Evaluating the HIV Infant Tracking System (HITSystem) to Improve Early Infant Diagnosis of HIV in The U.S. Military HIV Research Program/PEPFAR in the Southern Highlands using the HITSystem©

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1. Executive Summary:

The HIV pandemic remains a global public health problem, with particularly devastating effects in sub-Saharan Africa. Since the beginning of the epidemic, more than 60 million people have been infected with HIV and nearly 30 million people have died of HIV-related causes (UNAIDS Fact sheet, 2016). Data from 2009 indicate that approximately 68% of the estimated 33.3 million adults and children living with HIV were in Sub Saharan African (22.5 million) (UNAIDS, 2010). Almost 75% of all deaths due to AIDS occurred in sub-Saharan Africa: 1.3 million of 1.8 million globally. However, the number of AIDS-related deaths in sub-Saharan Africa has dropped due to the increasing availability of antiretroviral (ARV) medications. In sub-Saharan Africa, women now account for almost 60% (12.1 million of 20.3 million) of the adults living with HIV (UNAIDS, 2010). The number of children worldwide (age 0–14) living with HIV increased from 2.0 million in 2001 to 2.5 million by 2009, with approximately 90% of these children living in sub-Saharan Africa (UNAIDS, 2010). A great majority of these children are infected with HIV through mother to child transmission (MTCT), during childbirth or through breastfeeding, and a majority of these children will die before their second birthday if they are not initiated on ART (UNAIDS, 2010).

In Tanzania, as in other African countries, there has been a substantial and effective scale up of HIV treatment services. Unfortunately, services for the prevention of mother to child transmission of HIV (PMTCT) and identification of HIV exposed and infected infants have not kept pace. As a result, many infants who are infected with HIV are not properly identified and do not get the lifesaving medication they need.

Henry Jackson Foundation Medical Research International (HJFMRI), in partnership with Global Health Innovations (GHI), aimed to improve PMTCT and the identification and tracking of HIV-exposed infants in the Southern Highlands of Tanzania through an innovation developed by GHI called the HIV Infant Tracking System (HITSystem©). The HITSystem© utilizes automated alerts to overcome current PMTCT and Early Infant Diagnosis (EID) barriers by prospectively tracking HIV-infected pregnant women and their HIV-exposed infants. The purpose of the evaluation was to (1) evaluate the capacity of the HITSystem to improve (EID outcomes; (2) to identify the predictors of better EID and PMTCT outcomes among HIV-exposed infants and HIV-positive mothers respectively and (3) to evaluate the effectiveness of future modifications of the HITSystem in improving other care and treatment outcomes in the program.

The HITSystem was implemented in all facilities offering EID and PMTCT services in the Regions of Mbeya, Songwe, Rukwa, Ruvuma and Katavi from 2013 to 2018 in a staggered fashion i.e. starting with 15 facilities and scaling up to over 182 facilities in the five regions. The facilities were selected on the basis that they were seeing over 20 HIV- exposed infants and HIV-positive mothers who needed EID and PMTCT services in a month. The mothers were enrolled in the intervention on a voluntary basis. Those who consented to participate in the study provided their phone numbers which were entered into the HITSystem database and tracked from the time they attended the antenatal care (ANC) clinic and after they gave birth to when their children reached 18 months of age when they exited the tacking system.

Overall for the facilities where the HITSystem was initiated, >95% of all the infants were tracked from birth to the 18-month period. There was an improvement in initiation of opportunistic infections (OI) medication that reached 99.4% for all the facilities where the intervention was used. A total of 99.8% infants received their DNA PCR results and a total of 99.3% of positive infants requiring antiretroviral therapy (ART) were initiated on ART as required. The main limitations of the study included the fact that there were no control sites to compare the intervention to as the intervention was scaled up to all facilities after it became clear that the HITSystem benefits were all too clear. Additionally, the HITSystem requires internet access and hence there were challenges in data entry at some of the facilities where it was used due to the low internet coverage. For some of these facilities the data had to be entered into the database from another location. The system did not have an offline module. As the HITSystem was being used for research purposes, there is a need to scale it up for programmatic use and reduce the per facility cost.

In conclusion, the HITSystem was seen to have a great impact in improving EID and PMTCT outcomes and has been recommended by the Ministry of Health in Tanzania as one of the interventions to be used in the country. It is recommended that the HITSystem should have an offline module so that data entry can be done even when one is not connected to the internet, and that a cost-effectiveness analysis should be conducted to ensure system sustainability.

2. Project Background:

The HITSystem is a robust tool that allows clinicians, lab technicians, and program managers to track the time-sensitive interventions of PMTCT, EID and ART programs in a "real-time" manner using online entries to trigger action 'alerts' when time sensitive interventions are overdue. An integrated text messaging system sends automated text messages to mothers' cell phones when test results are ready or follow-up visits are needed. The ultimate goal of the HITSystem© was to increase the number of HIV-positive pregnant women receiving complete PMTCT care, improve uptake of EID by coordinating PMTCT and EID services, improve retention of HIV-exposed infants retained in EID services until 18 months, improve early ART initiation for infants diagnosed with HIV, and improve retention and clinical care outcomes of HIV-positive infants initiated on ART. The HITSystem was used to carry out an evaluation with the aim of improving the uptake of EID and POMTCT services in the southern highlands of Tanzania where HJFMRI works.

The evaluation was carried out in 161 health facilities offering early infant diagnosis of HIV (EID) services in southern Tanzania. These facilities were located in the regions of Rukwa, Ruvuma, Mbeya, Songwe and Katavi. The facilities were selected on the basis that they were seeing at least 20-40 HIV exposed infants per month. The evaluation began in September 2013 and was completed in September 2018. The total cost of the evaluation was $633,630.50. The general objective of this evaluation was to improve the uptake of EID and PMTCT services in the southern highlands using the HIV Infant Tracking System (HITSystem).

The specific objectives of the study were as below:

1. To evaluate the HITSystem's capacity to improve the 1) retention, 2) timely provision of 8 time-sensitive intervention benchmarks for EID services, and 3) EID outcomes (including infant positivity rate by 18 months, infant mortality, etc.)
2. To identify among HIV-exposed infants predictors of (1) incomplete EID care, (2) time periods most vulnerable to loss of contact, and (3) infant outcomes.
3. To evaluate the HITSystem's capacity to improve the 1) retention, 2) timely provision of benchmarks for PMTCT services, and PMTCT outcomes (including maternal mortality, pregnancy outcomes, infant linkage to EID, and infant HIV status at first test)
4. To identify among HIV-infected mothers predicators of 1) incomplete PMTCT care, 2) time periods most vulnerable to loss of contact, and 3) poor PMTCT outcomes.

5. To evaluate the future modifications of the HITSystem, including in-progress modules to improve 1) pediatric and 2) adult HIV care including: retention in ART treatment, ART adherence, and immunologic/virologic outcomes (viral load and CD4).

3. Evaluation Design, Methods, and Limitations

3.1 Evaluation Type & Design:

This impact evaluation was carried out in 161 health facilities where the HITSystem was implemented. Implementation of HITSystem (EID module) started in 2013. The PMTCT module was introduced to all HITSystem sites simultaneously in January 2016 and the combined EID/PMTCT was introduced to all facilities that began implementing the HITSystem after January 2016. HITSystem program staff collected de-identified pre-intervention data from implementing facilities, which was compared to post-implementation data collected in the HITSystem.

Key indicators that were used to measure performance outcomes are detailed below:

1. **OI prophylaxis Y/N, age OI administered:** % and age receiving OI prophylaxis
2. **DBS collection Y/N, age at DBS collection:** % with DBS collected; Age at DBS collection
3. **Number of days from DBS collection to receipt of sample at laboratory**: % received at lab; TAT of receipt at lab
4. **Number of days for testing cycle**: PCR test date, dispatch of results to hospital (Control)/ PCR results posted (HITSystem): % sample with result indicated; TAT of results
5. **Mother notified of results Y/N, date of notification, # of days from receipt of results to notification of mother:** % mothers notified of infant status; TAT of notification
6. **ART initiation of HIV+ infants Y/N, date initiated and number of days from notification to initiation:** % positive infants; % positive infants initiated on ART; TAT of ART initiation; Infant age at ART initiation
7. **Re-test HIV exposed infants at 13.5 months (or other specified time point according to the Tanzania National EID Algorithm):** Y/N, infant age at re-test: % negative infants receiving 13.5m (or other specified time point according to the Tanzania National EID Algorithm)

Pre-intervention data from EID patients receiving care during the year prior to implementation of the HITSystem was compiled by every infant file recorded in the HIV Exposed Infant (HEI) Registry from the twelve months prior to HITSystem implementation at each facility. All data collected for the retrospective review was coded, thus no identifying patient data was collected.

To determine whether the HITSystem improved longitudinal EID service provision and outcomes, we compared infant outcomes and the proportion of mother-infant pairs still enrolled at each step of the EID cascade between pre- and post- HITSystem periods. Patterns of EID utilization (characterized as complete or incomplete) were also reviewed. Incomplete EID care was defined as one or more of the following: (1) DBS not collected, (2) Mother not notified of result, (3) HIV-positive infant not started on ART, (3) High-risk infants (as defined by national Tanzania guidelines) who have not received the appropriate ART prophylaxis regimen or have not received prophylaxis for the required duration, (4) HIV-exposed infant not re-tested at 13.5 months (or other specified time point according to future updates of the Tanzania National EID Algorithm) and (5) HIV exposed infant not tested at 18 months or 12 weeks following the cessation of breastfeeding (whichever is later or other specified time point according to future updates of the Tanzania National EID testing Algorithm). EID utilization was reported as proportions for categorical data and as mean (SD), range for continuous data. To determine predictors of incomplete EID care utilization,

demographic data collected by the HITSystem (e.g., maternal age, education level, disclosure status, distance from hospital, household income) was analyzed.

A retrospective review of HITSystem program data to assess PMTCT-related outcomes of HIV-positive pregnant women was also done. All data collected for the retrospective review was coded, thus no identifying patient data was collected. PMTCT outcomes along the cascade of care included: ART initiation (if not already on ART at time of pregnancy), attendance at PMTCT appointments, a hospital delivery, and infant enrollment in EID prior to hospital discharge.

The 8 intervention points that were evaluated for PMTCT were:

1. **Enrollment:** N (%) enrolled among those identified HIV+; Gestational age at enrollment and Prenatal meds received
2. **Pre-ART Lab results:** Time (days) to results; Time (days) to ART; N(%) starting ART the next clinic day
3. **ART initiation:** N(%) returned for ART; Gestational wk at initiation
4. **Appointment reminders:** N (%) ANC appointments kept
5. **ART adherence:** N(%) 36 week VL undetectable; N(%) refill appts kept,
6. **Hospital delivery:** N (%) delivered at hospital; N (%) infants with correct ART prophylaxis (regimen and duration)
7. **EID enrollment:** N (%) Enrolled at delivery; Infant age at enrollment
8. **Retention until Infant result:** N (%) loss to follow up total; N (%) at each point when loss to follow up occurred

Pre-intervention data was abstracted from the PMTCT paper registry or an electronic medical record, if one was utilized prior to HITSystem introduction. As with the process for EID, clinical data from the mother-infant pairs are captured directly into the HITSystem at PMTCT enrollment and each subsequent visit. The data are all de-identified. The PMTCT provider is the primary person(s) entering data directly into the system. However, lab and pharmacy personnel also facilitate entry of relevant data that are critical for prompting the algorithm. Maternity providers also play a critical role by linking the infant's information (most critically, infant's date of birth) to the mother's HITSystem file prior to discharge. All relevant data to measure the targeted PMTCT outcomes are entered and maintained in the HITSystem. For analyses, de-identified HITSystem data can be exported to an excel spreadsheet which includes only a PMTCT unique identifier code; mothers' names are not reported in the spreadsheet. As with the process for EID, to determine whether the HITSystem improved longitudinal PMTCT service provision and outcomes, maternal and infant outcomes and the proportion of mothers with complete PMTCT services provision between pre- and post- HITSystem periods were compared.

3.2 Sampling strategy:

The initial plan was to pair facilities (i.e. control against intervention sites) that were located in the same region and which had similar numbers of PMTCT and EID enrolments. This was done for the initial 15 sites in the first year of implementation of the intervention. However, when the intervention was seen to be working well, it was rolled out to all remaining facilities. All facilities that were enrolled into the HITSystem had to have between 20-40 enrolments per month.

3.3 Data collection methods and rationale:

See description of data collection methods under the Evaluation Type and Design section.

3.4 Data handling procedure:

The pre-intervention data from all sites was manually entered into a secure database and the HITSystem data entered directly into the system by the provider at each facility. All HITSystem data was handled with integrity and confidentiality. All staff were trained to promote standardized and objective collection and recording of patient information. Data entered in the HITSystem was routinely reviewed by HITSystem personnel for legibility, consistency, and completeness. All data was stored in a password-protected database that was backed up through a secure connection.

All staff who used the HITSystem at program hospitals were trained to promote standardized and objective collection and recording of patient information. Data entered in the HITSystem was routinely reviewed by HITSystem personnel for legibility, consistency, and completeness. Data sets entered every month were routinely checked and cleaned for inconsistencies. This was done by extracting all the data into an excel sheet and reviewing it.

3.5 Data analysis plan:

STATA v10 statistical software was used to perform descriptive statistical tests, using Chi-squared tests to compare proportions and t-test to compare mean values between pre and post implementation of the HITSystem©. Logistic regression was used to calculate odds ratios for predictors of poor retention, and survival analyses conducted to identify most vulnerable periods for patient drop out. Generalized estimating equation (GEE) will be used to control for potential clustering effects among clinics.

3.6 Evaluation limitations:

Initial challenges with data cleanliness in the HITSystem database were addressed through data cleaning, once identified. Additionally, the HITSystem is web based and relied on internet connectivity. There were challenges with the connection in some facilities resulting in delays in data entry or missing data.

3.7 Summary of stakeholder engagement:

The study was carried out in collaboration with Regional Medical Officers of each of the five regions of HITSystem implementation. Additionally, healthcare workers at the pediatric clinics were trained to carry out data abstraction at the sites where they work. This helped them to manage the process of data entry at the facility level. There was also involvement of government staff from the Mbeya Zonal Referral hospital as study investigators on the protocol, and government staff based at the facilities where the study was carried out. International stakeholders that were involved in the study included the Global Health Innovations who designed the HITSystem and The University of Kansas Medical Centre, both from the USA.

3.8 Ethical Considerations:

The study was approved by the Mbeya Medical Research and Ethics Committee (MMREC), National Institute of Medical Research (NIMR) and Walter Reed Army Institute of Research (WRAIR) IRBs. The protocol received approval from WRAIR Human Subjects Protection Branch on 11 August 2014 and received a not research determination given this was a program evaluation activity. Annual renewal of approvals was done thereafter. The HITSystem was a program evaluation that did not involve collection of information beyond that already collected in routine service provision (i.e. Maternal antenatal treatment history, provision of EID steps and outcomes, and patient's contact information (phone and physical). There was no additional human subjects participation. Furthermore, since all data collected retrospectively and prospectively was de-identified, the scope was consistent with program monitoring and evaluation and all reviewing IRBs determined there was no need for utilization of informed consent beyond standard consenting procedures in a routine clinical care setting.

3.9 Deviations and adjustments from the approved SOW/Protocol:

There were no deviations from the study procedures. All study procedures were carried out as indicated in the protocol.

3.10 Procedures used to ensure data quality:

The quality of the data was ensured through reviewing all of the data entered in the HITSystem database using the patient source document files located at the health facilities. Additionally, data quality was ensured through supportive supervision and mentorship training of health facility staff to ensure that they followed standard procedures of data entry. Standard operating procedures for data entry were developed and shared with all facilities using the HITSystem. Data queries were also run centrally on a monthly basis for all the sites and the data cleaned of any discrepancies.

4. Findings and conclusions:

4.1 Key Findings for program improvement in relation to evaluation questions:

In summary, the utilization of the HITSystem at the health facilities in the southern highlands of Tanzania helped to improve PMTCT and EID outcomes in the following ways:

1. All mothers who were enrolled in the PMTCT component of the intervention were successfully tracked and given an opportunity to have their infants tested for EID.
2. Greater than 99% of the infants who were HIV-exposed were initiated on OI Prophylaxis.
3. All of the EID samples collected for testing were tracked successfully to the testing laboratories and their results tracked back to the health facilities where they originated from, ensuring that all samples were accounted for.
4. The HITSystem improved ART initiation for all infants identified to be HIV positive with more than 95% of all positive infants being initiated on ART.
5. The Time to ART initiation for positive identified infants improved.
6. Mothers in the PMTCT program were tracked for their viral load and other care indicators, which in turn helped to improve their treatment outcomes.
7. The overall turnaround time for EID testing i.e. from sample collection to testing and return of results to the facilities and initiation of appropriate care improved.

4.2 Conclusions:

Overall, the study findings show that the HITSystem improved EID and PMTCT outcomes. More than 95% of all the children diagnosed to be HIV positive were initiated on ART in HITs facilities as compared to non-HITs facilities where the positive enrolled in care was less than 75%. The HITSystem was shown to improve EID as all samples that were collected were accounted for, including all tests done and initiation of treatment for those who were diagnosed to be HIV positive. In terms of OI prophylaxis, more than 99% of HIV-exposed infants received OI prophylaxis in HITS sites as compared to less than 80% who received it in non-HITS sites. The HITSystem sites also performed better for the 13.5- and 18-month retests with more than 70% of retests being done here as compared to non-HITSystem sites that had performance of 50% and below.

4.3 Recommendations:

Overall, the HITSystem helped to improve PMTCT and EID outcomes in all facilities where it was implemented. Challenges of lost samples, loss to follow up of mothers and infants enrolled in the PMTCT and EID programs and late initiation of positive infants on life saving ART were all addressed and improved. The next steps would be to address all the challenges that were identified during the evaluation stage of its implementation. This includes helping to design an offline platform that can be used for data entry when there is no internet access, carrying out a cost-effectiveness analysis so as to have a sustainable system and to ensure that the system can be integrated into daily routine activities of EID and PMTCT programs in Tanzania.

5. Dissemination plan:

Data generated from the HITSystem have been shared in different forums including Ministry of Health meetings on pediatrics. Indeed, the Tanzanian Ministry of Health and the National AIDS Control Program recognize these features as a best practice and are considering broader implementation. Additionally, the generated data will be shared in presentations in local and international conferences and also published in peer reviewed journals. Findings from specific health facilities were shared with facility heads to ensure the information would be used to improve facility performance.

6. References:

1. UNAIDS Factsheet (2016). Online. Available from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

2. UNAIDS Global Report (2010). Online. Available from: http://www.unaids.org/globalreport/documents/20101123_GlobalReport_full_en.pdf.

3. UNICEF, Statistics by Country, KENYA. Updated 2003. Available at: http://www.unicef.org/infobycountry/kenya_statistics.html

7. Appendices:

a. **Approved Evaluation SOW/Protocol:** {Attached}
b. **Data collection instruments/tools:** {Attached}
c. **Abridged bios of the evaluation team:** {Attached}
d. **Conflict of interest statement**
e. **Evaluation costs**
f. **Project Results Framework**

7e. **Conflict of interest statement**: The evaluation staff certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the protocol discussed in this report.

7f. **Evaluation cost:** The total cost of the evaluation was $633,630.50 over 6 years.

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7g. Project results framework

	INDICATOR	DEFINITION How is it calculated?	BASELINE What was the original value?	TARGET What is the target value?	DATA SOURCE How will it be measured?	FREQUENCY How often will it be measured?	RESPONSIBLE Who will measure it is done?	REPORTING Where will it be reported?
Goal	1. OI prophylaxis Y/N, age OI administered	1. % infants receiving OI prophylaxis 2. Age of OI prophylaxis	1. Less than 50% 2. More than 8 months	>95%	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports
	2.DBS collection Y/N, age at DBS collection	1. % infants with DBS collected 2. Age at DBS collection	1. Less than 50% 2. More than 8 month	1. >95%. 2. Two weeks	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports
	3.Number of days from DBS collection to receipt of sample at laboratory	1. % DBS received at lab 2. TAT of DBS receipt at lab	1. Less than 50% 2. More than 30 days	1. 100% 2. One week	Laboratory log books	Monthly	Study staff, Laboratory Staff RCH nurses	Study reports
	4.Number of days for testing cycle: PCR test date, dispatch of results to hospital (Control)/ PCR results posted (HITSystem)	1. % of DBS sample with result indicated 2. TAT of results	1. Less than 50% 2. More than 30 days	1. 100% 2. Two weeks	Laboratory log books	Monthly	Study staff, Laboratory Staff RCH nurses	Study reports
	5.Mother notified of results Y/N, date of notification, # of days from receipt of	1. % mothers notified of infant status 2. TAT of	1. >50% 2. More than 20 days	1. 100% 2. One week	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports

	results to notification of mother	notification						
	6.ART initiation of HIV+ infants Y/N, date initiated, # days from notification to initiation	1. % positive infants 2. % positive infants initiated on ART 3. TAT of ART initiation 4. Infant age at ART initiation	1. >5% positive infants 2. <50% positive infants initiated on ART 3. >30 days 4. >7 months	1. <2% positive infants 2. 100% positive infants initiated on ART 3. <5 days 4. <6 weeks	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports
	7. Re-test HIV exposed infants at 13.5 months (or other specified timepoint according to the Tanzania National EID Algorithm) Y/N, infant age at re-test	1. % negative infants receiving 13.5m (or other specified timepoint according to the Tanzania National EID Algorithm) 2. Antibody retest 3. Age at retest Outcomes from steps 2-5 for infants with positive antibody test 4. % positive infants	1. <50% 2. <50% 3. 13.5 months, 18 months 4. >5% positive infants	1. >90% 2. >90% 3. 100% 4. <2% positive infants	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports

	8. Re-test HIV exposed infants at 18 months Y/N, infant age at re-test (or 12 weeks following the cessation of breastfeeding, whichever is later)	1.% negative infants receiving 18m antibody retest 2.Age at 18m retest (or other specified timepoint according to the Tanzania National EID Algorithm) 3.% positive infants	1. <50% 2. >18 months 3.>5% positive infants	1. >90% 2. 18 months 3.<2%	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports
Outcomes	Improved uptake of EID and PMTCT services	EID and PMTCT Scores	-	-	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports
Outputs	Higher infant survival and reduced infections with HIV	EID and PMTCT Scores.	-	-	HEI Registers, HITSystem database	Monthly	Study staff, Facility Staff RCH nurses	Study reports