## Cuba eliminates mother-to-child transmission of HIV and congenital syphilis: a call to action for the Americas Region

On June 30, 2015, the World Health Organization (WHO) validated Cuba as the first country in the world to eliminate mother-tochild transmission of HIV and congenital syphilis as public health problems. What makes this achievement especially laudable is that Cuba is a nation with limited economic resources. With an estimated Gross Domestic Product (GDP) of USD 9,900 (2010), Cuba ranks 114<sup>th</sup> of 230 nations on this global economic indicator<sup>(1)</sup>.

Following the 2007 launch by WHO of the global initiative on elimination of congenital syphilis as a public health problem, in 2010, the Pan American Health Organization (PAHO) initiated a regional strategy with the broader goal of dual *Elimination of Mother-to-Child Transmission of HIV and Congenital Syphilis* (i.e., "Generations Free of HIV and Syphilis")<sup>(2)</sup>. The Americas regional initiative supports the integration of HIV and syphilis screening programs in antenatal care and builds on more than 15 years of regional commitment towards congenital syphilis elimination<sup>(3,4)</sup>.

With no vaccine against either HIV or syphilis on the immediate horizon, what does it mean to eliminate mother to child transmission of HIV or syphilis "as a public health problem"? The rationale behind these initiatives takes into account that, for pregnant women with prevalent or new infections, highly effective interventions exist to prevent transmission from mother-to-child. Even when HIV or syphilis transmission continues at low levels within communities, if infections are detected and treated early in pregnancy, infants will be born free of the diseases<sup>(5)</sup>.

Syphilis is an old disease that has fallen off the radar screens of many providers and the funding streams of many health ministries despite the policies for systematic antenatal syphilis screening that exist in most nations<sup>(6)</sup>. However, syphilis continues to affect about 1.4 million pregnancies each year, including approximately 107,000 pregnancies in the Americas region<sup>(7,8)</sup>. Untreated syphilis in pregnancy is often devastating, resulting in an adverse pregnancy outcome in more than half of maternal infections<sup>(9,10)</sup>. Furthermore, since the overwhelming majority of syphilis infections in pregnancy are asymptomatic, many of the perinatal deaths caused by syphilis remain undiagnosed; they are "unexplained" stillbirths, neonatal deaths, or low birth weight infants.

Prevention of mother-to-child transmission of HIV (PMTCT) is a true public health success story. Since the 1994 landmark study proving that antiretroviral medications prevent perinatal HIV transmission, increasingly successful treatment regimens have been identified<sup>(11)</sup>. Today, using an evidence-based set of comprehensive interventions, HIV transmission from mother to child can be reduced to less than 1%<sup>(12)</sup>. The situation is even simpler for syphilis: for pregnant women with syphilis, a single maternal dose of 2.4 mu intramuscular penicillin before 20-24 weeks gestation can treat the fetus against *T. pallidum*, the causative agent of syphilis<sup>(9,10)</sup>. Both of these prenatal interventions are recommended by WHO as part of the basic antenatal care package and are national policy in most nations<sup>(6,13)</sup>. Antenatal HIV screening and treatment are affordable even for low income countries; and antenatal syphilis screening and treatment are almost universally cost-effective and even cost-saving in many countries<sup>(14,15)</sup>.

While integration of HIV and syphilis testing in the perinatal period seems an obviously beneficial approach on the surface, in real-world settings implementation has been more difficult to achieve than expected. HIV is a firmly established priority on the global health agenda, and national HIV programs are often sufficiently well-funded to be carried out to scale. However, the continued stigma associated with this infection, misconceptions about potential transmission risk (even among health providers), and "HIV exceptionalism" have made HIV screening a challenge, even in the context of PMTCT. Integration of PMTCT into routine antenatal services is often limited<sup>(16,17)</sup>. In some settings, lack of integration of the services has led to egregious missed opportunities for preventing perinatal mortality<sup>(18)</sup>.

Linking antenatal HIV and syphilis screening can be a "winwin" because HIV testing is normalized, leading to higher uptake, and syphilis testing and treatment are not overlooked in poorly funded or weakly coordinated programs<sup>(19)</sup>. The development of dual rapid tests for both syphilis and HIV on a single device is a recent innovation, and several such tests are already marketed. These dual syphilis/HIV tests allow testing for both infections with a single finger prick during the antenatal care visit; thus, if either test is positive, treatment can be initiated immediately. In addition to limiting patient loss to follow up, such tests are easy to use and interpret, and can save time for busy health providers<sup>(20)</sup>.

In addition to clinic based antenatal clinic services, eliminating MTCT of HIV and syphilis is supported by combined primary prevention of HIV and STIs at the community level and by reproductive health services for women. Equally important is national commitment, because fundamentally EMTCT is a policy issue that requires supportive leaders, continuing visibility, and ongoing justification for sufficient resources to sustain these basic programs. Country programs can benefit from guidance documents using approaches that are standardized and evidence-based. For example, PAHO has developed a set of operational tools to help countries working on the priority areas of data quality, program organization and services, appropriate attention to human rights, and laboratory quality. For the Americas, laboratory infrastructure continues to be challenging in some settings. A recent survey of laboratory directors from PAHO member countries found more than 30% of laboratories providing syphilis testing for antenatal care settings did not participate in an external quality control program, and about the same proportion did not have a national syphilis testing algorithm for pregnant women. Additionally, half of all participating laboratories serving antenatal clinics reported a stock-out of one or more essential reagents or supplies during the previous year<sup>(21)</sup>. To address this situation, PAHO, in collaboration with the Ministry of Health in Brazil and the Centers for Disease Control and Prevention (CDC), published in 2015 a guidance document on syphilis testing in Latin America and the Caribbean, aimed at improving uptake, interpretation and quality of syphilis testing in different clinical and laboratory settings(22).

The WHO and PAHO targets for EMTCT of HIV and syphilis are pragmatic rather than onerous, and focus on a platform of basic maternal and child health (MCH) services rather than vertically funded programs. In the Americas, our regional goals are that countries achieve case rates of < 50 congenital syphilis cases per 100,000 live births and < 30 perinatal HIV infections per 100,000 live births, as well as a perinatal HIV transmission rate < 2% (non-breast feeding populations) for at least 2 years. Programmatically, countries must provide compelling data that these benchmarks have been achieved by also providing at least two years of data supporting that more than 95% of pregnant women are screened for HIV and syphilis, and more than 95% of women testing positive are adequately treated, in both the public and private sectors. Countries must show that EMTCT has been achieved not only at the national level but also at the country's lowest performing subnational administrative unit. This helps ensure high coverage and quality of services even among hidden or higher-risk sub-populations in which pockets of MTCT may continue to occur. Countries are also encouraged to provide data indicating that overall STI/HIV prevention services are sufficiently strong to support low community prevalence of these infections. Such programs help ensure that women become aware of their infections prior to conception and can obtain supportive services to prevent MTCT, and that women (and their partners) do not become infected or re-infected during pregnancy.

WHO estimates that each year 350,000 babies die of syphilis infection and another 240,000 are perinatally infected with HIV, dooming most to an early death<sup>(6,23)</sup>. Most of these infections occurred among women who received antenatal care services, and about one in seven of these perinatal deaths occured in the Americas region<sup>(6)</sup>. That preventable infant mortality still occurs despite the existence of an effective and affordable public health intervention (i.e., early detection and prompt treatment) is unnerving and supports EMTCT of HIV and syphilis as an appropriate call to action. No public health elimination effort is easy. However, the validation of Cuba as the first country in the world to achieve EMTCT of HIV and syphilis demonstrates the potential for every country, regardless of income level, to achieve the targets set out by WHO and PAHO<sup>(24,25)</sup>. Cuba's success was realized on the back of its strong primary health care infrastructure, well synergized health systems, and large cadre of well-trained doctors and nurses providing basic health services, free-of-charge, for all. Cuba's organized data monitoring system tracking how well targets are met also played an essential role, as did its compliance with basic human rights principles and involvement with civil society organizations. Evidence-based clinical services, surveillance and data monitoring, program evaluation and continuous feedback, effective commodities distribution, and supportive laboratory infrastructure were all integral in supporting Cuba in achieving EMTCT. These basic public health tools can help other countries in the region achieve elimination.

EMTCT of HIV and congenital syphilis are aspirational goals, but the benefits are enormous and relevant for most countries in our region. Syphilis and HIV screening and treatment are markers of antenatal care quality; and improving quality of basic MCH services supports better maternal and infant outcomes beyond the prevention of perinatal HIV and syphilis. Higher screening coverage ensures services reach the most vulnerable and hidden women who often do not reach antenatal care and contribute disproportionately to poor infant and maternal outcomes. The initiative's demands for robust, high quality interventions, laboratory systems, and data are all necessary elements for any strong national health program. Supporting the dual elimination of MTCT of HIV and syphilis is a bold step in improving health services overall. Let us hope that Cuba is only the first country in the Americas Region to achieve and sustain elimination of MTCT of HIV and syphilis through prioritizing stronger MCH systems.

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## REFERENCES

- Countries of the World. GDP per capita country ranks (2013). Available at: http://www.photius.com/rankings/economy/gdp\_per\_capita\_2013\_0. html. Accessed in:
- Pan American Health Organization. Strategy and Plan of Action for the elimination of mother-to-child transmission of HIV and congenital syphilis. 50<sup>th</sup> Directing Council, 62<sup>nd</sup> Session of the Regional Committee. Resolution CD50.R12. Washington: PAHO; 2010.
- Pan American Health Organization. Regional HIV/STI plan for the health sector 2006-2015. Washington: PAHO; 2004.
- Pan American Health Organization. Plan of action for the elimination of congenital syphilis. Washington: PAHO; 1995.
- World Health Organization. The Global elimination of congenital syphilis: Rationale and strategy for action. Geneva: WHO; 2007.
- Hossain M, Broutet N, Hawkes S. The elimination of congenital syphilis: a comparison of the proposed World Health Organization action plan for the elimination of congenital syphilis with existing national maternal and congenital syphilis policies. Sex Transm Dis. 2007;34(7Suppl):S22-30.
- Newman L, Kamb M, Hawkes S, Gomez G, Say L, Seuc A, et al. Elimination of mother-to-child transmission of HIV and syphilis in the Americas. PLoS Med. 2013;10(2):e1001396
- Pan American Health Organization. 2014 Update: Elimination of Motherto-Child Transmission of HIV and Syphilis in the Americas. Washington: PAHO; 2014.
- Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. Bull World Health Organ. 2013;91(3):217-26.
- 10. Qin J, Yang T, Xiao S Tan H, Feng *T*, Fu H. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. PLoS One. 2014;9(7):e102203.
- Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al. Reduction of Maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. New Engl J Med.1994;331:1173-1180.
- Chasela CS, Hudgens MG, Jamieson DJ, Kayira D, Hosseinipour MC, et al. Maternal or infant antiretroviral drugs to reduce HIV-1 transmission. N Engl J Med. 2010;362:2271-2281.
- World Health Organization. WHO antenatal care randomized trial: manual for the implementation of the new model. Geneva: WHO; 2001. (WHO/ RHR/01.30).
- Ishikawa N. Utilizing resources effectively for the first "90": Strategic approaches to testing pregnant women for HIV across high and very low prevalence settings. WHO consolidated guidelines on HIV testing services – Support tools. Presented at the 8<sup>th</sup> IAS Conference on HIV Pathogenesis, Treatment & Prevention, 2015 July 20, Vancouver, Canada.
- Kahn JG, Jiwani A, Gomez GB, Hawkes SJ, Chesson HW, Broutet N, et al. The cost and cost-effectiveness of scaling up screening and treatment of syphilis in pregnancy: a model. PLoS One. 2014;9(1):e87510
- Swartzendruber A, Steiner RJ, Adler MR, Kamb ML, Newman LM. Introduction of rapid syphilis testing in antenatal care: A systematic review of the impact on HIV and syphilis testing uptake and coverage. Int J Gynaecol Obstet. 2015;130(Suppl1):S15-21.
- Tudor Car L, Van Velthoven MH, Brusamento S, Elmoniry H, Car J, Majeed A, et al. Integrating prevention of mother-to-child HIV transmission (PMTCT) programmes with other health services for preventing HIV

infection and improving HIV outcomes in developing countries. Cochrane Database Syst Rev. 2011;(6):CD008741.

- Peeling RW, Mabey D, Fitzgerald DW, Watson-Jones D. Avoiding HIV and dying of syphilis. Lancet. 2004;364(9445):1561-3.
- Strasser S, Bitarakwate E, Gill M, Hoffman HJ, Musana O, Phiri A, et al. Introduction of rapid syphilis testing within prevention of mother-to-child transmission of HIV programs in Uganda and Zambia: a field acceptability and feasibility study. J Acquir Immune Defic Syndr. 2012;61(3):e40-6.
- Yin YP, Ngige E, Anyaike C, Ijaodola G, Oyelade TA, Vaz RG, et al. Laboratory evaluation of three dual rapid diagnostic tests for HIV and syphilis in China and Nigeria. Int J Gynaecol Obstet. 2015;130(Suppl1):S22-6.
- Luu M, Ham C, Kamb ML, Caffe S, Hoover KW, Perez F. Syphilis testing in antenatal care: Policies and practices among laboratories in the Americas. Int J Gynaecol Obstet. 2015;130(Suppl1):S37-42.
- 22. Pan American Health Organization. Guidance on syphilis testing in Latin America and the Caribbean: Improving uptake, interpretation and quality of testing in different clinical settings. Washington: PAHO; 2015.
- Joint United Nations Programme on HIV/AIDS. 2014 Progress Report on the global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive. Geneva: UNAIDS; 2014.
- Gulland A. Cuba is first country to eliminate mother to child HIV transmission.BMJ. 2015;351.
- Editorial. Cuba: defeating AIDS and advancing global health. Lancet. 2015;386:104.