

## IMPACT UNIVERSAL: End of Project Report

Project number: .....

Organisation name: University of KwaZulu-Natal, Durban, South Africa

Project Name: A PILOT TO EVALUATE THE ACCEPTABILITY AND FEASIBILITY OF PROVIDING  
ROUTINE HIV TESTING OF ALL 6 WEEK OLD INFANTS ATTENDING IMMUNIZATION  
CLINICS

Project period covered by this report: October 2007 to June 2008 (completion)

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### Project Summary:

The Impact Universal Testing – Feasibility study sought to evaluate the acceptability, utility and feasibility of routine HIV testing of infants at 6-week immunization visits. The specific aims were to learn:

1. How feasible is it to provide routine post-natal testing as a routine service within a primary health care system? What is the uptake of results at subsequent immunization clinics? How feasible is follow-up to ensure that infant test results are delivered? What additional financial costs or other burdens on clinic flow might be anticipated from this additional testing?
2. How acceptable is post-natal testing to mothers, other caregivers, local community and health-care providers (nurses and counselors) as a means of determining infant HIV status and also the status of mothers?
3. What is the utility of routine post-natal testing? Does it allow for earlier identification of infected children born to known HIV-infected mothers and the identification of children whose maternal antenatal status was negative or unknown? Does testing provide a useful way of evaluating program effectiveness on a population level?

### Project Outcomes:

Objective	Outputs against objective
1. Complete a research study as per protocol	Study completed
2. Complete the study write – up for public dissemination	Write-up completed and submitted to peer-reviewed journal
3. Present findings to Provincial and National Departments of Health	Results presented
4. Present findings to the international scientific community	Presentation due to be given at the CROI conference, Montreal, in February 2009
5.	

Provide below a written overview as to how this project has performed against its original targets, providing explanations as to any opportunities or constraints that have affected project performance:

The project was completed as per the original protocol.

The study was implemented between October 2007 and February 2008 at three clinics in KwaZulu Natal – Caluza, Mpumuza and Bothas Hill.

Trained counsellors invited mothers bringing their infants for immunisation at three primary health care facilities in KwaZulu Natal, to give permission for their infants to be tested for HIV. KwaZulu Natal is the largest Province in South Africa with an HIV prevalence rate of ~39% among women attending antenatal clinics(11). Mothers who agreed were also asked about their own prior experiences of HIV testing and PMTCT services. Inclusion for testing was limited to infants attending any of the first three immunisations i.e. at 6, 10 or 14 weeks of age. The testing method, return appointment and provision of results were explained to groups of mothers while waiting for the immunisation.

If a mother gave signed consent for her infant to be tested then blood was collected from the infant by heel prick onto filter paper. Filter paper samples were dried and transported to the laboratory once per week. Dried blood spot (DBS) samples were labelled with a sample ID number that was linked to infant details on a separate record sheet. Infant DBS samples were first tested for HIV antibodies (Vironostika HIV Uni-Form II plus O, Biomerieux, Netherlands). Samples that were found to have HIV antibodies were then tested for HIV by DNA PCR (AMPLICOR HIV-1 DNA test version 1.5, Roche Diagnostics, USA).

Prior to requesting consent the implications of potential results were explained:

1. The infant's dried blood spot has HIV antibody present. At this age, HIV antibodies will be maternal antibodies and will therefore indicate maternal infection. In this situation:
  - a. The mother may already know that she is positive (ANC testing or testing prior to the pregnancy);
  - b. She may have tested negative at the antenatal clinic and believed that she was HIV uninfected – she might have been in the window period or became HIV infected after ANC testing;
  - c. She may not have known her HIV status prior to this test.
2. If HIV antibody is present the infant's dried blood spot will be tested for HIV by DNA PCR. This test may be positive or negative and will indicate the HIV status of the infant.
3. The result of the HIV antibody or PCR tests may be indeterminate and a repeat sample is needed.

Staff were trained to clearly explain each of these scenarios and how to respond to questions. Mothers were also given the opportunity to individually talk more about testing and possible results. The counsellors were trained on how to post-test counsel mothers in each of these scenarios. Infants who were not accompanied by the mother were not included even if the caregiver was the legal guardian.

Mothers were given an appointment date about two weeks later to return for results. If mothers were unable to attend the appointment, she could also speak to counsellors at the next scheduled immunisation date. Three counsellors were present at each clinic, each day. After results were returned to the clinic, a system of unique identifiers and passwords (chosen by the mother at the time of testing) was used to ensure confidentiality.

At post-test counselling, if antibodies were present on the infant DBS the mother was advised that she herself was probably HIV infected and referred to the routine HIV services in the clinic for confirmation. If HIV DNA testing of the DBS was also positive, then counsellors advised mothers that their infant was probably infected and similarly referred for confirmatory testing; prophylactic cotrimoxazole was also started. Mothers and infants who were subsequently confirmed HIV-infected were immediately referred for assessment for ART. Each of the clinics were 'stepdown' facilities that were able to perform CD4 testing and dispense antiretroviral drugs if therapy was started at the nearby ART initiation site.

All mothers who had brought their infants for immunisations, irrespective of whether they had agreed to HIV testing of their infants, were also invited to participate in exit interviews following the immunisation. Information collected through the exit interviews was not linked with earlier interviews or the status of mother or infant. Questions included how they felt when given the option of their infants being tested and what were the advantages or disadvantages of infant testing.

Sample size. In a prior surveillance project, there was 87% acceptance by mothers for anonymised screening of their infants that adopted the same laboratory testing algorithm (8). In this study, to detect a similar 85% uptake +/- 5% at the 95% confidence level, we needed to approach 195 mothers with the offer of infant HIV testing. About 200 mothers were therefore approached at each clinic.

Analysis approach. The primary outcome was acceptability of the offer of infant testing. Acceptability was assessed first by the proportion of women who agreed to testing of their infants and secondly by the number of mothers who returned for results. Additional aspects explored included the time interval until mothers returned for results if not on the scheduled appointment date, and whether return rates varied by HIV status of the mother (either according to antibody status of the infant or by maternal self-reported HIV status). Simple frequency distributions were calculated for responses collected from the exit interviews. Although HIV prevalence rates would be available, this was not the primary outcome and sample size was not based on this estimation. SPSS version 15.0 (SPSS Inc., Chicago, Illinois) was used to analyse the data. A p value <0.05 was considered as statistically significant.

The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and also by the KwaZulu Natal Department of Health.

## **Results**

Between November 2007-February 2008, 646 mothers of infants brought to three peri-urban primary health care facilities in KwaZulu-Natal were approached by study counsellors regarding HIV testing of their infant. Of these, 584 (90.4%; 95% CI 87.8%, 92.5%) agreed to testing (giving signed written consent) and DBS samples were collected from their infants on the same day. Mothers' details and self-reported experiences of HIV testing are included in table 1. About 98% women reported having ever tested for HIV and almost all stated that they had received results. 266 women reported having swallowed nevirapine in the labour ward even though only 233 self-reported being HIV infected. Among mothers who reported being HIV infected, about 70% said their infants received sdNVP while almost a quarter did not know whether their child had received anything.

Of the 584 mothers who agreed to infant testing, 332 (56.8% ; 95% CI 52.7%, 60.9%) subsequently returned for the results of their infants. Of those who returned, 160 (48.2%) came back on the scheduled appointment date. Of those mothers who came at a time other than the scheduled date, 80% came about 4 weeks after the first attendance. Data on both HIV antibody status of DBS and date of scheduled appointment for results and post-test counselling were available on 520 infants and mothers. There was no significant difference in return rates ( $p=0.092$ ) according to antibody status of the DBS (Table 2). However, women who self-reported being HIV positive were more likely to return than women who

self-reported being HIV negative ( $p=0.001$ ). Combining the rates of initial uptake and returning for results, 51% (332/646) of infants and mothers were informed of, or had their HIV status confirmed through this approach.

Overall, 247 of 584 (42.3%) infant dried blood spot samples had HIV antibodies present which is comparable to estimates of antenatal HIV prevalence. Of these, 54/247 (21.9%) samples were positive for HIV DNA by PCR. This equates to 9.2% (54/584) of all infants tested. Results of antibody testing were equivocal in 20 dried blood spots. Among women who self-reported being HIV uninfected, 7.2% of their infants had HIV antibodies indicating that these mothers were in fact HIV-infected. These mothers may have been in the window period when tested antenatally or had become HIV-infected since then, or had opted to tell the team that they were uninfected. The vertical HIV transmission rate from these mothers to their infants was 38%.

Women's perspectives on being offered testing of their infants are summarised in Table 3. The vast majority stated that they were generally comfortable with being offered testing of their infant (Table 3a). Few remarked that they were anxious, shocked or frightened by the invitation. A small number were surprised by the presence of counsellors and the offer of testing. Reasons given for not testing (Table 3b) included anxiety, fear and indecision. A small number commented that their infant had been tested elsewhere and the result was pending. When asked about the advantages of testing (Table 3c), confirmation of HIV status was widely acknowledged and about half of women recognised that it would enable opportunities for antiretroviral therapy. Only about one quarter of mothers realised that confirming the infant's and her own HIV status would directly inform what would be the best infant feeding practice; even fewer mothers knew about cotrimoxazole prophylaxis. Women described a number of perceived disadvantages. About a quarter of women commented that the prospect of testing and the implications were 'frightening', or the process was 'too quick', or that they were concerned that it revealed HIV status. 580 of 646 (89.8%) mother interviewed said they would recommend testing to others.

Counsellors were consistently positive about the testing strategy stating that it had several benefits for infants and mothers. They commented that, in general, mothers were 'excited' by the opportunity to learn their infant's status and that the approach was 'important for all of South Africa'. However they commented that there was little space and privacy in the clinics and that it was hard to look after an infant if the mother started crying. Other difficulties reported included mothers who refused subsequent care, or who were angry or confrontational after being post-test counselled; in particular the complexities when HIV positive mothers had not disclosed their status to their partner or family.

During the implementation phase of the study a total of 18 counsellors and field staff were employed in addition to 2 supervisors and one data entry clerk. One consultant was employed for training and supervision.

Additional costs were encountered for travel of supervisors and training activities.

*Perlcom* – a local IT company - developed a database for data capture and data storage and assisted in merging of HIV results and data extraction

### **Current status**

The data has all been entered and cleaned and the data analysed by a statistician in the College of Health Sciences, UKZN. A manuscript has been prepared and submitted to a peer-reviewed journal.

The concept and results have been presented to the Provincial and National Departments of Health in SA.

The results will also be presented at the Conference on Retrovirus and Opportunistic Infections (CROI) in Montreal in Feb 2009. This is probably the leading international HIV-AIDS scientific meeting.

#### Lessons Learned:

In this study, routine HIV testing of infants attending primary health care clinics for immunisation was acceptable and feasible. If routinely implemented, more than half of infants and mothers would have known their status at about 6-10 weeks of age after which they could gain access to a continuum of care. With better awareness within communities and a more 'routine' approach being offered by staff, this number could increase. In this study more than half of the peripartum infected infants were thereby identified and referred for HIV treatment. This contrasts sharply with the experience of PMTCT programmes in which routine HIV testing of infants is achieved in only 8% HIV-exposed infants(12). Routine implementation would also serve to identify, and refer for treatment and care, women who previously thought they were HIV uninfected but who had become HIV infected during pregnancy. In high HIV prevalence settings, this approach has the potential for significantly increasing the number of mothers and children gaining access to HIV treatment and care.

We gauged acceptability by the number of women who accepted testing of their infants and, perhaps more importantly, the number of women who returned for the results. About 93% of women agreed to testing of their infants after full explanation of the process including implications for themselves. There was no significant difference in return rates ( $p=0.092$ ) according to DBS antibody status suggesting that mothers decisions were not significantly influenced by their actual HIV status (Table 2). Both the initial acceptance rates and the return for results data suggest that infant HIV testing is acceptable.

Mothers not returning on the scheduled date tended to return about 4 weeks later which may have coincided with the next immunisation visit. Considerations such as money or other commitments might have precluded them from coming for the 'extra' post-test counselling visit, whereas they felt able to combine it with the next immunisation visit. Other mothers may have chosen to come back on the next immunisation visit in order to disguise their return for results.

We implemented an opt-out HIV pre-test counselling approach, but with the option of one-on-one counselling, and individualised post-test counselling. Although immunisations are offered every day of the week, mothers still informally adhere to certain patterns of attendance, resulting in certain days of the week being inundated. We therefore appointed three counsellors per clinic who together were able to cope with the abbreviated counselling and testing strategy.

Although this study suggests that this would be a feasible approach to achieve early infant diagnosis, the demands on the counsellor teams were complex and more intense than are perhaps immediately evident. Considerable planning and training of counsellors was undertaken to ensure that each were able to manage the various anticipated scenarios. These included mothers believing that they were HIV uninfected and therefore not taking any intervention, only to learn that they and perhaps their infants were actually infected. Such scenarios are not included in routine HIV counsellor training and hence our supervisory team carefully monitored how counsellors were coping. They actually managed well and the training seemed to have equipped the counsellors with the necessary competencies. If such a strategy were scaled up, several questions would need to be addressed such as whether a lesser intensity of pre- and post test counselling would result in lower uptake of testing or return for results, or increased stress for the mother. In the study we implemented a password system that protected the confidentiality of the infant's results and therefore the mother's HIV status. If taken to scale, similar consideration would be needed in case the infant was brought for a later immunisation by another caregiver.

The testing approach described can only be used in first 1-2 months of an infant's life when maternal antibodies are definitely present and a high level of sensitivity could be expected. At this age, the approach is efficient and could bridge the gap between antenatal services and opportunities for postnatal care. In older infants and in those who were breastfed, it would be necessary to detect HIV DNA by PCR without any consideration of antibody status; this would have significant cost implications and would limit its utility in determining maternal HIV status.

An ethical question we faced was whether our team had an obligation to seek out the infants and mothers who were found to be HIV-infected but who did not return for results. We did not do so, principally because in our explanation to mothers we indicated that we would provide the results only at the clinics, and that we would not solicit addresses or phone numbers. Had we done so and included this in our pre-test information, mothers may have felt vulnerable and not agreed to testing. Our approach was consistent with current HIV testing at public health facilities in South Africa namely, patients return for results, as and when they choose.


In addition to the vast majority consenting to their infants being tested, mothers also expressed their acceptance in the exit interviews. Most mothers felt comfortable with the idea of testing, understood the value of early diagnosis and would recommend it to others. Some may have felt that testing of their infant was less daunting than testing again themselves, knowing that it would infer their own HIV status. Only a small proportion expressed anxiety and this was reflected in the small proportion that refused testing. Of note, few mothers acknowledged the value of knowing their own HIV status in guiding decisions on infant feeding practices.

Good News Stories:

HIV testing of all infants attending immunisation clinics in this study was acceptable and feasible. In high prevalence settings, the routine offer of HIV testing at immunisation clinics to young infants and/or mothers could enable both to receive early treatment that could avert the early morbidity and mortality that is seen all too frequently. Mothers demonstrated their understanding of the potential gains of knowing their own and their infant's status.

In your opinion how has this project improved South Africa's response to HIV and AIDS:

It has informed the National and Provincial Departments of Health (and the international community) of not just the feasibility of such an approach but also some of the complex issues that would need to be considered before wide-scale implementation.

	
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