A Framework for Elimination of Perinatal Transmission of HIV in the United States

An abstract

The availability of effective interventions to prevent mother-to-child HIV transmission and the significant reduction in the number of HIV-infected infants in the United States have led to the concept that elimination of mother-to-child HIV transmission (EMCT) is possible. Goals for elimination are presented. We also present a framework by which elimination efforts can be coordinated, beginning with comprehensive reproductive health care (including HIV testing) and real-time case-finding of pregnancies in HIV-infected women, and conducted through the following: facilitation of comprehensive clinical care and social services for women and infants; case review and community action; allowing continuous quality research in prevention and long-term follow-up of HIV-exposed infants; and thorough data reporting for HIV surveillance and EMCT evaluation. It is emphasized that EMCT will not be a one-time accomplishment but, rather, will require sustained effort as long as there are new HIV infections in women of childbearing age. Pediatrics 2012;130:1–7

AUTHORS: Steven Nesheim, MD,a Allan Taylor, MD, MPH,a Margaret A. Lampe, RN, MPH,a Peter H. Kilmarx, MD,a Lauren Fitz Harris, MPH,a,k Suzanne Whitmore, DrPH,a Judy Griffith, RN, MS,a Melissa Thomas-Proctor, MS,a Kevin Fenton, MD, PhD,a and Jonathan Mermin, MD, MPHa

aCenters for Disease Control and Prevention, National Center for Viral Hepatitis, HIV/AIDS, Sexually-Transmitted Disease and Tuberculosis Prevention, Division of HIV/AIDS Prevention, Atlanta, Georgia; and bAssociation of Schools of Public Health, Washington DC

KEY WORDS
elimination, HIV, mother-to-child, perinatal, transmission

ABBREVIATIONS
ARV—antiretroviral
CDC—Centers for Disease Control and Prevention
EMCT—elimination of mother-to-child transmission
FMR—Fetal and Infant Mortality Review
MCT—mother-to-child transmission
PHSC—Perinatal HIV Services Coordination
PMTCT—prevention of mother-to-child transmission

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-0194

doi:10.1542/peds.2012-0194

Accepted for publication May 23, 2012

Address correspondence to Steven Nesheim, MD, DHAP/NCHHSTP, Centers for Disease Control and Prevention, MS E-45, 1600 Clifton Rd, Atlanta, GA 30333. E-mail: sxn9@cdc.gov

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2012 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.
The reduction of perinatal transmission of HIV in the United States and many other areas of the world is a success story of the HIV epidemic. Policies directed at identification of HIV-infected pregnant women have been essential to efforts to prevent mother-to-child transmission (MCT) of HIV, beginning in the United States with the recommendation in 1985 for testing of high-risk women and avoidance of breastfeeding by HIV-infected mothers. With the increasing scope of testing recommendations and refinements in the use of antiretroviral (ARV) agents in pregnant women, the estimated annual number of HIV-infected infants has declined substantially, but transmissions continue to occur. Most new infections are attributable to failures to perform well-established interventions (ie, “missed opportunities”). The improved implementation of these interventions would further reduce the annual number of infections. This article outlines a framework to improve the prevention of mother-to-child transmission (PMTCT) of HIV, advocating the goal of elimination of mother-to-child transmission (EMCT) in the United States.

**SCOPE OF THE PROBLEM**

The rate of perinatal transmission of HIV in the absence of intervention during the prenatal period or labor and delivery is estimated at 18% to 32%. With the introduction of combination ARV therapies in the late 1990s, and the use of elective cesarean delivery, when appropriate, the number of perinatally infected infants with AIDS declined by >95%. Rates of perinatal HIV transmission have been reduced to <2% in other industrialized countries. In the United States, the annual number of estimated perinatal HIV infections peaked in 1991 at 1650 and declined sharply thereafter, with an estimated transmission rate of 2.2% of HIV-exposed infants born in the 15 US sites conducting the Enhanced Perinatal HIV Surveillance system during 2005–2008. Studies demonstrate mother-to-child transmission rates <1% when non-breastfeeding women and infants receive all appropriate PMTCT interventions and women’s plasma HIV viral load is suppressed to undetectable levels. Nationwide, an estimated 151 perinatally infected infants were born in 2008.

Infants in the United States continue to be infected with HIV at a time when perinatal transmission could theoretically be further reduced given the known efficacy of available interventions. Every perinatal HIV infection represents a sentinel public health event, often indicating a woman whose HIV infection was undiagnosed before or during pregnancy, who received no or inadequate prenatal care, or who failed to receive other appropriate interventions to prevent transmission of the virus to her infant. Opportunities to prevent infant HIV infection thus encompass much of the breadth of women’s and perinatal health, and these factors comprise a series of events known as the Perinatal HIV Prevention Cascade (Table 1). Data from the Pediatric Spectrum of Disease study demonstrated that more than one-half of infant infections (56%) between 1996 and 2000 were associated with receipt of suboptimal prevention interventions. More recent data from the Enhanced Perinatal HIV Surveillance system of the Centers for Disease Control and Prevention (CDC), which includes data on the pregnancies of HIV-infected women, indicate that 1 or more missed opportunities were present in 74% of infected infants, compared with 52% of uninfected infants, and more than one-half of infant infections were attributable to missed opportunities. In theory, some of the continued transmissions could be due to issues not addressed in the Perinatal HIV Prevention Cascade (eg, maternal acute infection during pregnancy, ARV resistance, but there is minimal evidence to support this proposition. Given the known effectiveness of preventive interventions from the preconception period through an infant’s first year of life, it is likely that most of the remaining ongoing perinatal HIV transmissions in the United States are attributable to program elements that can be improved. With such improvement, it should be possible to further reduce HIV MCT in the United States.

Substantial challenges remain. Particular attention needs to be given to the first element in the Perinatal HIV Prevention Cascade; that is, prevention of HIV infection in women and girls of childbearing potential, especially African-American and Hispanic women. Heterosexual transmission remains the principal source of exposure among HIV-infected women. An important recent step forward in this area was the demonstration in 2011, by study 052 of the HIV Prevention Trials Network, that early ARV treatment of HIV-infected men and women can reduce

**TABLE 1** Cascade of Events for the Successful Prevention of MCT of HIV

- Prevention of HIV infection in women and girls of childbearing potential
- Identification of infection among women of childbearing potential
- Assurance of adequate preconception care and family planning services for HIV-infected women
- Early identification of HIV infection of pregnant women through universal prenatal screening
- Provision of adequate prenatal care for women who have HIV infection
- Maximal reduction of maternal viral load through appropriate use of ARV drugs
- Cesarean delivery when maternal viral load is not maximally suppressed
- Provision of neonatal ARV prophylaxis
- Neonatal replacement feeding as well as maternal support for lactation suppression

Downloaded from by guest on April 14, 2017
transmission to heterosexual partners by 94%.18 Studies suggest that the higher rates of infection among African Americans in the United States are related to a number of social-factors, such as tight social and sexual networks, and poverty.19 The distribution of perinatal HIV infections demonstrates significant health inequity: African-American infants accounted for 69% of diagnoses of perinatal HIV infection in 2004–2007, although only 15% of infants are African American. The degree of health inequity seen in the perinatally infected population is even greater than that among adults and adolescents with HIV infection.20 Finally, the annual number of perinatal HIV exposures is even greater than that among adults and adolescents with HIV infection.20

In April 2008, the CDC sought expert consultation on preventing perinatal HIV transmission in the United States. Federal and state public health professionals, clinicians, researchers, and representatives of national professional organizations and advocacy organizations met over a 3-day period and discussed relevant data and potential new directions for PMTCT. After the meeting, action steps and an implementation plan were developed in a series of follow-up conferences. The consultants concluded that elimination of perinatal HIV transmission in the United States is possible and should be pursued.

**ELIMINATION OF HIV MCT IN THE UNITED STATES**

In April 2008, the CDC sought expert consultation on preventing perinatal HIV transmission in the United States. Federal and state public health professionals, clinicians, researchers, and representatives of national professional organizations and advocacy organizations met over a 3-day period and discussed relevant data and potential new directions for PMTCT. After the meeting, action steps and an implementation plan were developed in a series of follow-up conferences. The consultants concluded that elimination of perinatal HIV transmission in the United States is possible and should be pursued.

“Elimination” in this context might be defined in terms of overall incidence of perinatal HIV infection or MCT rate. Achieving zero cases of perinatal HIV infection would not be feasible as long as women of childbearing age continue to acquire HIV, and their infections sometimes remain unidentifed. In addition, some perinatal HIV transmission continues despite the use of recommended ARV prophylaxis and avoidance of breastfeeding. With the annual number of perinatal HIV infections in the United States estimated in the 100 to 200 range, a reduction of 1 order of magnitude was considered achievable by the consultants, which would yield an annual number considerably <100. We established elimination goals, including an incidence <1 infection per 100 000 live births and an MCT rate of <1% among HIV-exposed infants. With ~4.1 million live births and an estimated 8700 births to HIV-infected women (as estimated for 2006), these targets would be 41 and 87 cases, respectively. All jurisdictions will be able to estimate the incidence. The MCT rate can only be estimated in those jurisdictions that can determine the number of HIV-infected women giving birth annually (ie, HIV exposure). These 2 approaches provide different information (eg, MCT rate will vary with the number of HIV-infected women giving birth), and it is expected that the 2 numbers will not always increase or decrease in parallel within a jurisdiction. Note that both of the proposed goals would have been substantially less than the most recent estimate of 151 HIV-infected infants born in 2009.12

An effective set of tools to prevent perinatal HIV transmission has been identified. Some of the remaining transmissions may be the result of incomplete adherence by patients and providers, an issue that could be minimized through intensive case management for all pregnant women with
HIV infection. Assuring full implementation of the perinatal HIV prevention strategies for all HIV-infected pregnant women will result in fewer cases of HIV-infected infants. However, a major barrier to achieving that objective is that health departments in most jurisdictions in the United States do not currently have the resources or systems in place to identify HIV-infected pregnant women during the pregnancy (as opposed to after the birth of the infant) that would facilitate linkage with necessary services to optimize the woman’s health and prevent transmission. Given that the racial/ethnic disparities of HIV are striking in the perinatal epidemic, and given the social and medical morbidities afflicting minority communities, elimination of perinatal HIV transmission is a compelling challenge.

We developed a new framework directed at the goal of eliminating perinatal HIV transmission in the United States, using input during the consultation and over the ensuing months, as action steps and an implementation plan were developed. In line with the Office of National HIV/AIDS Policy National HIV/AIDS Strategy (http://www.whitehouse.gov/administration/eop/onap/nhas), this framework aims to reduce HIV incidence, increase access to care for HIV-infected individuals and optimize their health outcomes, decrease health disparities, and increase collaboration among federal agencies engaged in HIV prevention and care activities. The conceptual bases for the framework are that our current activities have brought us to all one way, the large majority of “ongoing” mother-to-child HIV transmission results from incomplete implementation of known efficacious interventions, and that improvement is possible in each intervention. The financial issues at all levels of government in recent years and the competing priority populations clearly restrain the amount of resources that can be devoted to EMCT. The emphases on women’s care and the concept that real-time “case-finding” is the identification of pregnancy in an HIV-infected woman are not new. What is new in the framework is the recognition that its interactions can perhaps bridge some of the financial gaps evident in our era and its recommended consistent use of public health personnel to assure the availability of programs to difficult-to-reach persons. What is also new is the recommendation of detailed review of select cases, with the goal of continuous quality improvement. This component was incorporated into the CDC’s recent HIV prevention cooperative agreement with health departments. Not only does the approach allow community discussions, which can lead to local systems change, but it also can serve as an important source of questions for implementation research. Implementation research will be necessary, regarding the degree of interactions, and the levels of governmental interaction (local, state, and federal) required to achieve the framework’s goals. Likewise, cost-related research will be necessary. No comprehensive estimate exists for the cost of existing PMTCT efforts, which involve complex expenditure by the Health Resources and Services Administration, the Centers for Medicare & Medicaid Services, the CDC, and state and local governments. With the lifetime cost of treating an HIV-infected infant estimated at $270,000, annual prevention of 100 additional cases prevents the expenditure of $27,000,000.

The framework is illustrated in Fig 1. Its twin foundations are: (1) to assure that HIV care includes comprehensive reproductive health, family planning and preconception care services and that women of childbearing age are tested for HIV according to CDC recommendations; and (2) to conduct comprehensive, real-time case finding of all HIV-infected pregnant women and their exposed infants. These 2 large tasks are conducted under the concept of Perinatal HIV Services Coordination (PHSC). As more women have access to HIV testing and are linked to HIV services, it is projected that a greater proportion of HIV-infected women will be identified before pregnancy. PHSC in each state (or jurisdiction) will assure comprehensive, real-time case finding early enough for appropriate intervention through linkage to care and services. PHSC would ideally occur in every jurisdiction, even if the burden of HIV during pregnancy is very small; in such jurisdictions, it may be helpful to have these functions combined with other related activities, such as the prevention of other perinatally acquired infections. With the financial realities facing all levels of government, and the fact that most HIV-infected pregnant women are, in fact, in care, it will not be possible, and may not be necessary, for PHSC to actively monitor each woman once it has been determined that she is in care. Conversely, for those women recognized as not in care, finding cases in real time would enable the conduct and coordination of the following components of the EMCT framework: facilitation of comprehensive clinical care and social services for women and infants; detailed review of select cases to identify and address missed prevention opportunities and local systems issues through continuous quality improvement (eg, consideration of every perinatal transmission of HIV as a sentinel event that prompts detailed case review and community action); research and long-term follow-up to develop and ensure safe and efficacious PMTCT interventions; and thorough data reporting for HIV surveillance and EMCT evaluation.
The framework also promotes and, to some extent, depends on interactions between the various components (eg, case review). Community action could change clinical services or improve data reporting, or clinical services could generate new areas in need of research and identify cases for review.

For purposes of this discussion, a “case” is a pregnancy in an HIV-infected woman. Case-finding includes active and passive identification of HIV-infected pregnant women. It requires both universal HIV testing (and reporting to the PHSC function) of pregnant women and a mechanism for detecting pregnancy among women with established HIV infection. It may be accomplished by laboratory-based reporting to the public health department, active case-finding by PHSC staff or disease-intervention specialists, direct reporting by providers (eg, through use of a perinatal HIV hotline), or other means.

The case-finding function will be distinct from traditional HIV surveillance. The use of surveillance data for program management is seen as an important concept, but there is significant variation among states in the degree to which surveillance-based data are usable for intervention. Traditional surveillance systems for perinatal HIV infection remain a critical function at local, state, and national levels for program planning and resource allocation. Surveillance systems will benefit from these more timely and more comprehensive case-identification activities if systems allow transfer of data between these systems.

Clinical management for HIV-infected pregnant women and their infants is credited with much of the documented reduction in perinatal HIV transmission; that is, it is clear that not all of the work described here will be performed by the PHSC. Local expertise in clinical care has been nurtured by the support for clinical activities provided by the Health Resources and Services Administration, under the Ryan White HIV/AIDS Program Act. In this discussion, the term “case management” includes guidance for and linkage to these clinicians, as well as other psychosocial and ancillary services that are necessary to overcome challenges in the very complex lives of women with HIV infection and pregnancy. Assuring these linkages for pregnant women with HIV infection will be a key function of the PHSC. Under the financial restraints of recent years, jurisdictions will need to determine the degree of their involvement with individual HIV-infected pregnant women. Recent national health care reform may enhance EMCT through reimbursement for preventive care and by facilitating access to care.

Looking at EMCT from a woman’s health perspective expands PMTCT activities into the area of reproductive decision-making. Furthermore, the emphasis on maintaining HIV-infected women in care between pregnancies underscores the need to test all women, as well as their partners, for HIV, regardless of their pregnancy status; only if women are identified can they be in care. Infected women will certainly be identified as testing is extended to more partners of known HIV-infected men. Reproductive decision-making by HIV-infected persons will also clearly include these female partners of HIV-infected men. Increased identification of HIV infection before pregnancy, and maintenance of more women in care would result in more opportunities to optimize HIV-infected women’s health before pregnancy, particularly with new treatment guidelines recommending ARV treatment at an earlier point in the disease. Proper attention to women’s HIV care will allow providers and patients to work to prevent unintended pregnancy. In the past, case-finding for PMTCT may have largely been conceptualized as HIV testing of pregnant women with unknown HIV status. The proportion of HIV-exposed pregnancies identified among women already in care will
increase as the proportion of HIV-infected women in care increases. Because missed opportunities for PMTCT are frequently the result of failures of local health systems, the CDC has worked with partners to develop a community-based, continuous quality improvement methodology. This methodology is modeled after the Health Resources and Services Administration–funded Fetal and Infant Mortality Review (FIMR) program and was demonstrated to be an effective tool to improve perinatal HIV prevention systems in 3 pilot communities. The CDC has since funded an FIMR–HIV Prevention Methodology National Resource Center and a limited number of community programs. With consent, this prevention methodology summarizes the experience from the mother’s perspective through an interview, and medical records are abstracted to assess in detail systems factors and individual factors that contribute to missed opportunities for PMTCT. Community action teams, composed of local leaders, implement the suggested system improvements, which are further assessed through subsequent case reviews. Because each case of perinatal transmission occurs in diverse and ever-changing communities and health care environments, it will be important to review and support local systems that serve HIV-infected women and their infants. Such systems improvements could also affect other perinatal infections (eg, hepatitis B infection, syphilis). In common with HIV, these infections are undergoing significant reductions in incidence, have effective biomedical interventions, and at least in the case of congenital syphilis, most often occur among women in lower-resourced areas. Investigating and improving these systems will likely benefit many HIV-uninfected women by improving maternal and child health services overall. In addition, coordination and integration of efforts to reduce other perinatal infections (eg, hepatitis B, syphilis) could be undertaken by the same personnel; such collaborations might be particularly advantageous in jurisdictions with fewer cases of 1 or more of these infections. A substantial proportion of women may be affected by >1 of the infections that share modes of transmission. In some jurisdictions, challenges such as distinct funding streams and local organizational structures will hinder such a collaborative approach.

To be fully effective, this approach to elimination will require ongoing research focused on the implementation of the known interventions, as well as identifying what proportion of ongoing transmission is attributable to factors not addressed in the Perinatal HIV Prevention Cascade. The PMTCT regimens used are always evolving and expose thousands of children to ARV medications every year. Research to monitor the long-term safety and efficacy of these interventions for both women and ARV-exposed children needs a long-term plan and sustained action. Ongoing monitoring and evaluation are also necessary because some policies have had limited uptake, such as repeat HIV testing of pregnant women during the third trimester. Benefits can be expected as these policies become more generally implemented. Elimination of perinatal HIV transmission will more likely be achieved if there is a high degree of coordination and active collaboration at local, state, and federal levels.

As long as there are new HIV infections in women of reproductive age, 100% “elimination” of HIV MTCT cannot be achieved. In the current phase of the epidemic, with low numbers of infants infected annually, one could predict that prevention of the annual “residual” cases will become increasingly difficult. We also note the example of the World Health Organization European region, which in 2005 adopted as a goal the elimination of perinatal transmission by 2010; with increasing numbers of cases attributed to new infections in drug-injecting women, this goal has been postponed to 2015. We propose that the current phase warrants a new approach to prevention of perinatal HIV transmission. This approach includes recognition that these cases represent some individuals who are among the most difficult to reach by clinicians, thus warranting an increased role for public health. In this approach, a focus on appropriate overall medical care for HIV-infected women is recognized as the best way to prevent HIV infection of infants. Finally, elimination of perinatal HIV transmission will not be accomplished simply by crossing a single threshold: every year, systems will be required to provide state-of-the-art prevention and care to an increasing population of HIV-infected women and HIV-exposed children.

REFERENCES


A Framework for Elimination of Perinatal Transmission of HIV in the United States

Steven Nesheim, Allan Taylor, Margaret A. Lampe, Peter H. Kilmarx, Lauren Fitz Harris, Suzanne Whitmore, Judy Griffith, Melissa Thomas-Proctor, Kevin Fenton and Jonathan Mermin

Pediatrics; originally published online September 3, 2012; DOI: 10.1542/peds.2012-0194

Updated Information & Services
including high resolution figures, can be found at:
/content/early/2012/08/28/peds.2012-0194

Citations
This article has been cited by 3 HighWire-hosted articles:
/content/early/2012/08/28/peds.2012-0194#related-urls

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2012 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
A Framework for Elimination of Perinatal Transmission of HIV in the United States

Steven Nesheim, Allan Taylor, Margaret A. Lampe, Peter H. Kilmarx, Lauren Fitz Harris, Suzanne Whitmore, Judy Griffith, Melissa Thomas-Proctor, Kevin Fenton and Jonathan Mermin

Pediatrics; originally published online September 3, 2012;
DOI: 10.1542/peds.2012-0194

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/early/2012/08/28/peds.2012-0194