Prevention of mother-to-child transmission of HIV in Africa: successes and challenges in scaling-up a nevirapine-based program in Lusaka, Zambia

Elizabeth M. Stringer\textsuperscript{a–c}, Moses Sinkala\textsuperscript{a–d}, Jeffrey S. A. Stringer\textsuperscript{a–c}, Elizabeth Mzyece\textsuperscript{c}, Ida Makuka\textsuperscript{c}, Robert L. Goldenberg\textsuperscript{a,c}, Pascal Kwape\textsuperscript{e}, Martha Chilufya\textsuperscript{e} and Sten H. Vermund\textsuperscript{a,c}

\textbf{Background:} Nearly half of perinatal HIV infection is preventable with nevirapine (NVP), which has transformed the ability to confront this transmission route in resource-limited settings.


\textbf{Results:} The first 12 months cost US$221 000 and enabled 178 district health employees to be trained in voluntary counseling and testing: 17 263 pregnant women were counseled for HIV, 12 438 (72\%) were tested, and 2924 (24\%) were found to be infected with HIV. NVP has been taken by 1654 (57\%) mothers and 1157 (40\%) babies. It is estimated that at least 190 infants have been spared HIV infection (11 per 1000 counseled women or 65 per 1000 identified HIV-infected women).

\textbf{Conclusions:} Prevention of mother-to-child HIV transmission is feasible and cost effective in resource-limited settings. In Lusaka, thousands of women have received voluntary counseling and testing and NVP therapy under the present scheme. Patient attrition and non-adherence represented a major source of program inefficiency, which requires to be systematically addressed.

\textit{AIDS} 2003, 17:1377–1382

\textbf{Keywords:} HIV, AIDS, Zambia, nevirapine, perinatal, transmission, mother-to-child, sub-Saharan Africa, southern Africa, women, pregnancy, child, infant, cost-effectiveness

\section*{Introduction}

Zambia is one of the most urbanized sub-Saharan African countries, with fully half of the nation’s 10.2 million people living in cities and over one million living in the capital Lusaka. Each year, more than 40 000 babies are born in Lusaka’s 24 public clinics and the University Teaching Hospital. One in four of these infants are delivered to an HIV-infected mother [1,2] and, in the absence of intervention, one in ten (roughly 4000 per year) will become infected themselves [3]. The discovery that as many as half of these infections are preventable with intrapartum and neonatal, single-dose nevirapine (NVP) [4] has transformed the ability to confront this transmission route in Lusaka, where, despite considerable resource limitations in the public
sector, the low cost of the drug and the ease of its administration have permitted rapid expansion of perinatal HIV prevention services.

Prior to initiation of the present program, HIV testing in Lusaka had been available to some expectant mothers in one Lusaka District public clinic and at the University Teaching Hospital through a national pilot program supported by the United Nations. Three other Lusaka District clinics had ongoing perinatal HIV research activities in place and many women were able to access prevention services through those initiatives. In November 2001, the Call-to-Action program was initiated to expand voluntary HIV counseling and testing and NVP availability to all the clinics in the Lusaka District quickly, effectively, and with a view towards long-term sustainability; the program was funded by the Elizabeth Glaser Pediatric AIDS Foundation. This report describes progress and challenges in the first year of bringing these services to scale in a large, urban center in sub-Saharan Africa.

Methods

Training

The initial goal was to offer voluntary counseling and testing and prophylactic antiretroviral medication to at least a subset of pregnant women in each of the city’s nine public delivery centers. Five of the nine public delivery centers were targeted for program initiation; no changes were made to the programs in the three clinics with research initiatives or to the United Nations–supported national pilot program in one clinic. In collaboration with the Zambian Counseling Council, a competency-based, ‘on-the-job’, 10-week voluntary counseling and testing training program was developed. The initial training session occurred over a 4-week period and was for midwives only (n = 39); it involved group instruction followed by each trainee observing at least three pre-test counseling sessions, three post-test sessions for HIV-seronegative women, and three post-test sessions for HIV-seropositive women. Upon completion of this section, another weekend didactic session was held. Subsequently, each trainee performed at least nine counseling sessions (as above) in her own clinic under direct supervision of an experienced counselor. Each nurse-midwife candidate was evaluated by a written examination that satisfied requirements for a UNAIDS-sanctioned training certificate. The training period used the same record keeping, counseling approaches, and NVP distribution that are now used for routine care.

Patient flow

In the Lusaka District antenatal clinics, pregnant women typically present for care in the early mornings, by

<table>
<thead>
<tr>
<th>PCR</th>
<th>R</th>
<th>NR</th>
<th>RBd</th>
</tr>
</thead>
<tbody>
<tr>
<td>__</td>
<td>__</td>
<td>___</td>
<td>___</td>
</tr>
</tbody>
</table>

Fig. 1. Stamp placed in maternal antenatal record for documenting HIV pre-test counseling, acceptance or refusal of testing, HIV status, and receipt of maternal and infant nevirapine. PCR, patient counseled and refused testing (will be approached again at a subsequent visit); PCA, patient counseled and accepted testing; R, reactive (HIV-infected); NR, non-reactive (HIV uninfected); I, indeterminate; RMd, reactive, mother given the drug; RBd, reactive, baby given the drug.

strong community and clinic tradition. An initial general pregnancy-oriented health talk is given to all women presenting for antenatal care, which includes discussion of the high prevalence of HIV among pregnant women in Lusaka, the risk of perinatal transmission, and the benefits of HIV testing and NVP. Women are encouraged to ask questions during the morning talks and may even be shown a NVP tablet. Women are then counseled individually in private rooms by the midwives, after which they are asked whether they would like to be tested for HIV. Women who express an interest at this point sign a brief consent form and their blood is drawn for HIV serology. The woman’s antenatal book is then coded to indicate whether she refused or accepted testing. An inked stamp was initially used to impress the form for recording these data (Fig. 1) but the form is now incorporated into the bulk printed antenatal record card. The stamp includes a place for HIV test results, and for documentation of receipt of NVP for both mother and infant. After having blood drawn for the HIV test, women are asked (but not required) to wait in a small waiting area until their results return, usually within 1 h. If a woman prefers to return on another day for her results, the counselor keeps the unopened results in a secure cabinet. In practice, very few women have opted not to receive their test results the same day. Post-test counseling of HIV-infected women who have completed 26 weeks of gestation includes distribution of a 200 mg NVP tablet with instructions to ingest at the onset of labor. Women who have not completed 26 weeks of gestation are given the tablet when they reach that gestational age or upon presentation in labor, whichever comes first. Women are encouraged to bring partners for voluntary counseling and testing or for counseling alone. Participation of men is not yet occurring in large numbers.

The Determine HIV-1/2 (Abbott Laboratories, Abbott Park, Illinois, USA) rapid test kit has been used so that women can receive their test results within 1 h. A confirmatory Capillus HIV-1/HIV-2 (Cambridge Biotechnology, Galway, Ireland) rapid test is performed for all positive Determine results. Determine HIV-1/2 test
kits were initially procured at a reduced price through Abbott Corporation. They are now being donated free of charge. NVP has been secured at no cost from Boehringer Ingelheim Corporation through the VIR-AMUNE Donation Programme, administered through Axios International in Dublin, Ireland [5].

**Staffing and remuneration**

Counseling for HIV in high-prevalence settings is time consuming and can be emotionally exhausting. As such, it represents a considerable strain on an already under-staffed midwife pool working in the busy antenatal clinics. Nurse midwives were compensated by allowing them to rotate counseling duties on their off-days for extra pay. A counseling schedule for the nurse midwives was prepared at the beginning of each month and midwives on this schedule delivered the perinatal health talks and provided the voluntary counseling and testing each day. These nurses were paid at a rate that was commensurate with hourly rates during their regular duties in these same clinics.

**Labor and delivery**

Lusaka District statistics indicate that most women deliver in a health center; however, it is suspected that a moderate number of women deliver at home. Unfortunately, these numbers are difficult to collect and so efforts to date have focused on women who deliver in health centers. When a woman presents in labor, the code in her obstetrical record is examined to determine whether she is HIV infected. HIV-infected women are asked whether they ingested the NVP tablet. If a woman reports having taken the tablet more than 48 hours prior to presentation or if she reports vomiting within 30 minutes after ingestion of NVP, she is given an additional NVP dose from a secure stock kept on the labor ward. Pill counts are correlated with the registered doses administered periodically to ensure that stocks are used only for patients needing medicine. Infants born to participating mothers are given NVP syrup prior to discharge home, typically within 12 h of delivery. If a woman states that she plans to deliver at a site other than a participating facility (e.g., her village or a clinic closer to her extended family), or if she is transferred to the University Teaching Hospital, 0.6 ml NVP syrup is drawn into a 1 ml syringe and wrapped in aluminum foil and plastic. The woman is given the syringe and told how and when to administer it to the infant. If an HIV-infected woman delivers at home and brings her infant back to the clinic within 1 week, the infant is given NVP.

**Infant feeding and follow-up**

In the Lusaka District, nursing staff recommend 6 months of exclusive breastfeeding to all postpartum mothers. Women identified as HIV infected are also encouraged to do this unless they can afford formula feeding (highly unusual in this patient population).

Because HIV polymerase chain reaction assays are costly and not available routinely in Lusaka, and since the majority of women choose to breastfeed, mothers are encouraged to bring back their infants at 15–18 months of age for HIV serology testing.

**Implementation and expansion**

The program began in two medium-volume clinics providing delivery services in Lusaka, each with approximately 150 deliveries per month. The nurses at these facilities had no prior training in voluntary counseling and testing or prophylactic provision of antiretroviral therapy. Once the program at the two facilities was well established, it was expanded to three high-volume centers where the nurse midwives already had some training in voluntary counseling and testing. Once the program was functioning in these five sites, training was expanded to five so-called ‘satellite clinics’, which provide antenatal and postnatal services but referred patients for delivery. It is anticipated that the program will expand to all 24 Lusaka District health clinics by March 2004.

**Results**

**Integration**

The program has been successfully integrated into existing antenatal services in the Lusaka District. The nurse midwives in the clinics are now accustomed to performing counseling and the lab technicians perform the rapid HIV tests alongside other antenatal services. In clinics that are particularly busy, the nurse midwives have been trained in rapid testing to assist the lab technicians when necessary. In the satellite antenatal clinics that do not have laboratories, the nurse midwives perform all of the rapid testing.

**Patients treated**

Over the 12 months that the program has been operational, 17,263 women have been counselled and 12,438 (72%) have been tested. HIV infection was confirmed in 2,924 women (24% seroprevalence). Same-day test results were given to almost all patients tested (97%). Of the 2,924 seropositive women, 1,654 (57%) collected a NVP tablet (Table 1). The discrepancy in the number of women issued NVP compared with those who test positive was partly, but not entirely, a result of the lag time between gestational age at testing (22 weeks) and the gestational age at NVP issue (26 weeks). To date, 1,157 infants (40% of eligibles) have been given NVP syrup. Tests have been taken by 86 partners in the program.

Assuming a 40% cumulative transmission rate through breastfeeding, [3], that this risk can be reduced by 41% [95% confidence interval (CI), 16–59] with single-dose
NVP [6], and that the NVP benefit would only derive to those mother–infant pairs who received both the intrapartum and postpartum doses, it was estimated that at least 190 (95% CI, 74–273) infants have been saved from infection to date. Other than reports of sadness and fear over learning of one’s HIV-seropositive status, we have observed no adverse reactions to voluntary counseling and testing or to NVP.

Cost effectiveness

The total cost of the program during its 12 months of operation has been US$221 170. This included US$60 000 in start-up costs, such as counselor and clinician training, minor clinic renovations, purchase of two used vehicles, and a computer and printer. Also included are US$161 170 in recurring costs: salaries for full-time and part-time staff, HIV test kits, blood draw supplies, office supplies and various other incidentals. These figures do not include expatriate salaries or travel expenses, which have been supported by related US National Institutes of Health and private foundation research and training grants. If the start-up costs are subtracted from the overall expenditure so far, the cost of administering the entire program is US$9.34 per patient counseled, US$12.96 per patient tested, US$55.12 per seropositive woman identified, or US$848.26 per infection averted.

Discussion

Zambia’s HIV prevalence rates are among the highest in the world. While simple and cost-effective measures are now available to prevent mother-to-child transmission, implementation is not as straightforward as it may seem. Until recently, most nations in the developing world, including Zambia, have lacked the appropriate personnel, training, and infrastructure to deliver these interventions effectively on a scale commensurate with the huge burden of infection. The Lusaka Call-to-

Table 1. Process indicators from the first 12 months of antenatal voluntary counseling and testing in the first seven Lusaka Urban District Clinics included in the Call to Action program in Zambia.

<table>
<thead>
<tr>
<th>Stage of program intervention</th>
<th>No. women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received HIV-related counselling</td>
<td>17 263 (4)</td>
</tr>
<tr>
<td>Tested for HIV</td>
<td>12 438 (72)</td>
</tr>
<tr>
<td>Women confirmed HIV infected</td>
<td>2924 (24)</td>
</tr>
<tr>
<td>Women given nevirapine at 26 weeks of gestation or greater</td>
<td>1654 (57)</td>
</tr>
<tr>
<td>Total infants receiving nevirapine</td>
<td>1157 (40)</td>
</tr>
</tbody>
</table>

As estimated from the logs kept by the trained nurse midwife counselors; it is not possible to determine the proportion of women in each clinic who are actually receiving counseling because of the way in which antenatal records are kept at present.

Overall seroprevalence in those actually tested.

One of the most challenging components of the program has been to determine its true population coverage rate. In Lusaka, and indeed most of sub-Saharan Africa, pregnant women carry their antenatal records with them. Therefore, while it is straightforward to determine how many counseled women agree to testing, it is more difficult to know what proportion of eligible women are actually getting testing in the various communities served by each clinic. It is clear that the program does not succeed in counseling each and every woman, largely because of staffing and space limitations. In addition, while acceptance rates for testing are 72%, still more than one in five women decline HIV testing. With continued community mobilization and improved counseling skills of the nurses, it is anticipated that the proportion accepting testing will improve.

The most concerning observations are that only 57% of women who tested seropositive were documented as having taken possession of the NVP tablet to date, and that only 40% of infants born to program participants received NVP syrup. Many other studies have noted a similar attrition phenomenon [7]. The number of women and infants receiving NVP should at any given time be lower than the number of identified HIV-infected mothers because of a ‘lag time’ between when women are tested and when they receive NVP. However, we suspect that a significant proportion of the women in our program are not returning to the clinic for receipt of NVP. In practice, this has been very difficult to document, since HIV testing in our setting is anonymous, and we cannot send clinic personnel into the community to locate and question those who elect not to return for care. In recently conducted focus groups with antenatal women, stigma, fear of partner abuse, fear of more rapid death once knowing ones’ status, and not wanting to prevent their babies from getting HIV if there is no maternal treatment available were all reasons women gave for not testing and not taking NVP. Others have postulated similar reasons for refusal of testing, NVP or partner disclosure, such as stigma and fear of violence and desertion [8,9]. We hope that generalized stigma-reduction messages in the target communities will, over time, work to mitigate program dropout. We also expect that, as perinatal prevention services and even treatment become more widely available, testing and medication adherence will improve. Finally, we hope that involvement of men in ongoing perinatal programs will help to increase the number of women and infants who are compliant with interventions to reduce mother-to-child transmission of AIDS 2003, Vol 17 No 9
HIV [10]. We are currently exploring offering partner and couples counseling on weekends.

The costs reported here exceed by several times those estimated in published economic models, including our own [11,12]. There are several potential reasons for this. First, the econometric models may have underestimated certain factors that are critical in real practice, such as the need for full-time coordinating staff, replacement drugs, fuel for vehicles, etc. Second, formal cost-effectiveness analysis would credit a program for averted medical care associated with prevented disease. Therefore, in order to compare the present report directly with prior models, one would have to estimate the cost savings to the medical system of the 190 infant HIV cases we believe have been prevented. Third, and probably most important, a major detriment to the cost effectiveness of our program is the considerable attrition of patients from the system [9]. We may spend considerable resources counseling and identifying them only to have them disappear and not benefit from the intervention. Obviously, retention of patients represents a critical area for evaluation and improvement in our program. Progress in this area, coupled with third-party test kit and drug donations, will likely increase the cost-effectiveness of our program considerably.

Perhaps the single most important element of the program’s initial success has been the strong commitment from the Lusaka District Health Management Board, which is now promoting ‘universal HIV counseling with optional testing’, similar to that increasingly common elsewhere [13]. Despite the challenges we have experienced, the potential public health impact of a program like ours is enormous. Expanded voluntary counseling and testing, improved acceptance of HIV-infected persons, and the extensive community education that accompanies the program will likely provide benefit far beyond the infant lives saved with NVP therapy. Since the NVP component of the program has been uncomplicated and safe, [14], we feel strongly that any facility that successfully offers voluntary counseling and testing to antenatal mothers should also offer prophylactic antiretroviral drugs such as NVP or short-course zidovudine. Early experience in Lusaka suggests that a large-scale, NVP-based perinatal HIV prevention program is feasible and sustainable, especially when drug and test kits are donated and start-up costs are provided. In the next year, we hope to be able to show that antiretroviral treatment services can be integrated into existing perinatal prophylaxis services. Toward that end, we have obtained funding to provide combination antiretroviral treatment to pregnant and postnatal mothers, fathers, and children with AIDS in one Lusaka District facility. Activities began in early 2003 through funding organized by the MTCT, plus a consortium at Columbia University [15]. While we focus on increasing the coverage of our perinatal programs, we believe that finding ways to integrate antiretroviral therapy into these programs will become increasingly important.

Acknowledgements

We thank Drs Rosemary Kumwenda, Elwyn Chomba, Margaret Siwale, Chiipepo Kankasa, Rosemary Sunkutu, Ben Chiirwa, Dirk Buyse, Catherine Wilfert, Trish Devine Carlin, Chuck Hoblitzelle, and the nurses and midwives in the Lusaka District for their contributions.

Sponsorship: The work is supported by the Call-to-Action initiative of the Elizabeth Glaser Pediatric AIDS Foundation. Investigators receive support from the US National Institutes of Health (U01 AI47972-02, D43 TW01035-04, K23 HD01411-01, K01 TW05708-01). Nevirapine is obtained through a donation program from Boehringer Ingelheim Inc. via the Axios Foundation. Test kits have been obtained at no cost from Abbott Pharmaceuticals.

References

10. Shutes E, Vwalika C, Kasonde P, Sinkala M, Kankasa C, Allen S, et al. Involvement of men in programs to prevent mother to...
child transmission of HIV. XIV International Conference on AIDS. Barcelona, July 2002 [abstract MoOrF1032].


