

Ending Sexual HIV Transmission: Lessons Learned from Perinatal HIV

Q1 Shannon Weber, MSW,*
Robert M. Grant, MD, MPH

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Data presented at the 2015 Conference on Retroviruses and Opportunistic Infections (February, Seattle, WA) confirmed that oral emtricitabine/tenofovir used as preexposure prophylaxis (PrEP) for HIV infection was highly effective. The Ipergay and PROUD studies both demonstrated an 86% reduction in HIV incidence in men who have sex with men randomized to receive active drug (McCormack & Dunn, 2015; Molina et al., 2015). The HPTN 067 ADAPT trial showed that high levels of PrEP adherence occurred in a sample of young women (Bekker et al., 2015). The Partners Demonstration Project revealed near elimination (96% reduction) of sexual HIV transmission with an integrated approach offering antiretroviral therapy (ART) for an HIV-infected partner and PrEP for an HIV-uninfected partner (Baeten et al., 2015). In that study, there were only two HIV transmissions and neither had detectable drug levels at the time of HIV acquisition. Surveillance from San Francisco demonstrated that PrEP was scaling up, with 10% to 15% of men who have sex with men already taking PrEP, and that PrEP uptake was highest in people who would benefit the most (Grant et al., 2015). The San Francisco modeling suggested that a reduction in HIV transmission would be possible with countywide scale-up of PrEP, with a further reduction in incidence and higher rates of viral suppression. It is time to widely disseminate an integrated treatment and prevention paradigm to end HIV transmission.

The success of perinatal HIV prevention highlights possibilities for consideration in the broader HIV

epidemic. Widely heralded as one of the greatest public health successes in the United States, perinatal HIV transmissions declined from 1650 in 1991 to 151 by 2009, a greater than 90% reduction (Nesheim et al., 2012). Several interventions led to this success: (a) routine prenatal HIV screening, (b) rapid HIV testing during labor and delivery, (c) maternal ART and infant ART prophylaxis, and (d) infant replacement feeding. Vital work remains to maintain these successes and achieve the elimination of perinatally transmitted HIV (Nesheim, Harris, & Lampe, 2013).

While perinatal HIV prevention efforts have been unique, including a time-limited focus, special motivations to protect infants, and increased opportunities for intervention when pregnant women engage in care, some themes are shared by prevention of perinatal HIV transmission and sexual HIV transmission (Figure 1). Reviewing successes from perinatal HIV prevention can inform a collective strategy to end sexual HIV transmission (Table 1).

Integrated HIV Treatment and Prevention

The Perinatal HIV Prevention Cascade first proposed by the Institute of Medicine in 1998 (Stoto,

*Shannon Weber, MSW, is the Director of HIVE, San Francisco General Hospital, University of California, San Francisco, California, USA. (*Correspondence to: Shannon.Weber@ucsf.edu). Robert M. Grant, MD, MPH, is a Principal Investigator at Gladstone Institutes, Professor of Medicine at University of California, San Francisco, California, and Chief Medical Officer at San Francisco AIDS Foundation, San Francisco, California, USA.*

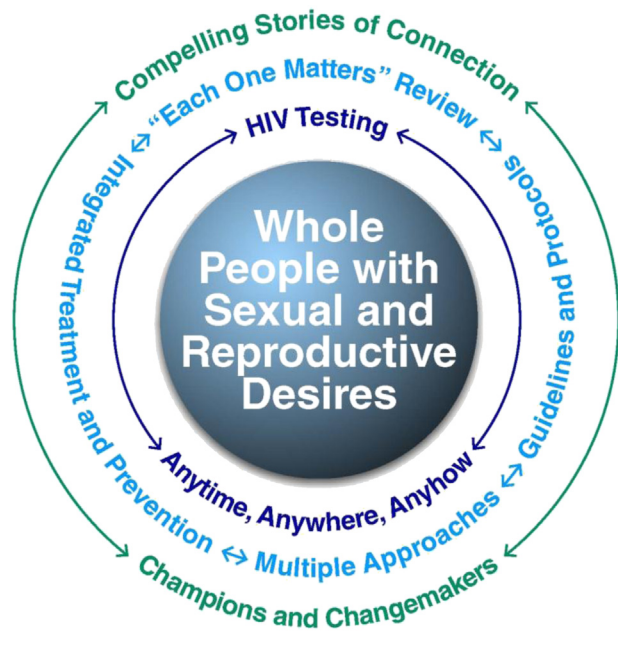


Figure 1. Ending sexual HIV transmission.

Almario, & McCormick, 1999) served as a guide for U.S. perinatal HIV stakeholders to develop the tools, interventions, and local infrastructure necessary to achieve a reduction in vertical HIV transmission. As knowledge evolved, the cascade was updated, integrating new technologies and interventions, providing a context for targeted efforts at national and local levels. In 2012, the Centers for Disease Control and Prevention (CDC) proposed a framework for the elimination of perinatal HIV transmission in the United States (Nesheim et al., 2012).

While the HIV treatment cascade has been widely discussed (Gardner, McLees, Steiner, Del Rio, & Burman, 2011) and the White House Executive Order on the HIV Care Continuum Initiative (White House Executive Order, 2013) began the broad conversation about gaps in the treatment cascade, these discussions did not include prevention components to fully realize the potential benefits of current behavioral and biomedical interventions. Treatment for prevention of perinatal HIV transmission necessarily combined with critical ancillary services for an integrated treatment and prevention approach. The successful elimination of sexual HIV transmission will most easily occur at the crossroads of treatment and prevention activities.

Embracing and Offering Multiple Approaches

The landmark AIDS Clinical Trials Group 076 trial demonstrated the benefits of reducing vertical transmission by providing zidovudine to pregnant women living with HIV and their HIV-exposed infants. The subsequent broad implementation of these findings dramatically decreased perinatal HIV transmission rates from 25% to 11% (Connor et al., 1994). Innovation is required to further reduce infections through routine HIV screening, access to prenatal care, and expanded and fully suppressive ART regimens.

Likewise, the end of sexual HIV transmission will require multiple approaches rather than championing one favored idea. Early treatment, pre- and postexposure prophylaxis, routine HIV testing, client-centered counseling, male and female condoms, serosorting (the adaptation of sexual practices based on HIV status), and negotiated safety all have important and complementary roles to play. Multiple ideas and people will foster an evolution of ideas and their dissemination.

Whole People With Reproductive and Sexual Desires

In 2002, the World Health Organization published a pioneering definition of sexual health:

Sexual health is a state of physical emotional, mental, and social wellbeing in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence. (World Health Organization, 2002, p. 5)

Consistent with this definition, the conversation in perinatal HIV shifted from prevention of vertical HIV transmission to a broader focus on women's health (Burr, Fry, Weber, Armas-Kolostroubis, & Lampe, 2009). Earlier identification of HIV, primary HIV prevention, preconception care, and safe conception options became priorities. Extending reproductive

Table 1. Applying Lessons Learned From Perinatal HIV Prevention

Perinatal HIV Prevention Strategy	Theme	Opportunities to Expand to Sexual HIV Prevention
The original cascade combined treatment and prevention strategies, iterating with new methods.	Integrated HIV treatment & prevention.	Develop an iterative framework integrating HIV treatment and prevention.
Rapidly implemented new perinatal HIV prevention methods with an eye toward zero transmissions.	Embracing & offering multiple approaches.	Create a menu of proven approaches and options.
Expanded view of perinatal HIV prevention to include women's reproductive and sexual health.	Whole people with sexual & reproductive desires.	Greater emphasis on planning to allow reproductive and sexual well-being to thrive. More emphasis on the impact of treatment and prevention for the whole person.
USPHS, ACOG, CDC guidelines.	Guidelines, association opinions, protocols.	Integrate treatment and prevention guidelines with capacity building, including provider and patient toolkits for implementation.
Leveraging the best treatment and prevention services when and where a woman presents for care.	HIV testing everywhere, anytime, anyhow.	Fully routinize HIV testing by eliminating interrogations and offering testing at all points of contact; point of care antigen and RNA tests.
Review of transmissions and missed opportunities: locally grown, individual review, listening to the woman.	"Each one matters" systemic review.	Enhanced engagement with newly diagnosed and long-term HIV-uninfected people, to understand resilience and opportunities for systems change.
Champions can make institutional change and are found in diverse roles.	Champions and change-makers are everywhere.	Support first followers who champion the end of HIV transmission; recognize leaders at all levels; grow community support to eliminate transmission.
Protecting infants from HIV is a compelling story that mobilized resources and people.	A compelling story.	Develop a compelling story about human connection; reproductive and sexual wellbeing are essential for fostering humanity.

Note. USPHS = U.S. Public Health Service; ACOG = American Congress of Obstetricians and Gynecologists; CDC = Centers for Disease Control and Prevention; RNA = ribonucleic acid.

health care to men living with HIV is the next step in realizing comprehensive sexual and reproductive care. Planning for success rather than coping with missed opportunities allows for an ongoing conversation about reproductive life planning rather than viewing vertical transmission only through the lens of pregnancy.

Adapting a whole person/whole health approach to sexual HIV transmission would shift our language to one of sexual wellness, not just an absence of disease, or condom utilization, or adherence to ART. This approach requires recognizing reproductive and sexual desires and sexual fulfillment as goals deserving support. This is not just about the science of eliminating

sexual HIV transmission, it is also about fostering sexual health, engaging with people, and leveraging the motivation to lead satisfying sexual lives.

Guidelines, Association Opinions, Protocols

National guidelines provide standards for excellent care, set the tone for reimbursement, and serve as the basis for training. Perinatal HIV stakeholders benefited from a dedicated guidelines committee that published frequently updated, data-driven guidelines, now available as a living document ([Panel on Treatment of HIV-Infected Pregnant Women and](#)

Prevention of Perinatal Transmission, 2014). Likewise, the American College of Obstetricians and Gynecologists and CDC publications of opinions and recommendations shifted the landscape and provided a template for standard of care (American College of Obstetricians and Gynecologists, 2014).

The International Antiviral Society - USA prevention practice recommendations and CDC PrEP guidelines have established a standard of care for PrEP provision (CDC, 2014; Murrain et al., 2014). Provider education, capacity building, and consultation services are necessary for practice to change. A mechanism for frequently updating integrated treatment and prevention best practices would rapidly disseminate new information from research and real-world settings.

HIV Testing Everywhere, Anytime, and Anyhow

Perinatal HIV prevention interventions are based on knowing a woman's HIV status. Routine first-trimester opt-out HIV testing or rapid testing at labor and delivery was recommended as part of the CDC's 2006 routine HIV testing guidelines (Branson et al., 2006). Additionally, scale up of rapid testing in labor and delivery brought training and a new technology to labor and delivery staff, expanding opportunities for women to test for HIV—providing testing whenever she presented for care, regardless of gestational age, and without questions about risk factors. In contrast, general HIV testing is not universally routine. Those without identified risk factors are not always screened, and some testing programs require questions about sexual practices and substance use before a test is offered (Zheng, Suneja, Chou, & Arya, 2014).

“Each One Matters” Systemic Review

A single perinatal HIV transmission is devastating, typically triggering a series of formal or informal reviews, changes to protocols, or additional training. In 2005, the Fetal Infant Mortality Review method was adapted for review of perinatal HIV transmissions and missed opportunities (Lampe, Buckley, Abresch, Carlson, & Fitz Harris, 2014). The abstracted chart review and maternal interview reviewed by a community action team are key to

the success of this initiative. Understanding the woman's experience of overlapping facilitators and barriers to maximize her and her child's health is invaluable.

Every HIV transmission could be considered a sentinel event. Those who remain uninfected (Pascale, Sternin, & Sternin, 2010) and those newly diagnosed with HIV have vital information to inform systems change. In many counties, case investigations are performed for new HIV infections, although the focus is on identifying recent sexual partners rather than opportunities to improve services. Investigating all of the 50,000 new HIV diagnoses in the United States would be a formidable task. However, local and regional review of people newly diagnosed with HIV, and some people who remain HIV uninfected, could make this possible.

Champions and Change-Makers are Everywhere

National and local perinatal HIV successes have champions: those who work beyond grant objectives and job descriptions. Champions can make institutional change and are found at any point of the perinatal HIV prevention cascade, perhaps in unexpected places—the front desk receptionist, physician, lab technician, social worker, and patients themselves. Champions for ending sexual HIV transmission are emerging, sometimes also in unexpected places. As in other fields of innovation, the first followers, or adopters (Sivers, 2010), have a key role in transforming a good idea into a social movement.

A Compelling Story

Saving infants from HIV infection is a compelling story. Perinatal HIV transmission continues to occur at an unacceptable rate, highlighting how the last mile is sometimes the most difficult: Sustaining enthusiasm until the goal is reached is a challenge. We now have the possibility of ending sexual HIV transmission—itsself a compelling story. Although sex and sexuality are, at times, ensnared in stigma and suspicion, we can reframe the story to include our shared desires for human connection. It is time to change the story from one of risk reduction to one of possibility.

Conclusion

Given recent advances in scientific knowledge made possible in partnerships between communities and researchers, now is the time to commit to ending HIV transmission. Perinatal HIV prevention has come a long way, with lessons that can be adapted to end sexual HIV transmission. A community-driven, iterative, and integrated treatment and prevention roadmap is needed to guide individuals, communities, and governments toward zero HIV transmissions. Lessons learned from prevention of perinatal HIV transmission can be adapted and applied to the prevention of sexual HIV transmission. At the core is an appreciation of whole people who have sexual and reproductive goals. Routine HIV testing should be made widely available and without strings attached. An integrated treatment and prevention framework with multiple approaches is supported by practice guidelines and protocols. A systematic review that regards every infection as preventable provides feedback to continuously update the integrated framework. Ultimately, success requires champions and change makers to mobilize around a compelling story of human connection.

Disclosures

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References

- American College of Obstetricians and Gynecologists. (2014). *Committee opinion: Preexposure prophylaxis for the prevention of human immunodeficiency virus*. Retrieved from <http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Gynecologic-Practice/Preexposure-Prophylaxis-for-the-Prevention-of-Human-Immunodeficiency-Virus>
- Baeten, J., Heffron, R., Kidoguchi, L., Mugo, N., Bukusi, E., Katabira, E., ... Celum, C. (2015). *Near elimination of HIV transmission in a demonstration project of PrEP and ART*. Paper presented at the conference on Retroviruses and Opportunistic Infections (CROI). Seattle, WA.
- Bekker, L.-G., Amico, R., Hughes, J., Roux, S., Hendrix, C., Anderson, P., ... Grant, R.M. (2015). *HPTN 067/ADAPT Cape Town: A comparison of daily and nondaily PrEP dosing in African women*. Paper presented at the Conference on Retroviruses and Opportunistic Infections (CROI). Seattle, WA.
- Branson, B., Handsfield, H., Lampe, M., Janssen, R., Taylor, A., Lyss, S., & Clark, J. (2006). *Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings*. Retrieved from <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>
- Burr, C. K., Fry, R. S., Weber, S., Armas-Kolostroubis, L. N., & Lampe, M. A. (2009). Integrating reproductive health into HIV care of women in the United States: It is time. *AIDS*, 23(14), 1928-1930.
- Centers for Disease Control and Prevention (CDC). (2014). *Pre-exposure prophylaxis for the prevention of HIV infection: A clinical practice guideline*. Retrieved from <http://stacks.cdc.gov/view/cdc/23109>
- Connor, E. M., Sperling, R. S., Gelber, R., Kiselev, P., Scott, G., & O'Sullivan, M. J. (1994). Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *New England Journal of Medicine*, 331(18), 1173-1180.
- Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clinical Infectious Diseases*, 52(6), 793-800.
- Grant, R.M., Lui, A., Hecht, J., Buchbinder, S., Weber, S., Cohen, S., ... Glidden, D. (2015). *Scale-up of pre-exposure prophylaxis in San Francisco to impact HIV incidence*. Paper presented at the Conference on Retrovirus and Opportunistic Infections (CROI). Seattle, WA.
- Lampe, M., Buckley, K., Abresch, C., Carlson, R., & Fitz Harris, L. (2014). *Fetal and infant mortality review (FIMR)/HIV prevention methodology: A community-based, case review approach to identify and address systems issues contributing to mother-to-child HIV transmission*. Paper presented at the 20th International AIDS Conference. Melbourne, Australia.
- Marrazzo, J. M., del Rio, C., Holtgrave, D. R., Cohen, M. S., Kalichman, S. C., Mayer, K. H., ... Benson, C. A. (2014). HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society-USA Panel. *Journal of the American Medical Association*, 312(4), 390-409.
- McCormack, S., & Dunn, D. (2015). *Pragmatic open-label randomised trial of pre-exposure prophylaxis: the PROUD study*. Paper presented at the Conference on Retroviruses and Opportunistic Infections (CROI). Seattle, WA.
- Molina, J.-M., Capitant, C., Charreau, I., Meyer, L., Spire, B., Pialoux, G., ... Tremblay, C. (2015). *On demand PrEP with oral TDF-FTC in MSM: Results of the ANRS Ipergay trial*. Paper presented at the Conference on Retroviruses and Opportunistic Infections (CROI). Seattle, WA.
- Nesheim, S., Harris, L. F., & Lampe, M. (2013). Elimination of perinatal HIV infection in the USA and other high-income

619	countries: Achievements and challenges. <i>Current Opinions</i>	681
620	<i>on HIV/AIDS</i> , 8(5), 447-456.	682
621	Nesheim, S., Taylor, A., Lampe, M. A., Kilmarx, P. H., Fitz	683
622	Harris, L., Whitmore, S., ... Mermin, J. (2012). A framework	684
623	for elimination of perinatal transmission of HIV in the United	685
624	States. <i>Pediatrics</i> , 130(4), 738-744.	686
625	Panel on Treatment of HIV-Infected Pregnant Women and Preven-	687
626	tion of Perinatal Transmission. (2014). <i>Recommendations for</i>	688
627	<i>the use of antiretroviral drugs in pregnant HIV-1 infected women</i>	689
628	<i>for maternal health and interventions to reduce perinatal HIV</i>	690
629	<i>transmission in the United States</i> . Retrieved from http://	691
630	aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0/	692
631		693
632	Pascale, R., Sternin, J., & Sternin, M. (2010). <i>The power of posi-</i>	694
633	<i>tive deviance: How unlikely innovators solve the world's</i>	695
634	<i>toughest problems</i> . Boston, MA: Harvard Business Review	696
635	Press.	697
636	Sivers, D. (2010). <i>How to start a movement</i> . TED conference.	698
637	Retrieved from http://www.ted.com/talks/derek_sivers_how_	699
638	to_start_a_movement?language=en	700
639		701
640	Stoto, M. A., Almario, D. A., & McCormick, M. C. (Eds.).	702
641	(1999). <i>Reducing the odds: Preventing perinatal transmis-</i>	703
642	<i>sion of HIV in the United States</i> . Retrieved from http://	704
643	www.nap.edu/openbook.php?record_id=6307&page=R1	705
644	White House Executive Order. (2013). <i>Accelerating improve-</i>	706
645	<i>ments in HIV prevention and care in the United States</i>	707
646	<i>through the HIV care continuum initiative</i> . Retrieved from	708
647	https://www.whitehouse.gov/the-press-office/2013/07/15/exe-	709
648	cutive-order-hiv-care-continuum-initiative	710
649		711
650	World Health Organization. (2002). <i>Defining sexual health:</i>	712
651	<i>Report of a technical consultation on sexual health</i> .	713
652	Retrieved from http://www.who.int/reproductivehealth/	714
653	publications/sexual_health/defining_sexual_health.pdf	715
654	Zheng, M. Y., Suneja, A., Chou, A. L., & Arya, M. (2014).	716
655	Physician barriers to successful implementation of US Pre-	717
656	ventive Services Task Force routing HIV testing recommen-	718
657	dations. <i>Journal International Association of Providers in</i>	719
658	<i>AIDS Care</i> , 13(3), 200-205.	720
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