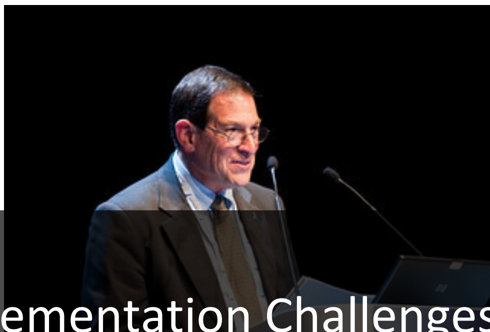

Operational and Implementation Challenges in Scaling Up PMTCT Programmes in Resource-Limited Settings

SESSION REPORT

Public Satellite Session at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2011)

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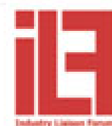
Co-hosted by IAS-ILF & UNICEF



Background

In 2010, the International AIDS Society (IAS)-Industry Liaison Forum (ILF) jointly with UNICEF and 14 other organizations (including WHO, UNAIDS, pharmaceutical companies, non-governmental organizations and community groups) released a consensus statement *Asking the Right Questions: Advancing an HIV Research Agenda for Women and Children*, which outlined 20 recommendations to advance HIV research for women and children. There are four specific recommendations (16-19) within that statement on conducting operational research in the prevention of mother to child transmission (PMTCT), which reflect the outcome of a high-level consultation led by UNICEF. As part of a continuing effort to promote HIV research according to the consensus statement, the ILF and UNICEF organised a satellite session at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2011), entitled “Operational and Implementation Challenges in Scaling up PMTCT Programmes in Resource-limited Settings”.

Mother to child transmission (MTCT) remains the primary source of new infections in paediatric populations in resource-limited settings. The current upscale of evidence-based programmes for PMTCT can serve as a vehicle to eliminate new HIV infections in infants. Identifying, recruiting, and retaining HIV-infected pregnant women in PMTCT programmes prove challenging in the cascade process. In turn, identifying HIV-exposed infants and subsequently linking them to care and prophylaxis programmes also are critical, and consequently, coordinated efforts are required for a more effective scale up of PMTCT programmes.

More recently, the UN General Assembly High Level Meeting on AIDS resulted in the adoption of a Political Declaration on AIDS by setting clear targets for the elimination of vertical transmission of HIV from mother to child by 2015. In light of the elimination plan, this IAS 2011 satellite session provided an overview of the scale-up efforts in PMTCT interventions and programmes in resource-limited settings, along with the operational and implementation issues associated with such efforts. Furthermore, the challenges in identifying HIV-exposed infants as a proxy for evaluating PMTCT programmes at a country level were highlighted, and the barriers in linking identified infants to care and/or prophylaxis programmes were also addressed. The ILF and its partner organizations well recognize that there is a unique and timely opportunity to work collaboratively to facilitate the process of a more successful PMTCT scale up towards elimination of vertical transmission of HIV.

Introduction

In welcoming participants, Co-chair Elly Katabira, President of the IAS, commented on the significance of this session, given the ILF’s historical role in addressing important issues around ethics in the conduct of HIV research. Furthermore, he described how the ILF took a

leading role in developing the HIV research agenda on children in resource-limited settings. Co-chair Jimmy Kolker, Chief of UNICEF's HIV/AIDS Section, commented on the need to understand the "real impediments in scaling up PMTCT and preventing MTCT", including both operational and implementation issues. In addition, Kolker noted that national protocols need to be adopted, while national programmes have to consider the integration of services, loss to follow up, stock outs, and other particularities in optimizing PMTCT services. On a positive front, he said that there is no need for "any new scientific breakthroughs" in order to achieve the results of PMTCT already observed in resource-rich countries.

PMTCT overview: current scale-up efforts and challenges in operations and implementation

Overview
By Angela Mushavi, Ministry of Health, Zimbabwe

Introduced by Jimmy Kolker, **Angela Mushavi** offered an overview of PMTCT scale-up efforts and the inherent challenges in implementation for resource-limited countries. Mushavi set the scene by describing the epidemiological landscape of HIV infection in Zimbabwe. The current adult prevalence of HIV stands at approximately 13.7%, while antenatal clinic (ANC) seroprevalence is estimated at 16.1%. New paediatric infections are estimated at 14,976, 90% of which are attributed to vertical transmission. Commenting that Zimbabwe is "a resource-constrained country but certainly not defeated", Mushavi noted that despite a fairly high attendance rate at ANCs, AIDS-related mortality remains "alarmingly high" (with 1,090 patients dying weekly).

The scale up of Zimbabwe's national PMTCT programme was initiated in 2002 with the introduction of single-dose nevirapine (sdNVP) for both HIV-infected mothers and their HIV-exposed infants, and led to the implementation of the World Health Organization's (WHO's) 2006 guidelines (using more efficacious regimens)[1] by 2009. With respect to the most recent WHO PMTCT guidance (2010), Mushavi indicated that Zimbabwe's national programme has chosen option A and is in the process of implementing it. In terms of geographic coverage, an estimated 95% of ANCs (n=1,560) across the country are providing PMTCT, while 77% are offering comprehensive

[1] Twice-daily AZT for the mother and infant prophylaxis with either AZT or NVP for six weeks after birth if the infant is not breastfeeding. If the infant is breastfeeding, daily NVP infant prophylaxis should be continued for one week after the end of the breastfeeding period.

PMTCT (which includes both on-site HIV testing and ARV prophylaxis). Referring to these as "very noteworthy outcomes", Mushavi cautioned that there is still some missed opportunity at sites where there is no HIV testing in place.

Mushavi commented on the critical support from Zimbabwe's partners in scaling up its PMTCT efforts, namely the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF). Interestingly, this support has implications for PMTCT services, with coverage being higher in partner-supported sites across Zimbabwe (Fig. 1). In reference to cotrimoxazole (CTX) prophylaxis, an inexpensive antibiotic for HIV-exposed infants, she indicated that only 53% of infants were receiving CTX in 2010.

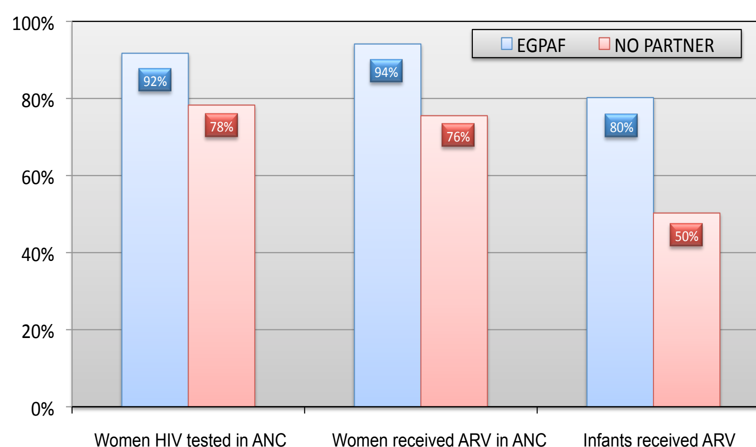


Figure 1. Comparison of partner-supported and non-partner-supported sites: Zimbabwe Ministry of Health and Child Welfare (MOHCW) 2009 data

Importantly, there has been a significant increase in early infant diagnosis (EID) polymerase chain reaction (PCR) tests being conducted since 2007. Mushavi highlighted some notable PMTCT achievements in Zimbabwe, including:

- Strong PMTCT partnership forum that supports scale up
- Transitioning to more efficacious regimens for PMTCT (moving to Option A)
- Revised Integrated Management of Adolescent and Adult Illness (IMAI)/Integrated Management of Pregnancy and Childbirth (IMPAC) curriculum with ongoing training and support supervision of staff
- HIV DNA PCR for early infant diagnosis of HIV available since 2007
- Support from government, donors and partners to provide resources for PMTCT scale up, including the Global Fund and the National AIDS Trust Fund.

Mushavi touched on the ongoing evaluation of point-of-care CD4 machines, and explained that there is no significant difference between point-of-care and lab-based machines. Regarding additional PMTCT challenges, she noted that "we still have a lot to do by 2015", and commented on low male participation rates in programmes and pregnant women presenting late to ANCs. Echoing her earlier theme on "missed opportunities" for PMTCT scale up in resource-limited countries, Mushavi argued that experts are too quick to develop guidelines, while monitoring to track PMTCT progress remains insufficient. In closing, she

underscored the challenge in human resources for healthcare delivery, coupled with procurement and supply chain management. Mushavi's parting message to the audience was that for elimination to be achieved, the sexual reproduction needs of HIV-infected women wishing to become pregnant would have to be targeted.

Challenges in identifying HIV-exposed infants, scaling up early infant diagnosis and linkage to prophylaxis, treatment and care programmes

Overview
By Charles Kiyaga, Ministry of Health, Uganda

Introduced by his fellow countryman, Elly Katabira, **Charles Kiyaga** provided an overview of Uganda's highly effective and successful EID national programme. Despite the programme's innovation, Kiyaga opened by cautioning on the persisting challenges confronting Uganda and other resource-limited countries when identifying HIV-exposed infants and linking them into care services. In describing the early infant diagnosis (EID) process as a cascade series, he identified where infants are lost, and commented on the spectrum of factors that account for this. The cascade, as Kiyaga noted, entails: a) identifying and testing an HIV-exposed infant; b) providing results and guiding caregivers through test algorithm; c) enrolling an HIV-infected infant in an ART clinic; and d) retaining the infant in care and/or treatment. In light of the rapid disease progression of HIV infection in infants, he argued that basic care services and prophylaxis should be offered to infants throughout the EID process.

Presenting data from an EID review of its national programme, Kiyaga explained that only 40% (98 of 244) of tested infants were eventually enrolled into care and treatment services. Alarmingly, 39% of positive infants never received results, and 35% of HIV-infected infants receiving results were never enrolled in care (Figure 2). He highlighted some of the drivers of loss in not identifying and testing exposed infants, including limited sensitivity and awareness by healthcare workers, coupled with a lack of a formal referral system for EID testing from "entry points" within health facilities (and off-site facilities).

Furthermore, the lack of a referral system for exposed infants identified before or at birth contributed to this loss. Regarding referrals from PMTCT programmes, Kiyaga presented data from one hospital showing that over 80% of HIV-infected pregnant women never brought their babies back for testing and care after delivery. In response to this, Kiyaga argued for strong, formalized PMTCT-EID linkages that can capture exposed infants before birth. Poor

documentation and tracking systems, coupled with a lack of consistent counselling and care provision, and long sample and result turnaround time, were predictive of not receiving a testing result and completing the testing algorithm.

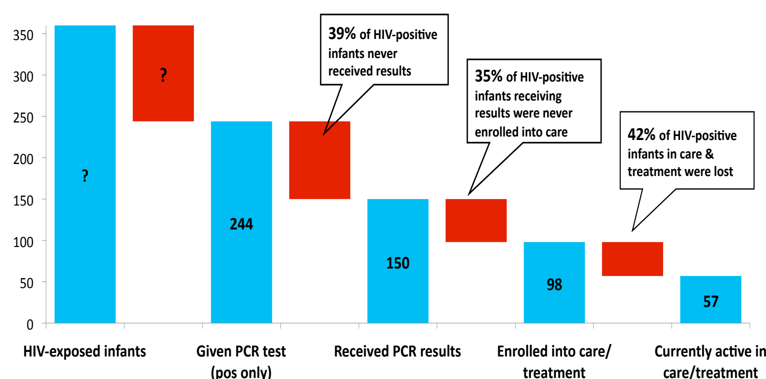


Figure 2. Infant retention continuum at 3 regional referral hospitals in Uganda (Sept 2007 – Feb 2009)

Kiyaga presented additional data to highlight the impact of exclusively centralizing EID services in a laboratory. Caregivers of infants having tests at an antenatal or ART clinic did not know where to return for results and follow up, while caregivers of infants who tested at the lab in outpatient department received no counselling or sensitization during sample collection. With all results given in the lab, there was no post-result counselling or care unless a caregiver took the initiative to seek it out.

Kiyaga commented on the issue of turnaround times, which had an adverse effect on whether caregivers received results or not. On average, caregivers had to wait 69 days to receive dried blood spot (DBS) results. In addition, in terms of turnaround time and retention, fewer caregivers received their results with longer turnaround time. Kiyaga also described some of the reasons for HIV-infected infants not being enrolled into care and treatment, which included the absence of a formal referral system to ART clinics, coupled with limited integration or communication between EID testing and an ART clinic. Retention into care after enrolment at an ART clinic was compromised if an eligible infant did not immediately initiate treatment. Furthermore, with respect to late identification and testing of exposed infants, only 40% of infants older than six months were tested for HIV. Kiyaga touched on age and attrition: 59% of infants older than three months were captured. He noted that capture and diagnosis of infants at a late age can lead to attrition after initiation on ARV treatment due to rapid disease progression.

In recognizing these challenges, Kiyaga described the country's efforts to strengthen its EID system, with a package of six complementary interventions. This was piloted in 21 health facilities of all levels in eight districts. The first step was to establish an "EID care point" within either a maternal and child health clinic or ART clinic where all exposed infant care and follow up was centralized. The second intervention was to integrate routine care into the EID

process and establish a regular visit schedule, followed by strengthening and standardizing counselling services for caregivers of exposed infants. The fourth intervention involved an effort to improve tracking tools to centralize data and follow infants longitudinally; this was followed by the establishment of a referral system for DBS testing and follow up at the EID care point. The final intervention was to establish a referral system for care and treatment at the ART clinic. Kiyaga added that the assessment of the pilot at several of the facilities showed high impact across all key areas of EID.

In closing, Kiyaga noted that challenges still exist, but the "EID system strengthening" model had demonstrated high impact and shown feasibility of implementation in Uganda. He also noted "the strengthening model has shown the value and feasibility of changing EID from merely a testing service to a longitudinal comprehensive care package for all HIV-exposed infants".

Panel discussion

Moderators: Session Co-chairs

Panel participants:

Karle Dehne	UNAIDS
Charles Holmes	PEPFAR
Helen Lee	University of Cambridge
Ying-Ru Lo	WHO
Angela Mushavi	Ministry of Health, Zimbabwe
Charles Kiyaga	Ministry of Health, Uganda

Following the presentations by Angela Mushavi and Charles Kyiaga, the session Co-chairs moderated a panel discussion with a diverse set of stakeholders. Each panellist had the opportunity to comment on the current scale-up efforts of PMTCT programmes in resource-limited settings. **Karle Dehne** from UNAIDS described how the field has to identify and address the major areas that merit greater focus, and specifically argued for full access to CD4 count assays and decentralization of laboratory testing services. Dehne also touched on the issue of how resources are financed and the implications on PMTCT impact. Of note, he underscored that the targets set out in the Global Plan for eliminating new HIV infections [2]among children can be realistically achieved in the presence of accountability and "real structural changes".

Charles Holmes, representing the US President's Emergency Plan for AIDS Relief (PEPFAR), described his organization's support of PMTCT programmes in more than 20 countries. In addition, Holmes indicated that PEPFAR has aggressive goals in place for PMTCT, which is reflected in its current guidelines. Furthermore, PEPFAR is excited about

[2] Countdown to Zero: Global Plan towards the Elimination of New HIV Infections among Children and Keeping their Mothers Alive

the 2015 plan, which is led by the 22 countries with the highest burden of MTCT; it will serve as a leading implementing partner.

Helen Lee, a professor from Cambridge University, addressed the particularities and challenges related to infant diagnosis. Commenting on the need to identify the key reasons for loss to follow up, she questioned the utility of testing given that 30-80% are lost after PCR. Furthermore, Lee cautioned that dried blood spots have yet to be established as a reliable tool in resource-limited settings, and noted that if a patient sample is compromised, the result will also be compromised. Citing a Chinese proverb that "there are a lot of pebbles", from a technical standpoint, she argued that the rate of false positive results is a barrier. It is, therefore, critical to examine the technical details that assure quality before prematurely funding scale-up of new testing technologies. Lastly, Lee proposed blinded quality control panels to determine such quality in EID.

Ying-Ru Lo from WHO referred to her organization's support of the Global Plan, and noted its role in providing technical support and normative guidance to countries. Lo noted that one of the key issues, from her organization's standpoint, is improving patient monitoring systems. Furthermore, she advocated for more debate on the emerging issues related to PMTCT and MTCT, and made reference to the recently published recommendations from Malawi.

Angelina Namiba, representing Positively UK, offered the perspective of a mother living with HIV. Namiba commented on how a woman and mother diagnosed with HIV is confronted with a complex range of issues, including disclosure of status, other children, delivery options, concerns over one's infant, and adherence to ARV treatment. Calling for greater support for HIV-infected women, she referred to a pilot programme set up by her organization, which provides opportunities for HIV-infected women to support and assist other women.

Importantly, Namiba stressed that “stigma kills”, and argued that the elimination targets will not be met if women are afraid to access care in the first place. She proposed a “robust system of maintaining human rights” to ensure that healthcare workers are not judgemental.

After the panellists’ remarks, the moderators opened up the floor to questions and comments by the audience. An initial comment touched on the issue of whether the right questions are being posed in the context of PMTCT scale up. Further to that, the issue was raised of whether the current approach of identifying HIV-infected infants is limited (with potential for more innovative ideas), and there was an argument that more work is needed to support mothers. In addition, Namiba commented that the role of faith-based organizations should be more carefully considered.

In recognition of maternal health, Katabira challenged the notion of following up only infants and children. Namiba also commented on the importance of using community as a resource, and quoted one HIV-infected mother (“I cannot begin to explain what it was to be supported by a woman who walked in my shoes”). Lo, in support of Namiba’s stance, described retention in care as critical in the overall response. In reference to Malawi’s rapid antibody tests when compared with some theoretical data, Lee noted that retention in care may be higher when a mother can see the positive result. Furthermore, follow-up results for CD4 counts and viral loads, when offered to the patients visually (e.g., a graph depicting a decline in viral load over time), can be an effective approach.

Holmes proposed a better integration of maternal and infant services, and argued that the time it takes to access care and services should be minimized. He also said that the field should explore the impact of conditional cash transfers and other incentivizing initiatives. Dehne commented that the original structure of PMTCT for sdNVP is “old news”, suggesting that the probable direction will be something like Option B+. Moreover, he indicated that stakeholders should consider the integration of ARVs into MTCT programmes. Namiba also spoke of the need for a monitoring system for the quality of implementation of PMTCT interventions.

Lo described the take up and/or adoption of WHO’s 2010 PMTCT guidelines, and made reference to Nathan Shaffer’s contribution in expediting the adoption of the 2010 guidelines (more rapidly than for the 2006 guidelines). Of note, WHO conducted a review of the 2006 guidelines prior to 2010 and determined that some key countries did not take up the 2006 guidelines (e.g., they kept sdNVP). Furthermore, Shaffer commented that the Global Fund would only support countries that are taking up the new guidelines, and indicated that WHO is currently working on an implementation guide.

In terms of engaging men, Namiba suggested that male partners should be tested together with women, which could enhance mutual support. Kiyaga commented on universal testing for infants, and noted that in Uganda's national programme, a mother who does not know her status is counselled for HIV testing, and in the case of refusal, the infant is screened and a dried blood spot sample collected. In response to a question from the audience on the issue of permanent contraception, Namiba emphasized that an HIV-infected woman's desire to have a child should be respected. Lo echoed that reproductive choices should be promoted for all women, including those infected with HIV.

Closing remarks

In thanking panel participants and everyone attending the satellite session, the Co-chairs remarked on the importance of addressing and overcoming the variety of challenges facing countries as they implement PMTCT guidelines in scaling up programmes. A key issue raised was accountability as a focal point, along with the paradigm shift towards thinking about keeping not only children but also mothers alive. Furthermore, institutional support by such organizations as the Inter-agency Task Team and other stakeholders will be fundamental in realizing the targets set out by the plan on elimination of MTCT. Parting comments by Katabira and Kolker were marked by a sense of hope and caution.

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About the ILF

The Industry Liaison Forum (ILF) is an initiative of the International AIDS Society (IAS) that brings together industry, independent investigators, non-governmental organizations, foundations and other stakeholders to enhance HIV treatment access and outcomes in resource-limited settings, with a particular focus on the role and responsibilities of industry. The ILF provides the unique platform that allows industry to engage, communicate and collaborate with other stakeholders to enhance HIV research, and thereby promote evidence-based health policy and health delivery in resource-limited settings.

The ILF fulfils its mission by: identifying research gaps; promoting targeted research; identifying challenges and best practices; analyzing available data and evidence; disseminating information; consulting and convening stakeholders; providing industry expertise; and supporting capacity building for research and health delivery.

As part of its new Strategic Plan (2012-2014), the ILF is committed to focusing on scientific, ethical and policy issues related to HIV research for women and children by identifying research gaps in this area.

For more information regarding ILF activities, please visit our website at http://www.iasociety.org/ilf.aspx, or follow us on Facebook & Twitter:

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Contact information:

International AIDS Society
Industry Liaison Forum
PO Box 28
CH-1216
Geneva, Switzerland
ilf@iasociety.org
Tel: +41 22 7100 800