 342 1824.

*Shared first authorship

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the view of the Centers for Disease Control and Prevention or the National Institutes of Health.

Summary and follow up communication from the participants of the Improving Early Infant Diagnosis Meeting, sponsored by the National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), 2016.

Abstract

In 2015, only 53 infants born in the United States acquired HIV, the lowest recorded number of perinatal HIV infections. Recognizing this significant achievement, we must acknowledge that the United States has not yet reached the goal of eliminating perinatal HIV transmission. This manuscript describes different approaches to perinatal HIV preventive services among five states and the District of Columbia as case studies. Continuous focus on improving identification, surveillance and prevention of HIV infection in pregnant women and their infants is necessary to reach the goal of eliminating perinatal HIV transmission in the United States.

Introduction

Perinatally acquired HIV infections among infants born in the United States have been steadily declining for more than 20 years[1]. After a dramatic (71%) reduction from 1630 infections in 1993 to 480 in 1996 following the introduction of zidovudine prophylaxis for pregnant women living with HIV and their infants, approximately 200 infants who were born in the United States acquired HIV infection annually in the first decade of the current century[2, 3]. In 2015, the Centers for Disease Control and Prevention (CDC) estimated only 53 infants born in the United States acquired perinatal HIV, the lowest number of perinatal HIV infections to date[4]. This reduction in perinatal HIV transmission is attributed to number of important interventions: a) implementation of routine opt-out HIV testing of all pregnant women[5]; b) introduction of combination antiretroviral treatment (ART) during pregnancy[6]; c) elective cesarean delivery for women with plasma HIV RNA viral load >1000 copies/ml[7]; and d) avoidance of breastfeeding by women living with HIV[8].

Despite the dramatic decline in the number of perinatal infections[3], at the national level we have not yet reached the target of elimination at the national level set by CDC as an incidence < 1:100,000 live births and a perinatal transmission rate < 1%[9]. In 2008 all United States HIV surveillance jurisdictions incorporated name-based HIV reporting, facilitating estimation of the incidence of perinatally-acquired HIV infection[10]. In 2015, the national incidence reported by CDC was 1.3/100,000 live births , which is still above the threshold for perinatal HIV elimination[9]. This target is even further out of reach for African American populations with a disproportionally high perinatal HIV incidence rate of 5.4/ 100,000 live births compared to 0.4/100,000 live births among White children[4].

The second target for elimination requires determining the perinatal HIV transmission rate; this has proven to be more challenging than assessing incidence. While the new cases of perinatal HIV are declining, the national transmission rate cannot be accurately determined because pregnancies and deliveries in women living with HIV in the United States are not routinely tracked. Funding for Enhanced Perinatal Surveillance (EPS) ended in 2011, and although Perinatal HIV Exposure Reporting is currently recommended by the CDC, there is no national mandate to report HIV infection during pregnancy. The annual number of HIV-infected women delivering in the United States was last estimated at 8,700 in 2006[11]. Indirect measures suggest that the number of pregnant women living with HIV rose in late 1990s and early 2000s; however perinatal HIV exposures reported to CDC by state and city surveillance systems suggested a potential decline in number of pregnancies with HIV of

approximately 20% from 2009 to 2013[12]. In fact, in a recent analysis the CDC estimated a 14% decline in the annual number of births to women living with HIV and as well as a decline in the annual number of women with HIV infection, approximately 5000, delivering infants in the USA[13]. Surveillance of pregnancy and HIV at the national level could significantly improve our knowledge about reproductive health and the pregnancy outcomes among women living with HIV in the USA.

Major obstacles to reaching elimination of perinatal HIV in the United States have been identified in several recent reports and include late diagnosis of HIV among pregnant women and suboptimal ART for their treatment and prevention of pediatric infections. Geographic and racial disparities of perinatal HIV outcomes continue to point to the Southern States and African American mother-child pairs as most vulnerable[14,15]. Current lack of a national surveillance system for tracking pregnancy outcomes in women living with HIV also needs to be addressed[16]. Moreover, all perinatally HIV-infected children born in the United States need to have timely access to the most current treatments, including early initiation of ART.

To address this goal of reaching the national perinatal HIV elimination targets, a meeting entitled Improving Early Infant Diagnosis was sponsored by the National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS) in May 2016, where the current status of perinatal HIV and HIV preventive strategies of the United States was reviewed. The six states and district (New York State, Louisiana, Illinois, Georgia, Florida and District of Columbia) with the high rates of HIV/AIDS and significant experience with perinatal HIV prevention were invited to participate with the goal of identifying barriers and facilitators towards reducing perinatal HIV transmission. In this manuscript we summarize, as case studies, regional approaches to perinatal HIV prevention and provide a consensus opinion on the way forward towards eliminating perinatal HIV transmission in the United States.

Case Studies

New York State

Epidemic landscape: In New York State, three coincident epidemics (HIV, injection drug use and crack cocaine) led to high prevalence of HIV infection in women and high perinatal HIV rates in the early to mid-1980s[17]. Since 1988 the Department of Health (DOH) has included universal dried blood spot HIV screening in the routine inborn-errors-of-metabolism screening of all newborns on the New York State[18]. Through this testing, 1,885 (0.66 %) women giving birth were found to be HIV-infected in 1989[19]; with a seroprevalence in the 13 most affected postal codes in New York City greater than 3%[18]. Considering transmission rates at that time of (25–33%), 471–622 infants were estimated to have acquired HIV infection in New York State in 1989.

Perinatal HIV prevention response: New York State began an unprecedented public health initiative involving rapid translation of new scientific discoveries into policy and practice through an extensive collaboration among health departments, health care providers, and community and advocacy organizations[20]. Several important initiatives were

undertaking some of which are summarized in Table 1. First, clinical guidelines to expand HIV counseling and testing were introduced in 1985, followed by case management programs funded through Medicaid and grants for HIV/AIDS (1990), supportive services for high-risk and HIV-infected women (1992) and co-located HIV/gynecological services (1993). In 1995 the New York State DOH Pediatric HIV Diagnostic Testing Service was implemented, closely followed by the clinical and targeted public education, regulation to require prenatal providers to routinely offer HIV counseling and testing to pregnant women. (Table 1) Other major initiatives included: un-blinding the newborn dried blood spot HIV test results with active public health follow-up of HIV-exposed infants, expedited HIV testing of women at delivery or their newborns in women without documented HIV test during the prenatal period, and recommendation for repeat testing in the third trimester to identify women with seroconversion during pregnancy[20]. (Table 1)

Recent updates: Since the 1990s, New York State experienced a steady decline in the prevalence of HIV in childbearing women and a dramatic decline in the number of new pediatric HIV infections. In 2013, only 2 cases of perinatal transmission were detected, a rate of 0.05 per 100,000 live births and 0.5 percent of HIV-exposed births[21], meeting CDC criteria for elimination of perinatal transmission[9]. However, after an 18-month period with no perinatal transmission, a new infant case occurred in early 2016[22]. Nevertheless, the extraordinary progress in reducing perinatal transmission in New York State through multi-sectorial collaboration points the way for other states to follow.

Illinois

Epidemic landscape: The first cases of AIDS were reported in Illinois in 1980. The first perinatal HIV diagnosis in Illinois was reported to the state in 1985. Since then, 506 perinatally transmitted HIV cases have been reported in Illinois through the end of 2013[4]. A state survey of all maternity hospitals in 2001 found that an average of only 72% of women presenting to deliver had a documented result from HIV screening during pregnancy. A coalition of advocates and public health partners worked to help enact legislation that would mandate the counseling and an offer of HIV testing to all pregnant women as early in the pregnancy as possible.

Perinatal HIV prevention response: In 2003, Illinois adopted a state law mandating the counseling and offering of a rapid HIV test at delivery to women without a documented HIV test result during the current pregnancy[23]. (Table 1) The law also mandated that maternal HIV test results be documented in the prenatal, labor and delivery and newborn charts. Four years later, the state law was amended to also mandate HIV testing of all infants born without a documented maternal HIV test result; parental consent is not required prior to newborn HIV testing. (Table 1) Positive results from rapid HIV testing in labor and delivery on either the mother or the infant are required to be promptly communicated to a state-sponsored perinatal HIV Hotline to ensure proper treatment and follow up of all cases[24]. The Hotline serves as a single point of entry and linkage to care for pregnant women with HIV and also as a connection to specialized perinatal HIV case managers, who provide field or home-based care for vulnerable women needing extra support. (Table 1)

Recent updates: The perinatal HIV services are sustained through public funding (the Illinois Department of Public Health and the Illinois Department of Women's Health) in partnership with private non-profit support (Pediatric AIDS Chicago Prevention Initiative) and the specialty HIV/Obstetric and HIV/Pediatric providers in the state. The CDC estimated that 18 infants born in 2012 in Illinois acquired HIV[12], and since that time, the number of children born in Illinois with HIV infection has decreased to 4 in 2013, 3 in 2014, 3 in 2015 and 1 in 2016 (personal communication, Cheryl Ward, Illinois DOH). Ongoing challenges include reducing rates of HIV seroconversion during pregnancy, implementing repeat 3rd trimester HIV testing without legislative mandate for repeat testing in pregnancy, and addressing ongoing stigma faced by women living with HIV infection.

District of Columbia

Epidemic landscape: Washington, DC has had high overall HIV prevalence for over a decade with a 2% prevalence reported in 2016[25]. Perinatal HIV transmission soared in 2005, and in that year the metropolitan DC area contributed to nearly 9% of new pediatric AIDS diagnosis in the nation[26].

Perinatal HIV prevention response: Introduction of name-based HIV reporting in 2006 and mandatory reporting of pregnancies in women living with HIV to the DC DOH in 2013 improved tracking of perinatal HIV exposure. (Table 1) DC DOH estimates ~80% of all pregnant women living with HIV are captured in HIV surveillance. Approximately 95% of pregnant women at higher risk for perinatal transmission, such as high maternal viral load, inadequate prenatal care or maternal mental health concerns are included in HIV surveillance (personal communication from Anitra Denson, MD, DC DOH). Without mandatory repeat HIV testing, the DOH of DC, Maryland (MD), and Virginia (VA), since 2007, recommended repeat HIV screening for all pregnant women during the third trimester and if not performed, and if maternal HIV status is unknown, rapid HIV screening during labor for mothers and infants at all regional healthcare facilities in the DC metropolitan and MD and VA suburban areas. (Table 1) Linkage to neonatal testing and care for the entire metropolitan area is centered at the Pediatric HIV program at Children's National Health System, which serves as the main provider of early infant diagnostics for an estimated 95% or more of perinatally HIV-exposed infants in the area.

Recent updates: Multi-sectorial collaboration helped decrease rates of perinatal HIV transmission DC. During 2013–2015, the Pediatric HIV program evaluated 388 HIV-exposed infants referred from the area, with 16% (n=62) representing high-risk exposures, and reported zero transmission events[27]. Unfortunately, two transmissions from the DC metropolitan area were reported in 2016 (personal communication, Natella Rakhmanina, Children's National Health System), factors associated with the transmission were reported in both cases and included lack of antenatal care and non-adherence to ART. Federal funding (Ryan White parts A and D) provide crucial support to the continuum of perinatal services including funding of a designated perinatal coordinator at Children's National Health System closely interlinked with regional healthcare facilities and health departments that provide testing and care to the HIV-infected mothers.

Georgia

Epidemic landscape: Georgia ranked fifth nationally in total number of new diagnoses of HIV infection in 2014; approximately 20% of these diagnoses occurred in females, including women of childbearing age[28,29]. Twenty-nine infants born in the state were diagnosed with HIV infection between 2011–2015, compared to 38 between 2006–2010 (personal communication, Pascale Wortley, M.D., Georgia Department of Public Health). Many factors at the state and local levels hinder elimination of perinatal HIV and need to be addressed, including increasing state support for programs to identify and link HIV-infected women to appropriate services, strengthening the perinatal HIV surveillance system and improving perinatal HIV prevention infrastructure at local delivery hospitals[30].

Perinatal HIV prevention response: In 2015, the Georgia Department of Public Health, in collaboration with Emory University, developed the Perinatal HIV Services Coordination (PHSC) program to close gaps in the perinatal HIV care continuum. (Table 1) The program connects local public health departments with healthcare providers and labor and delivery units to facilitate identification, linkage, and retention of HIV-infected pregnant women and HIV-exposed infants in care. The PHSC program initially focused on 11 birthing facilities in the Atlanta Metropolitan Statistical Area, with a plan to expand to rural Georgia. Additional objectives of the program include ensuring provision of antiretroviral drugs (ARVs) as treatment and prophylaxis, promotion of perinatal HIV exposure reporting, education of providers on national perinatal HIV prevention guidelines and evaluation of institutional infrastructure.

Recent updates: Initial findings of a survey to assess facilities and practices suggested that nine of the 11 centers that were surveyed failed to follow standard-of-care guidelines, including assessment of maternal HIV status during labor by rapid testing[31]. Nearly all providers were unaware of the National HIV Clinician Consultation Center, the organization supporting the national perinatal HIV hotline that provides immediate consultation for management of HIV in pregnancy[21]. Practices overall were highly variable, with only four of 11 centers stocking liquid formulations of nevirapine for infant prophylaxis. The PHSC program assisted hospitals to fill gaps identified by the survey with education and training to providers and implementation of an electronic notification system for reporting of perinatal HIV exposures to the Department of Public Health as part of state HIV surveillance.

Florida

Epidemic landscape: Florida's system for perinatal HIV transmission prevention includes a number of largely decentralized programs: Ryan White Programs Parts C & D supporting perinatal HIV prevention coordinators, 115 obstetrical hospitals and 35 birthing centers, Florida DOH surveillance reporting of deliveries to women living with HIV within 24 hours of the delivery (implemented in 2006), Baby Rxpress Program for postpartum zidovudine prophylaxis at no cost to families, and Children's Medical Services Pediatric HIV Referral Centers. (Table 1) Despite the these varied programs, Florida continues to rank in the top 3–4 states in the United States for annual perinatal HIV transmission[3].

Perinatal HIV prevention response: In 2016, the Florida DOH HIV Surveillance Program performed a retrospective review of de-identified data from the Enhanced HIV/Acquired Immune Deficiency Syndrome (AIDS) Reporting System for the years 2007 through 2014 to identify factors associated with perinatal HIV transmission risk[32]. (Table 1) From 2007 through 2014 they documented 4574 deliveries to women living with HIV and 70 HIV infections among infants born in Florida with an overall transmission rate of 1.5% through those years. The transmission rate ranged from 2.5% in 2007 to 0.5% in 2011, but it rose to 1.6% in 2016. Analysis of transmission risks showed that transmission was primarily associated with insufficient antenatal and prenatal care and a lack of HIV diagnosis and ARVs during pregnancy. Illegal substance use during pregnancy and breastfeeding was an additional risk factor.

Recent updates: To further decrease perinatal HIV transmission Florida aims to implement individualized patient care and supportive services for pregnant women at risk of HIV infection and more coordinated HIV testing and reporting. Remaining challenges include: HIV testing in pregnancy with repeat 3rd trimester testing and rapid testing in labor for women without documented HIV results, as well as addressing mental illness and substance abuse in women of reproductive age[33,34]. The state perinatal case report form is currently being revised to better identify more missed opportunities.

Louisiana

Epidemic landscape: In 2015, Louisiana had the second highest rate of HIV diagnoses in the United States[28], and from 2004– 2013, of 1728 identified HIV-exposed infants, 54 were determined to be infected with HIV[35]. Rates of perinatal transmission have declined over the years but surveillance and care for HIV-infected pregnant women and their exposed infants remains a challenge. Late diagnosis of HIV in pregnancy, lack of ART during pregnancy, labor and delivery were identified as missed opportunities in perinatal HIV prevention[35].

Perinatal HIV prevention response: Perinatal HIV exposure surveillance has been a part of the Louisiana STD/HIV surveillance unit since 1999 through the Enhanced Perinatal Surveillance (EPS) program and continued through core surveillance funding after 2011 when funding for the EPS program ended. (Table 1) Fetal Infant Mortality Review HIV methodology (FIMR/HIV) sites in New Orleans and Baton Rouge were established in 2009 to review and identify root causes of perinatal transmissions and high-risk perinatal exposures to HIV to prevent future transmissions. In 2014, Louisiana passed legislation requiring opt-out HIV and syphilis testing at the first prenatal care visit in the third trimester as well as at the first prenatal care visit. Additionally, while HIV during pregnancy is a reportable condition in Louisiana, most perinatal exposures are identified postpartum through active reporting to field epidemiologists that cover all nine regions of Louisiana. In an attempt to prevent future transmissions of HIV, the STD/HIV surveillance unit developed a pregnancy report form in 2016 to improve statewide reporting and to document continuum of care during pregnancy and postpartum period.

Recent updates: While perinatal transmissions have declined over the recent years, FIMR/HIV remains a primary element in the program's ability to identify and address

system issues relating to high-risk perinatal HIV exposures. Efforts have been made to implement the FIMR/HIV Community Action Team to evaluate the efficacy of legislation regarding third trimester testing, and the surveillance unit has been working with Medicaid to analyze screening data of pregnant women since the policy change in 2014. While reporting of HIV and syphilis during pregnancy remains a problematic, the program has made several efforts to improve provider reporting, (e.g. including the form in provider education packets and increased provider outreach through field staff.) Enhanced outreach is needed to improve timely reporting of disease during pregnancy and increase prevention efforts of perinatal transmission.

Discussion

As described above, various states and District of Columbia have adopted individual approaches to tackle perinatal HIV prevention. Some, such as New York State and Illinois, created a strong legislative and regulatory environment favoring HIV testing and treatment during pregnancy and in newborns. Others adopted more decentralized approaches with local HIV programs taking on various consulting and coordinating tasks within the prevention cascade. Each state and District of Columbia, however, has recognized the importance of strong surveillance programs, cohesive and coordinated action, and social and financial support for these programs to improve maternal HIV care and prevent pediatric infections. On the national level, lessons learned pointed to the need for knowledge and communication between states and regions on perinatal HIV issues. The NIH sponsored meeting served as a platform for the exchange of best practices and regional approaches to managing perinatal HIV; such exchanges should facilitate efforts to reach elimination of perinatal HIV transmission in the United States.

While there have been impressive gains in prevention of perinatal HIV transmission in the United States since the beginning of the epidemic, remaining gaps dictate the need to accelerate efforts to achieve elimination of perinatal HIV at the national level.

For the past decade, United States perinatal HIV guidelines have recommended nucleic acid testing (NAT) at 14–21 days of life for infants born to women living with HIV, with additional NAT testing at birth for infants at high risk for perinatal HIV[36]. Use of postpartum zidovudine with or without additional ARVs depending on the HIV exposure risk has become a recommended postpartum approach to the management of the HIV-exposed newborn. However, the 2013 report of “functional cure” case in an infant in Mississippi following initiation of combination triple ART at therapeutic doses within 30 hours of birth has put a new spotlight on the postpartum management of the infants with high risk exposures[37, 38]. The prolonged “remission” without ART in a Mississippi case pointed to potential benefits of very early initiation of combination ART including a reduction in the size the viral reservoir with intense treatment following the establishment of the infection[38]. The events of the “Mississippi baby” have not only led to promising research efforts but have also had an impact on clinical guidelines and practice in the United States and elsewhere. National experts report that physicians across the USA are increasingly doing diagnostic testing of high risk infants at birth, and some start postnatal ART rapidly within hours after birth, treating high-risk infants “presumptively” with doses ranging from those

used for prophylaxis to doses used for treatment while test results are pending[36,39, 40]. Currently, however, this approach and practice are challenged by the limited availability of appropriate ARV formulations for infants and the lack of data to inform dosing guidelines for those younger than 2 weeks of age[36]. Safety data, pharmacokinetic data, and appropriate ARV formulations for the newer more potent ARVs are critically needed for postpartum HIV prevention and treatment of neonatal HIV not only globally, but in the USA as well. Recent approval (2017) of the first integrase inhibitor raltegravir for neonatal use is promising; however, experience in clinical practice remains limited. These needs have prompted a number of important studies and clinical trials for a several ARVs and as well as the development of the formulations for newborns and young infants[41, 42, 43, 44].

Research is currently underway to optimize HIV treatment and prevention in neonates. In the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network study P1115, HIV-infected neonates are treated with an intensified 4-drug ART regimen to reach plasma HIV RNA suppression, and ART cessation is considered at ~2 years of age to assess for potential for remission[45]. P1115 study is generating important data about the pharmacokinetics of nevirapine in the first weeks of life and the dynamics of the latent viral reservoir in infancy[46]. Similar studies evaluating outcomes of very early ART on HIV reservoirs and potential for HIV remission are funded by the NIH and are in progress in several international settings[47, 48].

In the United States Treating Infants Early Study (TIES), also funded by NIH, aims to assess the safety and virologic outcomes of very early ART[49]. Recognizing that many clinicians are initiating infants with HIV on ART within the first days of life, frequently using off label investigational doses or regimens of ARV drugs outside of current guidelines, TIES is enrolling infants with HIV within community settings throughout the United States. With well-characterized clinical histories and banked specimens, children in the TIES cohort will also be candidates for future studies of remission or treatment reduction strategies.

Infants with HIV in the United States should have access to the best available therapies and to potentially curative interventions. In addition to studies supporting a biomedical research agenda, more implementation research, including research examining ongoing prevention practices and uptake of individualized care models for high risk pregnancies is needed to identify best practices in perinatal HIV elimination in the United States.

Conclusion

The dramatic reduction of perinatal HIV transmission is one of the most remarkable achievements in the history of the HIV epidemic. Since the first cases of pediatric AIDS were recognized in the USA more than thirty years ago, the collaborative efforts of scientists, clinicians, policy makers and community members have expedited the path from scientific discovery to clinical practice, bringing us to the threshold of perinatal HIV elimination. Throughout the United States most pregnant women now have access to HIV testing and safe and efficacious ART that benefits their own health and prevents perinatal HIV transmission. Similarly, HIV-exposed infants have access to timely diagnostic testing and effective ART. Although the United States has not yet achieved the targets for perinatal

HIV elimination, a precedent for HIV elimination has been set in some states and lessons learned from these successes need to be utilized in other regions.

Elimination of perinatal HIV in the United States is not a one-time event and reaching and sustaining this target will require continued persistent financial and logistic support. Repeat HIV testing during pregnancy, coordination of perinatal HIV services, and implementation and maintenance of perinatal HIV surveillance systems are critical to ensure continued success preventing new perinatal HIV infections. It is particularly critical when reaching the most vulnerable populations of women who face challenges such as substance abuse, disengagement from HIV care or have acquired HIV infection during pregnancy. National collaboration and research must continue to optimize ART strategies for mothers and infants, including studies aimed to achieve a cure as the goal of HIV elimination. Concerted coordinated efforts by scientists, care providers, policy makers, and communities will be required to maintain focus on improving identification, surveillance and prevention of HIV infection in pregnant women and their infants to achieve a once unthinkable goal of elimination of perinatal HIV infection in the United States.

Acknowledgments

We express our gratitude to Arthur Stone, Scientific Writer, NIAID, who provided scientific writing for the workshop; and to Anitra Denson. MD, MPH, Perinatal Coordinator HIV/AIDS, Hepatitis, STD and TB Administration, DC Department of Health; Cheryl Ward, Department of Health, Illinois, and Pascale Wortley, Department of Public Health, Georgia, for their reviews.

Drs. Devasena Gnanashanmugam and Natella Rakhmanina have led writing of the manuscript. Drs. Keith Crawford, Steve Nesheim and Elaine Abrams provided significant contribution to the design of this paper, the key themes and messages to convey, and to the design and execution of the workshop from which the material arises. These authors also provided significant critical review of all the data arising from the states and regions within the US and intellectual content for the paper. All authors above approve of the manuscript and agree to be accountable for all aspects of the work related to its accuracy or integrity.

Drs. Patrick Jean-Philippe, Lakshmi Jayashankar, Patricia D'Souza, Joseph Fitzgibbon, Keith Crawford, and Rohan Hazra all provided substantial contributions to the design of material in this submission, the key themes and messages to be conveyed, and to the design and execution of the workshop from which the material arises. These authors also contributed to providing content for this paper and to significant critical review. All authors above approve of the manuscript and agree to be accountable for all aspects of the work related to its accuracy or integrity.

Drs. Theodore Ruel, Guthrie Birkhead, Rana Chakraborty, Robert Lawrence, Anne Statton, Ashley Hoover, Barbara Warren and Somer Smith all provided critical regional content for this work reflecting practices and challenges in perinatal HIV prevention within the United States. All authors listed here contributed to drafting the manuscript. All authors above approve of the manuscript and agree to be accountable for all aspects of the work related to its accuracy or integrity.

Sources of support: No funding was secured for this study.

Reference List

1. Little KM, Taylor AW, Borkowf CB, et al. Perinatal Antiretroviral Exposure and Prevented Mother-to-child HIV Infections in the Era of Antiretroviral Prophylaxis in the United States, 1994–2010. Pediatr Infect Dis J. 2017;36(1):66–71. [PubMed: 27749662]
2. Lindegren ML, Byers RH,, Jr., Thomas P, et al. Trends in perinatal transmission of HIV/AIDS in the United States. JAMA. 1999;282(6):531–538. [PubMed: 10450714]
3. Taylor AW, Nesheim SR, Zhang X, et al. Estimated Perinatal HIV Infection Among Infants Born in the United States, 2002–2013. JAMA Pediatr. 2017;171(5):435–442. [PubMed: 28319246]

4. Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data - United States and 6 dependent areas. HIV Surveill Suppl Rep. 2018;23(4):1–51.
5. U.S. Public Health Service recommendations for human immunodeficiency virus counseling and voluntary testing for pregnant women. MMWR Recomm Rep. 1995;44(RR-7):1–15.
6. Feinberg MB. Report of the NIH panel to define principles of therapy of HIV infection. Morbidity and Mortality Weekly Report: Recommendations and Reports. 1998:iv–38.
7. Committee on Obstetric Practice. ACOG committee opinion scheduled Cesarean delivery and the prevention of vertical transmission of HIV infection. Number 234, May 2000 (replaces number 219, August 1999). Int J Gynaecol Obstet. 2001;73(3):279–281. [PubMed: 11424912]
8. Recommendations for assisting in the prevention of perinatal transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus and acquired immunodeficiency syndrome. MMWR Morb Mortal Wkly Rep. 1985;34(48):721–726, 731–722. [PubMed: 2999576]
9. Nesheim S, Taylor A, Lampe MA, et al. A framework for elimination of perinatal transmission of HIV in the United States. Pediatrics. 2012;130(4):738–744. [PubMed: 22945404]
10. Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2014. HIV Surveillance Supplemental Report. 2016;21(4).
11. Whitmore SK, Zhang X, Taylor AW, Blair JM. Estimated number of infants born to HIV-infected women in the United States and five dependent areas, 2006. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2011;57(3):218–222. [PubMed: 21372725]
12. Centers for Disease Control and Prevention. Pediatric HIV Surveillance. 2017; https://www.cdc.gov/hiv/pdf/library/slidesets/cdc-hiv-surveillance-pediatric.pdf. Accessed 10 April 2018.
13. Nesheim SR, FitzHarris LF, Lampe MA, Gray KM. Reconsidering the Number of Women With HIV Infection Who Give Birth Annually in the United States. Public Health Rep. 2018:33354918800466.
14. Nesheim SR, Wiener J, Fitz Harris LF, Lampe MA, Weidle PJ. Brief Report: Estimated Incidence of Perinatally Acquired HIV Infection in the United States, 1978–2013. J Acquir Immune Defic Syndr. 2017;76(5):461–464. [PubMed: 28991886]
15. Nesheim SR, Linley L, Gray KM, et al. Country of Birth of Children With Diagnosed HIV Infection in the United States, 2008–2014. J Acquir Immune Defic Syndr. 2018;77(1):23–30. [PubMed: 29040167]
16. Brady KA, Storm DS, Naghdi A, Frederick T, Fridge J, Hoyt MJ. Perinatal HIV Exposure Surveillance and Reporting in the United States, 2014. Public Health Rep. 2017;132(1):76–84. [PubMed: 28005487]
17. Nicholas SW, Abrams EJ. Boarder babies with AIDS in harlem: lessons in applied public health. Am J Public Health. 2002;92(2):163–165. [PubMed: 11818282]
18. Novick LF, Glebatis DM, Stricof RL, MacCubbin PA, Lessner L, Berns DS. Newborn seroprevalence study: methods and results. Am J Public Health. 1991;81 Suppl:15–21.
19. Birkhead GS, Pulver WP, Warren BL, et al. Progress in prevention of mother-to-child transmission of HIV in New York State: 1988–2008. J Public Health Manag Pract. 2010;16(6):481–491. [PubMed: 20885177]
20. Birkhead GS, Klein SJ, Warren BL, et al. Program and policy interventions for preventing mother-to-child transmission of HIV in New York State. J Public Health Manag Pract. 2010;16(6):492–504. [PubMed: 20885178]
21. Laufer FN, Warren BL, Pulver WP, Smith LC, Wright RL, Birkhead GS. Return on Investment From Expenditures Incurred to Eliminate Mother-To-Child Transmission Among HIV-Infected Women in New York State: 1998–2013. J Acquir Immune Defic Syndr. 2016;71(5):558–562. [PubMed: 26974414]
22. NYC HIV Epidemiology and Field Services Program. Perinatal HIV in New York City, 2016. 2017; https://www1.nyc.gov/assets/doh/downloads/pdf/dires/hiv-in-peds.pdf. Accessed 21 April 2018.
23. Illinois General Assembly. Perinatal HIV Prevention Act 140 ILCS 335. 2003 http://www.ilga.gov/legislation/ilcs/ilcs3.asp?ActID=2483&ChapterID=35. Accessed 16 May 2018.

24. Pediatric AIDS Chicago Prevention Initiative. 24/7 Illinois Perinatal HIV Hotline. 2016; http://www.hivpregnancyhotline.org/. Accessed 16 May 2018.
25. Annual Epidemiology & Surveillance Report, 2016 Government of the District of Columbia, Department of Health; 2017 https://dchealth.dc.gov/page/2016-hahsta-annual-reports. Accessed May 16, 2018.
26. Bureau of Surveillance and Epidemiology- HIV/AIDS Administration; District of Columbia Department of Health. District of Columbia HIV/AIDS Epidemiology Annual Report. 2007.
27. Ellenberger NGC, Hussein N, Ferrer K, Matulich A, Chamma N, Rakhmanina N. . Prevention of mother-to-child transmission of HIV in an urban area of the USA: are we doing too much. Paper presented at: 9th IAS Conference on HIV Science; July 2017, 2017; Paris, France Paper presented as poster abstract 4695.
28. Centers for Disease Control and Prevention. HIV Surveillance Report, 2015. 2016;27 http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Accessed 16 May 2018.
29. Georgia Department of Public Health. HIV/AIDS Epidemiology Section HIV Surveillance Summary, Georgia 2014. Available at: https://dph.georgia.gov/data-fact-sheet-summaries [Accessed 16 May 2018].
30. Camacho-Gonzalez AF, Kingbo MH, Boylan A, Eckard AR, Chahroudi A, Chakraborty R. Missed opportunities for prevention of mother-to-child transmission in the United States. AIDS. 2015;29(12):1511–1515. [PubMed: 26244391]
31. Smith SL, Chahroudi AM, Camacho-Gonzalez AF, Gillespie S, Wynn BA, Badell ML, et al. Evaluating facility infrastructure for prevention of mother-to-child transmission of HIV- a 2015 assessment of major delivery hospitals in Atlanta, Georgia. J Pediatric Infect Dis Soc 2018; 7(3): e102–e106. [PubMed: 29986059]
32. Florida Department of Public Health. Epidemiology of HIV Among Pediatric Cases in Florida through, 2014. 2014; http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/_documents/hiv-aids-slide-sets/2014/peds-2014-2.pdf. Accessed 16 May 2018.
33. Centers for Disease Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Morb Mortal Wkly Rep. 2006;55(RR14): 1–17.
34. Trepka MJ, Mukherjee S, Beck-Sague C, et al. Missed Opportunities for Preventing Perinatal Transmission of Human Immunodeficiency Virus, Florida, 2007–2014. South Med J. 2017;110(2): 116–128. [PubMed: 28158882]
35. State of Louisiana DOH, Office of Public Health. 2014 STD/HIV Surveillance Report. http://new.dhh.louisiana.gov/assets/oph/HIVSTD/2014_STDHIV_SURVEILLANCE_REPORT.pdf. Accessed 16 May 2018.
36. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. 2018 Available at: https://aidsinfo.nih.gov/guidelines/html/3/perinatal/0 [Accessed 16 May 2018].
37. Persaud D, Gay H, Ziemniak C, et al. Absence of detectable HIV-1 viremia after treatment cessation in an infant. N Engl J Med. 2013;369(19):1828–1835. [PubMed: 24152233]
38. Luzuriaga K, Gay H, Ziemniak C, et al. Viremic relapse after HIV-1 remission in a perinatally infected child. N Engl J Med. 2015;372(8):786–788. [PubMed: 25693029]
39. Persaud D, Deveikis A, Gay H, et al. Very early combination antiretroviral therapy in perinatal HIV infection: Two case studies. Paper presented at: Conference on Retroviruses and Opportunistic Infections 2014; Boston, MA Paper presented as oral abstract 75LB.
40. Bitnun A, Samson L, Chun TW, et al. Early initiation of combination antiretroviral therapy in HIV-1-infected newborns can achieve sustained virologic suppression with low frequency of CD4+ T cells carrying HIV in peripheral blood. Clin Infect Dis. 2014;59(7):1012–1019. [PubMed: 24917662]
41. Capparelli E, Maswabi K, Rossi S, et al. Nevirapine (NVP) concentrations in HIV-infected newborns receiving therapeutic dosing. Poster abstract 815: Conference on Retroviruses and Opportunistic Infections 2016; Boston, MA.

42. Acosta E, Clarke D, Chain A, Cababasay MP. Raltegravir (RAL) pharmacokinetics (PK) and safety in HIV-1 exposed neonates at high risk of infection (IMPAACT P1110). Paper presented at: 8th International Workshop on HIV Pediatrics 2016; Durban, South Africa.

43. Lau E, Brophy J, Samson L, et al. Nevirapine Pharmacokinetics and Safety in Neonates Receiving Combination Antiretroviral Therapy for Prevention of Vertical HIV Transmission. J Acquir Immune Defic Syndr. 2017;74(5):493–498. [PubMed: 28114187]

44. Clarke DF, Acosta EP, Chain A, et al. E. Raltegravir pharmacokinetics and safety in HIV-1 exposed neonates: dose-finding study. Conference on Retroviruses and Opportunistic Infections; 2017; Seattle, WA Paper presented as poster abstract 757.

45. United States National Institutes of Health. IMPAACT P1115: Very Early Intensive Treatment of HIV-Infected Infants to Achieve HIV Remission: A Phase I/II Proof of Concept Study. https://clinicaltrials.gov/ct2/home Accessed May 16, 2018.

46. Qin M, Chadwick EG, Bryson Y, Mirochnik M. Establishing a treatment dose of Nevirapine (NVP) for full-term neonates with perinatal HIV infection: IMPAACT P1115. Paper presented at: AIDS 2016; Durban, South Africa.

47. BHP Early Infant Treatment Study: A Clinical Treatment Trial of HIV+ Infants in Botswana. https://clinicaltrials.gov/ct2/home. Accessed May 16, 2018.

48. United States National Institutes of Health. Latency and Early Neonatal Provision of Antiretroviral Drugs Clinica Trial (LEOPARD). https://clinicaltrials.gov/ct2/home. Accessed May 16, 2018.

49. The Regents of the University of California. Treating Infants Early Study (TIES). 2015; http://ties.ucsf.edu/. Accessed 4 February 2018.

Table1.

Summary of perinatal HIV preventive services as described by state and regional case studies (incudes 5 states and District of Columbia)

State/District	Perinatal HIV Rates[1]	Major Interventions that Shaped PMTCT Services	Challenges
New York State	0–1.3 per 100,000 live births[2]	Implementation of the Pediatric HIV Diagnostic Testing Service (1995) Un-blinding the newborn dried blood spot HIV test results with active public health follow-up of HIV-exposed infants (1997) Regulations for expedited HIV testing at delivery for all women without a prenatal HIV test (1999) Recommendations for repeat testing in the third trimester to identify women with seroconversion during pregnancy (2007)	Security of the financial and political support for universal newborn DBS screening and other related programs
Illinois	2–4 per 100,000 live births	State law mandating the counseling and offering of a rapid HIV test at delivery to women without a documented HIV test result during the current pregnancy (2003) Expansion of the state law to mandate HIV testing of all infants born without a documented maternal HIV test result without parental consent (2007) Implementation of Perinatal HIV Hotline (2007)	Practical implementation of the 3rd trimester testing
District of Columbia	4–16 per 100,000 live births	Introduction of name-based HIV reporting (2006) Recommendations for repeat HIV screening during the 3rd trimester and rapid HIV screening during/ after the labor for mothers and infants with unknown status or lack of repeat testing in pregnancy (2008) Mandatory reporting of pregnancies in women living with HIV (2013)	Identification and management of high risk pregnancies
Georgia	4–16/ per100,000 live births	Perinatal HIV Services Coordination (PHSC) program to close gaps in the perinatal HIV care continuum (2015) PHSC program focused on birth facilities in the Atlanta Metropolitan Statistical Area, with a plan to expand to rural Georgia. Objectives of the program include provision of ARVs, promotion of perinatal HIV exposure reporting, education of providers and evaluation of institutional infrastructure (ongoing)	Sustainability of the perinatal HIV surveillance Implementation of HIV prevention programs in hospitals statewide
Florida	4–16 per 100,000 live births	Florida DOH surveillance reporting of deliveries to women living with HIV within 24 hours days of delivery (2006) Baby Rxpress Program for postpartum zidovudine prophylaxis at no cost to families and Children's Medical Services Pediatric HIV Referral Centers (2006) Retrospective review of de-identified data from the Enhanced HIV/Acquired Immune Deficiency Syndrome (AIDS) Reporting System by DOH (2016)	Scaling up HIV testing, HIV surveillance, Antenatal care for high risk pregnancies Implementation of repeat HIV testing in 3rd trimester
Louisiana	4–16/ per100,000 live births	Perinatal HIV exposure surveillance as part of the Louisiana STD/HIV (1999) Enhanced Perinatal Surveillance program (2011)	Improvement in access to ART for perinatal prevention Expansion of the enhanced perinatal HIV surveillance

[1] Estimated Rate of Perinatal HIV from 2010–2013. Source: Taylor AW, Nesheim SR, Zhang X, et al. Estimated Perinatal HIV Infection Among Infants Born in the United States, 2002–2013. JAMA Pediatr. 2017;171(5):435–442.

[2] Personal commination with Guthrie Birkhead, MD, MPH, Professor Emeritus, Department of Epidemiology and Biostatistics, School of Public Health, University at Albany