Towards eliminating perinatal transmission of HIV, syphilis and hepatitis B in Yunnan

A case study, 2005–2012
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Acknowledgements

This eight-year programme on the prevention of mother-to-child transmission (PMTCT) of HIV required the efforts of many dedicated teams of health professionals in Yunnan, and the generous support of various national and international organizations, as well as individual donors. Initiation of the project in 2005 would not have been possible without the generous donation from Tony Yeung and his Gracious Glory Buddhism Foundation. Other donors for the early phase of the project include the JT Tai Foundation, Oscar and Kevin Tang, Walter and Shirley Wong, and Miranda Wong Tang. Both funding and technical support from the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) was critical from 2007 to 2009, when the project expanded capacity-building to the township and village levels. Funding from Rotary International during this period filled the gap in supply of HIV rapid test kits. Initially, the Hong Kong ZeShan Foundation made donations to the programme in 13 counties during 2005–2009, and supported the integration of PMTCT of hepatitis B and syphilis in six of those 13 counties during 2009-2010. During 2009-2010, the Foundation supported further expansion of the programme to 26 counties.

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Dr Gui Xi’en, AIDS Clinical Advisory and Training Center, Wuhan, Hubei, China was part of the Aaron Diamond AIDS Research Center’s early efforts on PMTCT.

We wish to thank the Yunnan Bureau of Health (BoH), which gave its full support to the programme in the beginning, and continued to champion the project through all these years. We also thank all the health professionals at our sites who took part in the programme, including leaders of the local doctors from each China Centers for Disease Control and Prevention (CDC), antiretroviral (ARV) clinic, Maternal and Child Health (MCH) hospital, township health centre and village clinic.

Finally, we wish to convey our appreciation to all the women and families that participated in our programme. It was only with their trust that we were able to carry out our work.

The Chinese names start with Family name followed by first names whilst the European names start with first name followed by family name.
Abbreviations

ADARC  Aaron Diamond AIDS Research Center
ANC  antenatal care
ART  antiretroviral treatment
ARV  antiretroviral drug
AZT  zidovudine
BoH  Bureau of Health
CCDC  China Centers for Disease Control and Prevention
EID  early infant diagnosis
EPI  Expanded Programme on Immunization
HBIG  hepatitis B immune globulin
HBsAg  hepatitis B surface antigen
HBV  hepatitis B virus
iPMTCT  integrated prevention of mother-to-child transmission
L&D  labour and delivery
MCH  Maternal and Child Health (programme)
MoH  Ministry of Health
MTCT  mother-to-child transmission
NCAIDS  National Center for AIDS/STD Prevention and Control
NVP  nevirapine
PCR  polymerase chain reaction
PLHIV  People Living with HIV
PMTCT  prevention of mother-to-child transmission
RPR  rapid plasma reagin
TRUST  toluidine red unheated serum test
WHO  World Health Organization
YACC  Yunnan AIDS Care Center
YAI  Yunnan AIDS Initiative
China began to implement services for the prevention of mother-to-child transmission (PMTCT) of HIV in 2003. By 2012, the national programme was expanded to 1156 counties. In 2011, the national Maternal and Child Health (MCH) programme included prevention of congenital syphilis and hepatitis B and the programme was renamed “integrated PMTCT” or iPMTCT.

Yunnan province, located in southwest China, is severely affected by the HIV epidemic. The national and provincial governments made HIV prevention and treatment a priority in Yunnan. We describe the evolving and expanding PMTCT programme in Yunnan province informing the national scale up of PMTCT.

This case study is divided into two parts. The first part describes the HIV PMTCT programme from 2005 to 2009. These were important years during which the programme worked within the existing local health structure to build a solid foundation for implementing PMTCT services integrated with routine maternal and child health services.

The second part of this case study describes the iPMTCT programme from 2010 to 2012. In these three years, the triple antiretroviral (ARV) drug regimen for PMTCT of HIV was scaled up, and HBV and syphilis counselling and testing were added to those for HIV.

Over the project period, the use of triple antiretroviral prophylaxis for HIV-positive women was rapidly scaled up. In 2012 more than 85% of HIV-positive pregnant women received triple ARV prophylaxis, and 86% of the 205 syphilis-positive women who gave birth in 2012 received benzathine penicillin treatment during pregnancy. Infants born to mothers who had hepatitis B surface antigen were given a birth dose of hepatitis B vaccine and hepatitis B immune globulin.
Introduction

China began to implement services for the prevention of mother-to-child transmission (PMTCT) of HIV in 2003. During this decade of implementation, the services have gone through several rounds of expansion and evolution. The national PMTCT guidelines also went through significant revisions. The most recent national PMTCT guidelines were revised in 2010 to adopt the World Health Organization (WHO) option B antiretroviral (ARV) regimen for the PMTCT of HIV, and to integrate the PMTCT of viral hepatitis B (HBV) and syphilis in antenatal care, and during labour and delivery (L&D) along with HIV. In 2011, the national Maternal and Child Health (MCH) programme obtained sufficient funding from the central government to expand integrated PMTCT (iPMTCT) services to 1156 counties with a high HIV prevalence.

Yunnan province, located in southwest China, is a region that is most severely affected by the HIV epidemic. Therefore, Yunnan has always been a top priority area for the HIV prevention and treatment efforts of the Chinese Ministry of Health (MoH). The Aaron Diamond AIDS Research Center (ADARC), a private AIDS research centre based in New York, actively collaborated with the Yunnan health authorities early on to help build system capacity in providing HIV prevention and treatment services. When antiretroviral treatment (ART) was yet unavailable in China, ADARC initiated a pilot project in Yunnan to provide ART to patients. In 2005, ADARC initiated a demonstration project on the use of a triple ARV drug regimen to prevent mother-to-child transmission (MTCT) of HIV. Gradually, Yunnan built up the infrastructure necessary for providing ART and PMTCT services.

The purpose of this case study is to describe how iPMTCT services were delivered in our programme and to highlight the achievements and challenges of the collaborative efforts to improve PMTCT services in Yunnan over the past eight years. We hope that sharing our programme experiences would be valuable for others implement integrated HIV, syphilis and HBV PMTCT services in resource-limited settings and reach the WHO goal of “virtual elimination” of paediatric HIV and congenital syphilis by 2015.

This case study is divided into two parts. The first part describes the HIV PMTCT programme from 2005 to 2009. These were important years during which the programme worked within the existing local health structure to build a solid foundation for implementing PMTCT services integrated with routine MCH services. The second part of this case study describes the iPMTCT programme from 2010 to 2012. In these three years, the triple ARV drug regimen for PMTCT of HIV was scaled up, and HBV and syphilis counselling, testing and PMTCT services were added to those for HIV.

The PMTCT programme for HIV, 2005–2009 in Yunnan was implemented for a population of 44 million, of which an estimated 85 000 were living with HIV. The national and provincial governments made HIV prevention and treatment a priority in Yunnan. Under the leadership of the Yunnan Provincial Bureau of Health (BoH), prevention and treatment services were provided by the Centers for Disease Control and Prevention (CDC), the infectious disease clinics at designated comprehensive hospitals, and the Maternal and Child hospitals (Figure 1).
**Initial challenges**

In 2003, the national government initiated PMTCT services in two pilot counties in Yunnan. By 2005, all 129 counties of Yunnan province were covered by the national programme. Initially, it was challenging to integrate PMTCT into the MCH services due to several hurdles.

**Lack of expertise and capacity at MCH settings**

Health workers within MCH settings lacked both the knowledge and experience in the administration of ARVs, which was widely regarded as the domain of infectious disease doctors at specifically designated hospitals. Fear and stigmatization of people living with HIV was prevalent among MCH care providers at that time due to the low level of knowledge and contact with HIV-infected persons. Another major barrier for the MCH hospitals was that they did not have the equipment necessary to run confirmatory tests for the laboratory diagnosis of HIV, such as western blot and CD4 testing. The capacity for conducting these diagnostic laboratory tests was housed in the CDC and at designated comprehensive hospitals.

**Lack of collaboration linkages across MCH and ART clinics and the CDC**

The other major challenge was the lack of linkages and collaboration between the key service providers at the MCH and ART clinics, and the CDC in order to ensure timely test results and patient referrals. Health workers from the MCH hospitals also needed to have expertise in conducting and interpreting these tests at the CDC and ARV clinics to manage HIV-infected patients. Getting different agencies to work together was difficult, particularly from the perspective of the MCH due to the weak position in the local health system.
Lack of geographical access to the health services

Strengthening the continuum of care across the different levels of health-care facilities in the rural three-tier network was also essential. In 2005, HIV/AIDS-related services were concentrated at the county level or above, with very few services accessible at the townships and villages within the county.

The mountainous terrain of Yunnan province, coupled with underdeveloped transportation infrastructure in many parts, make it difficult for rural residents to access health services at the county level. It is not unusual for residents from a rural village to spend an entire day to get to the county, where the MCH services and hospitals are located. In the existing infrastructure, health workers at township health centres and village clinics are not professionally trained medical providers and do not have the expertise to treat serious medical issues. In 2005, uptake of health services among the rural population in Yunnan was also low. Coverage with antenatal care (ANC) was poor and hospital delivery rates were as low as 22% in some counties.

In this context, the ADARC, in collaboration with the Yunnan BoH, started implementing a pilot PMTCT project using triple ARV drug prophylaxis for HIV-positive pregnant women.
HIV PMTCT programme strategy and implementation (phase I), 2005–2009

Leadership of the Bureau of Health
In the project framework, leadership was critical for coordinating linkages between the health facilities within the local health system. Leadership mobilization efforts started at the provincial BoH, and were linked down to the county BoH at the project sites. The county BoH, the administrative entity that oversees the operations of all health facilities within its region, could play the vital role of facilitator and ensure smooth linkages between facilities.

Programme implementation structure
Through multiple consultations with provincial authorities and site assessment visits, 13 counties (Hongta, Tengchong, Longlin, Lancang, Linxiang, Gengma, Cangyuan, Gejiu, Kaiyuan, Wenshan, Yanshan, Mangshi, Longchuan) with a relatively high HIV prevalence and operational local ART clinics were chosen as demonstration sites.

PMTCT services were provided by the MCH hospitals in close coordination with ART clinics. In order to ensure the effective and safe implementation of triple ARV prophylaxis for PMTCT, the programme appointed the Yunnan Provincial AIDS Care Center (YACC) to be the managing organization for overall programme implementation (Figure 2). YACC is the government-designated institution for the supervision of ART in the province. For the PMTCT programme, YACC was responsible for managing ARV drug distribution to the sites, providing technical support, and close monitoring and evaluation of the programme. To better facilitate coordination between health institutions at all levels, a programme office was established at each of the county MCH hospital with a full-time programme coordinator hired by the project at each site. After the initial programme implementation, partnership was actively sought with other international institutions and nongovernmental organizations to strengthen different technical aspects of the programme.
Capacity-building for PMTCT

The project provided tailored PMTCT training for two types of target audiences. One major group of target trainees was the clinicians at MCH hospitals. This group consisted mostly of obstetricians and paediatricians in charge of providing PMTCT services and managing ARV prophylaxis for pregnant women. Another group consisted of township and village health workers, most of whom had less medical training than doctors at the county level. However, under our programme strategic framework, we needed to expand some PMTCT services to the township and village levels in order to increase access to services closer to their homes. After assessment visits to the township and village, we decided that the programme would try to build the capacity of the township and village doctors to provide HIV counselling and testing services to pregnant women, and refer HIV-positive women to the county MCH hospital for clinical management. Therefore, the training designed for providers at the county level focused on ARV management and clinical approaches to the PMTCT of HIV, as well as the overall public health perspective. In comparison, the training for health workers at the township and village levels contained more basic information on HIV/AIDS, with emphasis on building the knowledge and skills necessary to provide standard HIV counselling and rapid point-of-care testing services to pregnant women. Unlike the typical training for local health workers in the past, which consisted mostly of lectures to hundreds of people, our training programme involved a variety of participatory training methods and strictly kept the size of each group undergoing training small, in order to promote interactive learning.
Improving linkages and task shifting
Rapid test kits for HIV were distributed to township level health centres. At some sites, HIV rapid test kits were also distributed to selected village doctors in remote villages for easier access. The main task for the village-level doctors was to identify pregnant women early in their villages, provide basic antenatal care (ANC) and HIV counselling, and then refer the women to the township or county level facilities for HIV rapid testing. At township-level clinics, women got their ANC booklet, and received HIV counselling and testing as a standard part of their ANC visit. All women with a positive rapid test result had their blood samples sent immediately to the county CDC for confirmatory testing. Samples were also sent simultaneously for CD4 testing to avoid additional waiting time after the return of confirmatory test results. Any woman who screened positive initially at the township level was immediately referred to the county MCH hospital. ANC and PMTCT services for all confirmed HIV-positive women were managed by county level hospitals during pregnancy and delivery. For women who first tested positive only during delivery at the township level clinics, the programme made sure that emergency supplies of ARVs were stocked at the township hospital.

The programme also advocated for stronger linkages between the MCH, CDC and local ART clinics. Coordination meetings organized by the programme and by BoH sites took place to ensure that samples of pregnant women can be sent to the CDC without delay, and HIV confirmation test and CD4 tests results can be returned as soon as possible. Doctors from the MCHs also established closer ties with doctors at the ART clinics in order to provide closer monitoring of pregnant women on ARV, and intervene early in case of serious adverse reactions.
Box 1: Responsibilities of health workers at various levels

**Village-level**

Key personnel: village doctors, women leader, family planning staff

Key activities and services:
- Carry out public education events with assistance from township and county-level doctors.
- Identify and make first contact with pregnant women in the village early in pregnancy.
- Provide women and their families with basic information on ANC and PMTCT services.
- Refer women to higher-level clinics for ANC and HIV, hepatitis B virus (HBV) and syphilis testing and counselling.
- Report data up to township clinics, and assist township and county doctors to follow up women who have not been coming for ANC.

**Township-level**

Key personnel: women and children specialists at township clinic

Key activities and services:
- Issue pregnancy booklets to women at ANC clinics.
- Provide HIV, HBV and syphilis counselling and testing (using rapid test kits) at ANC and during labour and delivery (L&D).
- Refer women with positive rapid test results to the county MCH hospital for further confirmation and PMTCT services.
- Provide ARV prophylaxis during L&D to HIV-positive women who have not been identified during ANC, or cannot make it to the county MCH hospital for delivery.
- Monitor and evaluate village doctors.
- Report monthly data up to the level of the county MCH hospital.

**County-level**

County MCH
- Provide counselling and testing as a routine part of ANC and L&D services.
- Coordinate with the local CDC to transfer samples and get laboratory results back in the most efficient manner.
- Provide standard PMTCT services to HIV-positive women and HIV-exposed infants.
- Follow up HIV-exposed infants for 18 months post birth.
- Refer HIV-positive women post-delivery and HIV-positive children to CDC and ARV clinics for continued follow up and treatment.
- Provide monitoring and evaluation of township clinics, and report monthly data up to the prefecture and provincial levels.

County ARV clinic
- Manage HIV-positive patients on ART.
- Provide technical assistance to MCH doctors in cases of opportunistic infections and severe adverse reactions among HIV-positive pregnant women.
- Receive HIV-positive women post-delivery from the MCH hospital for continuing treatment.

County CDC
- Follow up people with HIV who are not yet on treatment.
- Provide HIV western blot confirmatory test, CD4 test and viral RNA test. Coordinate with the MCH hospital to make sure that those pregnant women who screened HIV-positive could get confirmatory and other test results back in a timely manner.
Establish a strong monitoring and evaluation system

Strengthening data reporting and linkage system is as critical as solidifying the referral system. The provincial MCH distributed standard PMTCT registries and monthly data report forms to county and township level hospitals. Every month, the registry information is tallied into report forms and sent to higher levels—township hospitals to county MCH, and then county to prefecture and provincial levels. Data communication and feedback between township hospitals and county MCH is important in helping the provider at this level to better understand and monitor their own services. The programme provided technical training and regular guidance to the providers to improve their capacity in data collection and analysis. The analysis of local data was essential to understand implementation gaps and improve the efficiency of the cascade of services.

National PMTCT guideline revision (2010): integrated PMTCT

Following the publication of WHO’s revised 2010 PMTCT guidelines, the China MoH promptly revised the national PMTCT guideline. The national guideline published in 2010 has two salient differences from the previous edition. First, the national guideline adopted the WHO Option B ARV regimen for PMTCT of HIV, which is the use of a triple ARV regimen for all HIV-positive pregnant women. Second, PMTCT services for syphilis and HBV were added alongside those for HIV. This meant that all pregnant women should receive counselling and testing services for HIV, syphilis and HBV combined as a standard part of their ANC package. Thus, this new version of the national guideline was called integrated PMTCT services or iPMTCT.
National iPMTCT implementation protocol summary (phase II), 2010–2012

Phase II included 13 additional sites (Longyang, Shuangjiang, Mengzi, Jianshui, Mile, Jinghong, Menghai, Mengla, Dali, Xiangyun, Ruili, Lianghe, Yingjina) and more comprehensive interventions for HIV, hepatitis B and syphilis.

Integrated counselling and testing for HIV, HBV and syphilis
Counselling and testing for HIV, HBV and syphilis are integrated into the MCH services and provided free to all pregnant women at health facilities. Women can receive counselling and testing services for the three tests simultaneously, both at ANC visits and during L&D (Figure 5). Rapid testing kits are used for the initial screening of all women. Women who receive an initial positive HIV rapid test result have their blood samples drawn for a western blot confirmatory test at the local CDC. Women with a positive syphilis rapid test result have the results confirmed by the toluidine red unheated serum test (TRUST) or rapid plasma reagin (RPR) test at the county MCH hospital.

Adherence counselling for antiretroviral therapy

Intervention for HIV-positive pregnant women and HIV-exposed infants
Once a woman is confirmed as being HIV-positive, she gets detailed post-test counselling on PMTCT interventions and HIV treatment. If she chooses to continue with the pregnancy, she receives regular ANC services as well as the tests required for HIV-infected persons. She is started on triple ARV prophylaxis/treatment as soon as she completes 14 weeks of pregnancy. The woman is closely followed up during pregnancy for ANC and monitored for standard treatment according to the national guidelines. Counselling and logistics are planned to ensure that the woman can arrive at the designated county level hospital in time for delivery. HIV infection alone is not an indication for elective caesarean section. Infants born to HIV-positive mothers are given nevirapine (NVP) or zidovudine (AZT) for 4–6 weeks. Exclusive formula feeding is recommended for infants and free infant formula is provided for 12 months. Early infant diagnosis using DNA polymerase chain reaction (PCR) is recommended at 6 weeks after

**Intervention for women who test positive for syphilis and syphilis-exposed infants**

Two courses of treatment with benzathine penicillin are recommended for syphilis-positive women; each course consists of three intramuscular injections (2.4 M IU) of benzathine penicillin one week apart. Infants born to syphilis-positive mothers who have not completed treatment at least a month before delivery receive one prophylactic intramuscular injection of benzathine penicillin (50,000 units/kg). The syphilis status of infants born to syphilis-positive mothers is assessed by a non-treponemal test every three months until the test becomes negative or the titre has decreased fourfold or more.

**Intervention for HBV-exposed infants**

Infants born to mothers who are positive for the hepatitis B surface antigen (HBsAg) are given a birth dose of hepatitis B vaccine and a dose of hepatitis B immune globulin (HBIG) (100 IU) as soon after birth as possible (within 24 hours). This is called the timely birth dose. The two other doses of hepatitis B vaccine are given at 1 and 6 months of age by the local CDC vaccination staff. The status of HBV-exposed infants is assessed at 12 months.

National implementation is supported by an integrated PMTCT training curriculum for health service providers developed in 2012. Visual aids/posters have also been developed to remind them of the interventions for detecting and managing persons with HIV, syphilis and HBV, and following them up (Annexes 1 and 2).

**ZeShan programme support**

Financial support from the ZeShan Foundation enabled expansion of the ADARC collaborative programme with Yunnan to 13 additional counties in 2010 (Table 1), resulting in a doubling of the number of programme sites to a total of 26 counties. These sites are in areas with a high HIV prevalence, and account for almost half of the HIV-positive pregnant women in the province annually.
Our programme protocol of Yunnan closely followed the national guidelines, with a couple of additions aimed at piloting areas that were not yet included in the government protocol. The programme provided free testing for the partners of women who tested positive for syphilis or HBV (partner HIV testing is covered by the government programme). For HBsAg-negative partners of HBsAg-positive women, the programme offered free catch-up hepatitis B vaccination. For partners of women who tested positive for syphilis, free treatment was extended as well to the partner through the programme. Our project also offered free HBsAg screening of HBV-exposed infants.

With the launch of the 2010 national iPMTCT guideline and strong government financial backing to ensure that supplies and drugs required for implementation could be covered, our programme continued its efforts to build local health system capacity so that standard and quality services could be implemented. At the same time, the programme continued to strengthen data collection, analysis and use at all the sites, so that health workers could better understand the progress and challenges through all the data they collected.

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**Table 1: County project sites**

<table>
<thead>
<tr>
<th>Period enrolled into program (year)</th>
<th>Program county/district</th>
</tr>
</thead>
</table>
Results in 2010–2012

ANC coverage in Yunnan improved dramatically in the past few years, reaching 96% in 2010. Good ANC coverage was key to the success of the iPMTCT programme.

**Coverage of testing for HIV, syphilis and hepatitis B**

Within the catchment area of the 26 programme sites, a total of 437,150 women gave birth between 2010 and 2012. Of these women, 98% (428,374) received HIV tests, up from 93.3% in 2009. During the first year of iPMTCT implementation in 2011, delay in procurement and distribution of testing kits during the early part of the year caused some women to miss their HBV and syphilis tests. In 2011, 83% of the women (115,000) received HBV and syphilis testing along with their HIV test. In the second year of programme implementation, HBV and syphilis testing of pregnant women reached 99% (Figure 3).

**Figure 3: Coverage of HIV, HBV and syphilis testing of women who gave birth at the 26 sites from 2009 to 2012**

The timeliness of HIV testing of women also improved at our project sites. Of the women who gave birth in 2009, 70.7% had received HIV testing during ANC visits; the remaining nearly 30% of the women got tested for the first time only when they came to the hospital for delivery. In 2012, 90.3% of the women who gave birth had received HIV testing during ANC visits (Figure 4).
Towards eliminating perinatal transmission of HIV, syphilis and hepatitis B in Yunnan: a case study, 2005-2012

Figure 4: Proportion of pregnant women who had an HIV test during ANC visits from 2009 to 2012

<table>
<thead>
<tr>
<th>Year</th>
<th>% of pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>71</td>
</tr>
<tr>
<td>2010</td>
<td>79</td>
</tr>
<tr>
<td>2011</td>
<td>86</td>
</tr>
<tr>
<td>2012</td>
<td>90</td>
</tr>
</tbody>
</table>

HBV, syphilis and HIV infection rates in pregnant women

Of the 161,000 pregnant women who gave birth in 2012 and had been screened, 4,849 (3.0%) tested positive for HBsAg, 539 (0.33%) for HIV and 205 (0.13%) for syphilis. The proportion of pregnant women with HBV was much higher than that of pregnant women with syphilis or HIV (Figure 5).

Figure 5: Number of women who delivered in 2012 detected with HIV, HBV or syphilis

<table>
<thead>
<tr>
<th>Virus</th>
<th>Number of women who delivered</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>4,849</td>
</tr>
<tr>
<td>HIV</td>
<td>539</td>
</tr>
<tr>
<td>Syphilis</td>
<td>205</td>
</tr>
</tbody>
</table>
Scaling up triple ARV prophylaxis during pregnancy

Over the project period, the use of triple ARV prophylaxis for HIV-positive women was rapidly scaled up. The proportion of identified HIV-positive pregnant women who received triple ARV prophylaxis increased from <50% in 2009 to >85% in 2012 (Figure 6).

Figure 6: Distribution of different prophylactic regimens used for HIV-positive women from 2009 to 2012

- **ARV antiretroviral; sdNVP single-dose nevirapine; scAZT short-course zidovudine; L&D labour and delivery**

Late discovery of HIV-positive pregnant women and late intervention

While the coverage of universal testing and provision of early testing improved considerably, a significant proportion of women were tested late in their pregnancy or tested only when they came to the hospital for delivery. Late identification of HIV-positive women meant that these women missed the optimal time to start ARV prophylaxis. Out of the 528 HIV-positive women who gave birth in 2012, 59 (11%) received ARV prophylaxis only during labour and delivery, and 13 (2.5%) women did not receive any prophylaxis (Figure 7). While some challenges (such as migrant women who return late to their hometown late during pregnancy) are part of a larger social phenomenon that is difficult for the health sector to address, other barriers could be overcome through further strengthening linkages within the local health system. For example, it was found that a considerable proportion of women who did not receive any intervention until delivery were actually women with a known HIV-
positive status before the current pregnancy. These women were registered with the CDC, yet for various reasons such as fear of stigma and discrimination, and fear of a negative impact on their family status if their HIV status became known, they tended to reject any follow-up, and deliberately avoided any contact with health institutions. Another group of women had presented for ANC during pregnancy at a local health facility, but had missed HIV testing. Such incidents could be further reduced by fixing the loopholes within the system.

**Figure 7: Implementation cascade of PMTCT for HIV from 2010 to 2012**

![Figure 7: Implementation cascade of PMTCT for HIV from 2010 to 2012](image)

**ARV antiretroviral medicines**
Testing and follow up of HIV-exposed infants

By May 2013, 1270 out of 1557 infants (81%) born to HIV-positive mothers from 2010 to 2012 had been tested for HIV. However, the health system needs to pay close attention to the follow-up and care of HIV-exposed infants. First, there was a delay in scaling-up early infant HIV testing. Most of the HIV-exposed infants in 2010 and 2011 did not receive early HIV testing, and received antibody testing only when they were 18 months of age, delaying the opportunity for early commencement of ART. This delay was due to issues related to the procurement of early infant diagnosis (EID) kits and customs clearances at the national level, which should be resolved in the near future. Treatment initiation for confirmed HIV-positive infants is also a problem. Many parents were reluctant to start treatment for their infants at an early age. Therefore, better counselling needs to be provided for parents to understand the importance of accepting treatment for their children. Another major issue was the higher mortality rate of HIV-exposed infants compared to infants in the general population. From 2010 to 2012, 50 HIV-exposed infants (3.2%) died at programme sites. This mortality rate was three times higher than the infant mortality rate of the general population in Yunnan (1.1%). Close to 50% of deaths among HIV-exposed infants were directly related to improper formula-feeding practices, which caused diarrhoea, malnutrition and pneumonia. The lack of timely follow-up of a sick child was a problem. In future, local health workers need to find ways to provide more effective feeding support to women and, at the same time, make greater efforts to be in touch with the family in order to provide timely intervention for a sick child.

Outcomes of HIV-exposed infants

Out of these 1270 infants born to HIV-positive mothers in 2010–2012 and tested, 24 infants (1.9%) tested positive for HIV. The MTCT rates among infants tested were stable from 2010 to 2012, which was below the national average. The national target rate of <5% for MTCT of HIV has been reached at the project sites. Out of the 24 infants detected with HIV, six have started ART, and only one started treatment before 18 months of age. Fifty HIV-exposed infants have died (3.2%); 40 of them died without HIV testing, and two were HIV-positive. HIV-free survival of HIV-exposed children was therefore only 95%.

Coverage of interventions for infants born to HBV-positive mothers

HBIG and timely birth dose of vaccine

Out of the 2803 and 4849 infants born to HBsAg-positive women in 2011 and 2012, respectively, 2526 (89.7%) in 2011 and 4783 (98.6%) in 2012 were given HBIG plus the first dose of HBV vaccine within 24 hours of birth. This amounted to a significant improvement in the two-year duration of the project.

Tracking HBV vaccination status of infants born to HBsAg-positive mothers

At our 26 project sites, the MCH programme tracked HBV-exposed infants to collect information on the coverage of the second and third doses of HBV vaccination. Monitoring infant vaccinations is typically the responsibility of the local CDC. However, the CDC collects HBV vaccination data for all infants in the general population, and does not differentiate between infants who are born to HBV-infected mothers and other infants. The population of HBV-exposed infants is particularly vulnerable to HBV infection, and therefore needs special attention. In 2011, only a few MCH sites had developed mechanisms to collect vaccination coverage data of HBV-exposed infants. Thus, after birth, only a very small percentage of children were tracked.
Towards eliminating perinatal transmission of HIV, syphilis and hepatitis B in Yunnan: a case study, 2005-2012

by the MCH for their vaccination status at 1 and 6 months in 2011 (Figure 8). There was a significant improvement in the tracking of HBV-exposed infants at most of the sites in 2012. Despite a high coverage of all three doses of the vaccine (>95%), out of the 4525 HBV-exposed infant case reports collected in 2012, 65% and 61% of the infants were tracked by MCH staff to confirm the completion of their second and third doses of HBV vaccination. Out of the 14 sites that had established a tracking mechanism that fully utilized the network of township and village doctors, confirmation of completion of all three doses of hepatitis B vaccine reached 98%.

Figure 8: HBV PMTCT implementation cascade in 2011 and 2012

Follow-up and outcome of HBV-exposed infants

Out of the 7309 HBV-exposed infants who had received HBIG and completed the three doses of HBV vaccination in 2011 and 2012, the project provided free HBV testing to 1293 (17%) infants at 8–9 months of age. The remaining HBV-exposed infants did not receive any follow-up testing as the national iPMTCT programme does not pay for it. Overall, 23 (1.8%) of these infants were detected to be HBsAg-positive. The HBV MTCT rate among the infants tested was 1.8% in 2012.
Free testing and catch-up vaccination for partners of HBV-positive women

Uptake of HBV testing among partners of HBsAg-positive women increased significantly during 2012. In 2011, only 110 (3.9%) partners of the 2803 HBV-infected pregnant women were tested, and 22 partners received catch-up vaccination. In 2012, 1825 (37.6%) partners of the 4849 HBV-infected pregnant women received HBV testing, and 876 HBV-negative partners (54%, 876/1624) received catch-up vaccination. Lack of awareness of HBV was the main reason for husbands’ refusing to undergo testing.

Coverage of interventions for syphilis-positive women and syphilis-exposed infants

Out of the 205 syphilis-positive women who gave birth in 2012, 176 (86%) received benzathine penicillin treatment during pregnancy, up from 82.5% in 2011. As with HIV-positive women, late discovery was the major reason for women not getting timely treatment. A total of 124 (60%) syphilis-exposed infants were tested for syphilis but no case of congenital syphilis was identified (Figure 9).

Figure 9: PMTCT implementation cascade for syphilis in 2011 and 2012
Achievements and challenges

Significant progress has been made in PMTCT services over the past three years. The coverage of pregnant women with integrated testing was more than 95% in 2012. The coverage of interventions for PMTCT increased to more than 80% for the three diseases in 2012. Although the follow-up of exposed infants has increased, it remains a challenge, in particular, for syphilis and HBV.

Follow up of HBV-exposed children: a heavy workload

Because of the higher prevalence of HBV, the number of infants born to HBV-positive mothers could be more than ten times the number of infants born to HIV-positive mothers at project sites. All the MCH sites have done an excellent job of providing the birth dose of vaccination and HBIG for HBV-exposed infants after birth. However, follow-up all the cases after they have left the hospital to collect information on the completion of the remaining two doses of vaccination (at 1 month and 6 months) remains a challenge. The follow-up system developed through the initial HIV PMTCT programme was meant for small numbers of HIV-exposed infants. Following up large numbers requires new systematic approaches. Most of the sites have made a remarkable effort to follow up HBV-exposed infants. Ten sites have achieved close to 100% confirmation of the infants’ second and third HBV vaccination shots. Other sites could learn from the best practices at these sites of how to utilize the local health network, including the township and village doctors and the CDC, to follow up exposed infants, instead of increasing the workload of the MCH hospital.

Syphilis testing: need for additional training to improve testing quality

Capacity for laboratory testing of syphilis remains an issue. The importance of estimating RPR or TRUST titres for follow-up of treatment is not well understood. Large variations have been observed in titre results on the same sample. Thus, additional training is needed to improve testing ability so that the treatment results of women and infants can be better monitored.

Improving the cascade of services to ensure elimination of MTCT

The MTCT rates among those tested are low but MTCT of HIV could decrease to below 1% if triple ARV prophylaxis is provided earlier. HIV-free survival should be improved by careful case-by-case assessment and support for infant feeding.
Lessons learnt

The commendable progress made by the integrated programme for PMTCT of HBV, syphilis and HIV in Yunnan are due to the following elements:

• Political and financial support by the government provided the critical basis for the iPMTCT programme. Additional technical and supplemental financial support from the project played an important role in rapidly building local capacity and improving service implementation.

• Strong leadership and high political commitment by health authorities at the provincial, prefecture/city, county, township and village levels resulted in rapid expansion of the programme.

• A standardized approach to iPMTCT using a standardized protocol and training package supported implementation.

• Strong coordination mechanisms and operational linkages existed between the MCH Programme, Expanded Programme on Immunization (EPI)/CDC, specialized services for HIV, syphilis and HBV, and village doctors.

• A continuous quality improvement model was used, based on strong monitoring and evaluation of the programme. The trend analysis of coverage of services, monitoring of the PMTCT cascade, MTCT rates and a systematic analysis of transmitted cases were useful in understanding programme achievements and gaps, and directing attention towards what needs to be improved.
Annex 1
Integrated HIV, syphilis and HBV PMTCT interventions during ANC, labour and delivery, and post partum

iPMTCT Patient flow and activities

ANC antenatal care; ART antiretroviral treatment; AZT azidothymidine; CBO community based organization; CTX cotrimoxazole; DNA PCR deoxyribonucleic acid polymerase chain reaction; HBV hepatitis B virus; HBsAg hepatitis B surface antigen; iTC integrated testing and counselling, 3TC lamivudine; iPITC integrated provider initiated testing and counselling, VL viral load.
### Annex 2

**Integrated interventions for the follow-up of HIV-, syphilis- or HBV-exposed infants in China**

#### Follow-up care of HIV, syphilis and HBV-exposed infants

<table>
<thead>
<tr>
<th>Activity:</th>
<th>Birth</th>
<th>4–6 weeks</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
<th>18 months</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV-EXPOSED</strong></td>
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<tr>
<td>Infant ARV prophylaxis</td>
<td>Daily nevirapine or twice daily AZT from birth to 4–6 weeks</td>
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<tr>
<td>Infant-feeding counselling and support or formula feeding</td>
<td>Encourage formula feeding</td>
<td>Consider breastfeeding only if conditions for safe feeding are not met</td>
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<td>Co-trimoxazole prophylaxis</td>
<td>No</td>
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<tr>
<td>Early infant diagnosis by HIV-DNA PCR testing</td>
<td>No</td>
<td>DNA PCR 1</td>
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<td>DNA PCR 2</td>
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<td><strong>SYphilis-EXPOSED</strong></td>
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<tr>
<td>Infant syphilis prophylaxis</td>
<td>Benzathine penicillin 2.4 MIU im x1</td>
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<td>Infant RPR testing</td>
<td>✔</td>
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<tr>
<td><strong>HBV-EXPOSED</strong></td>
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<tr>
<td>Infant HBV PEP</td>
<td>HBIG 100 IU im x1</td>
<td>HBV-1st dose</td>
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<td>HBV-2</td>
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<tr>
<td>Clinical assessment including signs &amp; symptoms of HIV and/or congenital syphilis</td>
<td>Evidence of HIV is not usually present at birth</td>
<td>Carefully assess for signs of congenital syphilis</td>
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<td>Growth and development</td>
<td>Refer if underweight</td>
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<tr>
<td>Check immunization status</td>
<td>Birth</td>
<td>HBV-1 BCG**</td>
<td>HBV-2</td>
<td>OPV-1, Hb-1</td>
<td>OPV-2, Hb-2, DTaP-1</td>
<td>OPV-3, Hb-3, DTaP-2</td>
<td>DTaP-3</td>
<td>HBV-3, MPSV-A</td>
<td>MV or MR, JEV-L</td>
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<td>1 month</td>
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* Safe replacement feeding means that safe water and sanitations are assured in the household and the community and the mother or other caregiver can relyably provide sufficient infant formula milk to support normal growth and development of the infant and can prepare it cleanly and frequently enough so that it is safe and caries a low risk of diarrhoea and malnutrition and can, in the first six months, exclusively give infant formula milk and the family is supportive of this practice and the mother or caregiver can access health care that offers comprehensive child health services. Note: previously referred to as AFASS (acceptable, feasible, affordable, safe, sustainable).

** In HIV-exposed infants, BCG is given after HIV status is concluded negative. For syphilis and HBV-exposed infants, BCG is given as per national schedule.

Note: A positive DNA PCR test result should always be followed by a confirmatory test. ART should be started as soon as possible. Do not wait for the confirmatory test result.

** HIV, syphilis, HBV-exposed Infant Fup, April 2015
** ARV: antiretroviral; AZT: azidothymidine; EID: early infant diagnosis; DTaP: Diphtheria, Tetanus, acellular Pertusis; JEV: Japanese encephalitis vaccine; DNA: deoxyribonucleic acid; HBV: hepatitis B; Hb: Hemophilus Influenzae Type b vaccine; MMR: Measles, Mumps, and Rubella vaccine; OPV: oral polio vaccine; MPSV: Menencoccal polysaccharide vaccine A,C; MV: measles vaccine; MR: measles and rubella vaccine; RPR: rapid plasma reagin.