Original Article

Consolidating HIV testing in a public health laboratory for efficient and sustainable early infant diagnosis (EID) in Uganda

Charles Kiyaga[a], Hakim Sendagire[a,b,*], Eleanor Joseph[c], Jeff Grosz[c], Ian McConnell[c], Vijay Narayan[c], Godfrey Esiru[a], Peter Elyanu[a], Zainab Akol[a], Wilford Kirungi[a], Joshua Musinguzi[a], and Alex Opio[a]

[a]Central Public Health Laboratories, Ministry of Health, 7-11 Buganda Road, Kampala 256 41, Uganda

[b]College of Health Sciences, Makerere University, Kampala, Uganda

[c]Clinton Foundation Health Access Initiative, Uganda

*Corresponding author.

Abstract Uganda introduced an HIV Early Infant Diagnosis (EID) program in 2006, and then worked to improve the laboratory, transportation, and clinical elements. Reported here are the activities involved in setting up a prospective analysis in which the Ministry of Health, with its NGO partners, determined it would be more effective and efficient to consolidate the initial eight-laboratory system for EID testing of HIV dried blood samples offered by two nongovernmental partners operating research facilities into a single well-equipped and staffed laboratory within the Ministry. A retrospective analysis confirmed that redesign reduced overhead cost per PCR test of HIV dried blood samples from US$22.20 to an average of $5. Along with the revamped system of sample collection, transportation, and result communication, Uganda has been able to vastly increase the HIV diagnosis of babies and engagement of them and their mothers in clinical care, including antiretroviral therapy. Uganda reduced turnaround times for results reporting to clinicians from more than a month in 2006 to just 2 weeks by 2014, even as samples tested increased dramatically. The next challenge is overcoming loss of babies and mothers to follow up.
Journal of Public Health Policy (2015) **36,** 153–169. doi:10.1057/jphp.2015.7; published online 26 March 2015

Keywords: HIV; laboratories; Early Infant Diagnosis (EID); Uganda

Introduction

Laboratory testing is critical for minimizing harm of HIV/AIDS, yet lab services remain largely unavailable in developing countries.[1,2]

The discovery of HIV cases in Uganda (1981) prompted discussions within the Ministry of Health (MoH) and with colleagues worldwide about a strategic response. From 1997 Uganda collaborated with the Joint United Nations Program on HIV/AIDS (UNAIDS) and by 2000 had enrolled 1000 patients on *antiretroviral therapy* (ART).[3] In 2000, the MoH assumed sole responsibility for managing ART, and then scaled up in 2003 with the World Health Organization (WHO) initiative to help increase to 3 million those on ARVs by 2005 in low- and middle-income countries.[4] Diagnosis and treatment of infants and mothers also increased.

Uganda has relied extensively on external funding and technical support operated through non-governmental organizations (NGOs), both international and domestic. They became *implementing partners* for the MoH – working together to achieve national goals.

The HIV/AIDS epidemic spread relentlessly in Uganda in the late 1980s and early 1990s, and peaked in urban areas by the mid-1990s. Antenatal prevalence (estimated for the general population, mainly from mothers at antenatal services) ranged from 25 to 30 per cent in heavily affected urban areas. From the 1990s it steadily declined across Uganda. From 2000 to 2010, HIV sero-prevalence stabilized at 5–10 per cent in urban areas and below 5 per cent in rural ones. A 2011 national survey showed prevalence up nationwide, to 7.3 per cent of adults aged 15–49 years, with higher rates among women (8.3 per cent) than men (6.1 per cent) and lower rates among the young: 4 per cent for young adults aged 15–24 years, and 0.6 per cent for children under age 5.[5,6] Uganda's population of about 30 millions in 2006 is close to 40 million in 2015 (http://countryoffice.unfpa.org/uganda/2014/12/23/11171/census_provisional_results_released_uganda_rsquo_s_population_at_34_9_million/).

The WHO recommends beginning ART for infected children under 2 years of age[7] immediately after diagnosis, because early treatment reduces infant mortality by as much as 76 per cent.[8] *Early Infant Diagnosis* (EID) describes a program to identify babies in need of treatment. Starting and retaining babies on ART depends in large part on identifying and treating mothers, and is a key to *preventing maternal-to-child transmission* (PMTCT) during pregnancy, labor, delivery, or breastfeeding. HIV/AIDS programs today focus on avoiding loss of patients at any step in the process. As the steps (see text box 1) have gained attention, they also gained a name: *PMTCT/EID cascade of care*.

Extending years of good health among people infected with HIV means they make greater contributions to society through parenting, growing

Box 1: The PMTCT Cascade of care

- Mother attends antenatal care (ANC), staff tests her for HIV.
- If positive, health worker counts mother's CD4 (evidence of impact of HIV on immune system).
- Health staff starts mother on ART for her own health or for PMTCT at ANC or refers her to an ART clinic to do so.
- Mother returns for follow up visits in ANC and adheres to PMTCT prophylaxis.
- Mother delivers in hospital maternity ward where she and baby receive postpartum prophylaxis.
- Hospital staff refer mother and baby to postnatal clinic for further care.
- Baby referred to *Exposed Infant Clinic* for dried blood sample (DBS) collected at 6 weeks or later (to test for HIV in blood).
- Baby receives results and completes EID testing algorithm[9] at the exposed infant clinic.
- Clinic staff refer HIV positive baby to ART clinic to start treatment.[10–12]

Source: Uganda's PMTCT Implementation Plan 2010 (Internal Document not published).

food, and other work.[13] Extending healthy life and increasing child survival also lessens burdens of care and sadness associated with death, which were so common before the availability of ART.[14] The WHO estimated that in 2011, only 35 per cent of infants worldwide born to mothers living with HIV received an HIV test within the first two months of life.[15] The rate in Uganda was 30 per cent. It was less than 10 per cent in the Global Plan to Fight HIV, TB, and Malaria's priority countries: Angola, Chad, the Democratic Republic of the Congo, Malawi, and Nigeria.[13]

Poor-quality and underused laboratories compromise HIV programs. They lack equipment and skilled lab personnel, experience reagent 'stock outs', use dysfunctional diagnostics and ill-defined standards for lab testing, and due to poor communication with lab workers, clinicians make inadequate use of testing.[16,17] The questions of why EID programs have been ineffective and how to improve them have attracted international attention.[18–22]

From 2006, Uganda offered EID services and scaled up PMTCT, responding to a global goal to eliminate mother-to-child transmission by 2015.[13] The Millennium Development Goals also helped attract new funds from abroad for Uganda's EID strategy that combines laboratory services, transportation of samples to labs, and clinical care (including PMTCT).

We describe below how Uganda approached improving, expanding, and consolidating the laboratory element of EID from 2006 to 2014. We highlight the advantages of consolidating laboratories within a public system in 2011. To confirm achievements and identify remaining challenges, we report results of a 2012 retrospective evaluation (2010–2012), and update our findings with program data from 2012 to 2014.

Uganda's Early Steps to Improve EID

In 2006, the MoH simplified EID by drying blood spots for transport and using polymerase chain reaction (PCR) analysis of HIV DNA. From 2005, targeted external funds, largely from the *US President's Emergency Plan for AIDS Relief* (PEPFAR), helped improve lab test quality and scale up HIV/AIDS prevention, *care*, and *treatment* programs.[23–25]

These terms have special meanings. Clinics recruit HIV-infected patients into *care* – visits every 2–3 months for prophylaxis against opportunistic infections, counseling in preparation for ART, and regular measuring of patients' CD4 counts. Once the CD4 falls to below about 350 cells/ml, clinicians start the patient on ART – the *treatment*.

Uganda's health system consists of four health center levels, supported by general and regional hospitals. In Kampala, the capital, is a national referral hospital. *Point of entry* health centers (near where patients live, Levels 1 and 2) performed no laboratory work. Hospitals, followed by health centers at levels 3 and 4, began collecting DBS for HIV testing from 2006 . By December 2009, 550 MoH facilities across the country had tested about 50 000 infants.[26] In 2010, 1700 health facilities produced dried blood spot samples (*Uganda's PMTCT Scale up Plan 2010*, Internal MoH document, unpublished).

A new EID Strategy Emerges (2010)

In 2008, the MoH established a National Advisory Committee for PMTCT, mostly of technical representatives of externally funded NGO

implementing partner organizations. A national *EID Coordinator* (author KC) oversees day-to-day program operations. He convened a *National EID Subcommittee* (Subcommittee) to develop a new strategy and served as its secretary. These two committees guide Uganda's EID program (within the MoH AIDS Control Program).

Why was a new strategy needed? In 2005, Uganda's HIV epidemic had stabilized at about 6.5 per cent prevalence in the general population.[5] With an estimated 1.4 million pregnancies annually and HIV prevalence of 7.2 per cent among pregnant women, which culminates into 100 800 exposed infants born per year, the EID program then projected how many babies would need to be tested from fiscal years 2010–2014 (Figure 1).

By May 2010, to improve the laboratory element of EID, the MoH had requested the Subcommittee to (1) analyze costs and operations of the EID program and to propose a more cost-effective and efficient laboratory network for DNA PCR testing, and (2) project operating costs for an optimal network (as had been done in Rwanda[21]).

The Subcommittee analyzed two other EID elements: sample transport, and how to engage and retain HIV-exposed infants in care. The MoH later used these tools to attract key donor resources and to 'sell' a new approach to NGOs and other stakeholders.

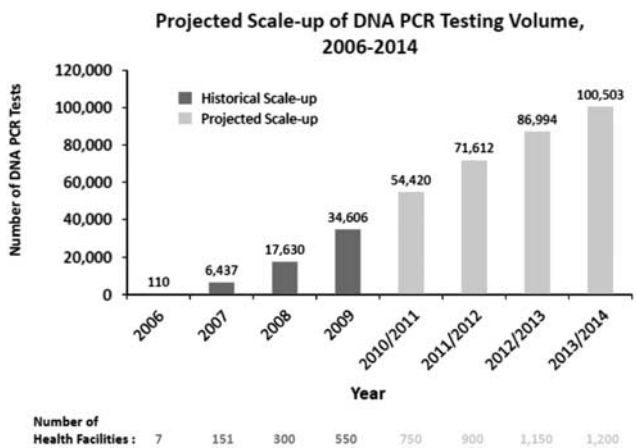

Figure 1: Projected scale-up of DNA PCR testing volume, 2006–2014.
Source: PMTCT Scale-up Plan 2010 (MoH internal document, unpublished).
Note: Data are for calendar years from 2006 to 2009 and from fiscal years (1 July – 30 June) from 2010 to 2014.

The Subcommittee classified laboratories by monthly sample testing capacity. Based on manufacturers' recommendations, manual PCR machines could process 840 samples/month and automated machine labs 2940 samples/month. Figure 2 compares the sample *capacity* for each lab to *actual numbers* tested. Backlogs and long lab turnaround times (TAT) plagued Gulu and Mbale labs with manual PCR machines. They received more samples than they could test efficiently. TAT at Kakira and Kabale often exceeded a month as they received few samples. These needed to be consolidated into a batch to run the machine.

The Subcommittee then considered three options for increasing efficiency and reducing costs as displayed in Table 1.

In 2010, the EID Subcommittee also projected laboratory use for each option (Figure 3).

In May 2010, the National EID Subcommittee projected costs for each option for the period 2011–2014 (Figure 4). Consolidation of the eight *partner-operated* research laboratories into one MoH-operated EID laboratory appeared to offer savings greater than $4.1 million over 4 years.

With support from the Clinton Health Access Initiative (CHAI) and based on projected numbers of samples, the Subcommittee predicted costs for each element of the testing process for each option for the period 2011–2014. Experiences in Kenya, Botswana, and South Africa informed the analysis.[27] Table 2 displays cost elements and totals by option. A single consolidated, central lab offered greatest savings, but not greatest capacity. By reducing recurrent costs (personnel, lab space,

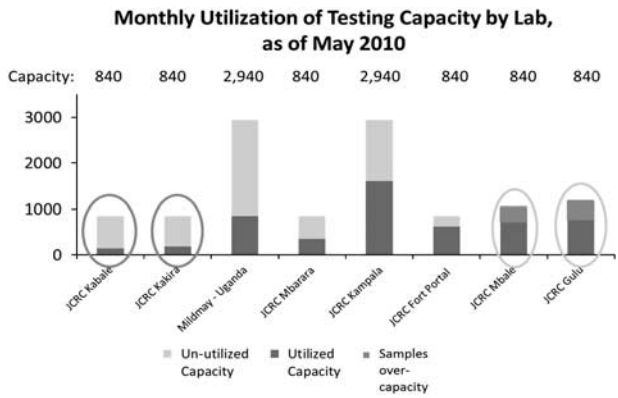

Figure 2: Monthly utilization of testing capacity by lab, as of May 2010.
Source: EID program review report 2010 (Internal MoH document, not published).

Table 1: Three laboratory system design options considered in 2010

Parameter	#1: Status quo, eight labs	#2: four labs	#3: one lab
No. of labs	8	4	1
Location of labs	Kampala Lweza Kakira Mbale Gulu Ft. Portal Mbarara Kabale	Kampala Mbale Ft. Portal Gulu	Kampala
No./Type of Equipment	Two automated Six manual	Four automated	Two automated
Lab technicians	One technician per manual machine Two technicians per automated machine Total: 10	Two technicians per automated machine Total: 8	Two technicians per automated machine Total: 4

Source: EID Program review report 2010 (unpublished internal document).

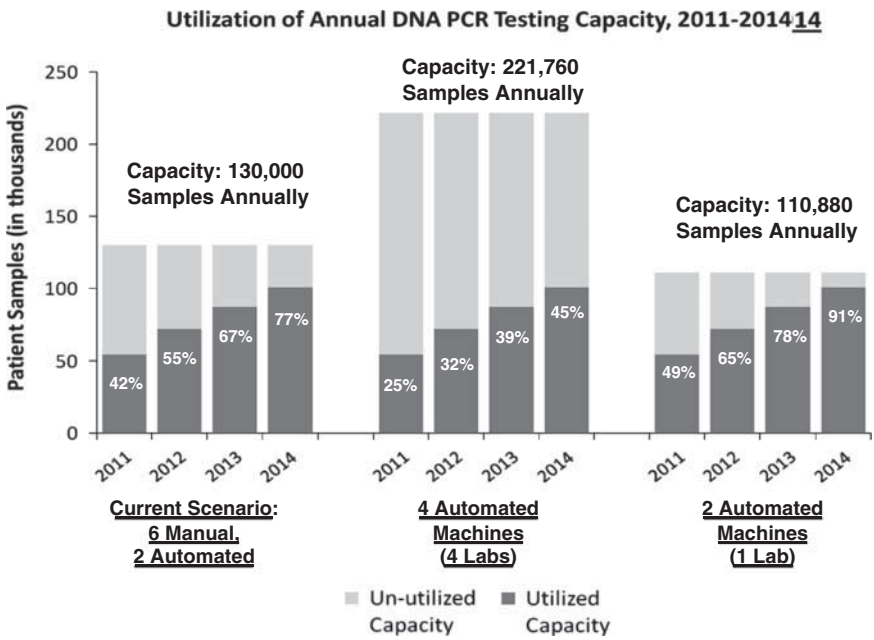

Figure 3: Utilization of annual DNA PCR testing capacity, 2006–2014.
Source: EID Program review report 2010 (Internal MoH document, not published).

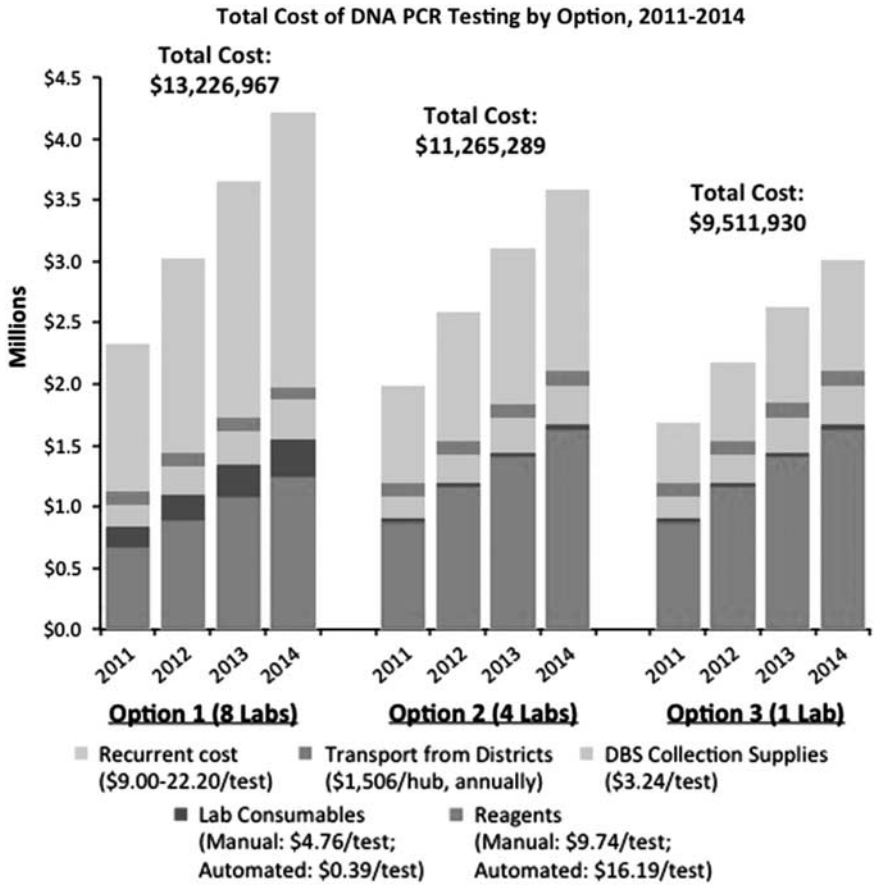

Figure 4: Total cost of DNA PCR testing anticipated for three options.
Note: Recurrent costs range from comparable labs in Botswana, Kenya, and South Africa; transport estimates from a financial optimization model owned by the Clinton Health Access Initiative (CHAI) with assumption designed by Uganda's Central Public Health Laboratories; DBS collection supplies, lab consumables, and reagents all projected using their 2010 costs.
Note: These data are based on international benchmarks and testing volume projections from our scale-up and, not real data from 2012.

power and water, service and maintenance, and administration) the EID program's cost per lab test appeared likely to drop from $22.20 (eight labs) to $10 (four labs), or to $6–$9 (one lab).

From 2006 to 2010, MoH efforts to expand EID had been constrained, not only by routine costs of testing in partner *research* facilities – but also by transport of DBS samples to the laboratories,

Table 2: Projected laboratory expenses by category for three options (2010)

	Current option of eight labs	*Four lab option*	*One lab option*
Reagents	$3 893 435	$5 076 035	$5 076 035
Consumables	$923 510	$122 276	$122 276
DBS collection supplies	$1 015 834	$1 015 834	$1 015 834
Transport to districts	$433 844	$457 944	$476 024
Recurrent costs[a]	$6 960 344	$4 593 200	$2 821 761
Total	$13 226 967	$11 265 289	$9 511 930

[a]Recurrent costs include: rent, manpower, utilities, and other operational costs.
This data is based on international benchmarks and testing volume projections from our scale-up plan.
Source: EID Program Review report 2010 (Internal document, not published).

processing samples at each facility within desirable time limits, and returning infants' HIV test results to their caregivers.[28] Average TAT through 2010 stretched well beyond the 30 days intended. When results are late, the providers cannot synchronize relaying these to caregivers returning with infants for the second set of vaccinations.[29] Missing this opportunity discouraged both patients and clinicians from HIV follow-up and complicated efforts to start HIV+ babies and mothers on ART.

Redesign Decision and Steps to Consolidate the EID Laboratory (2010–2011)

Having met to consider data from May 2010, the Subcommittee reached its program redesign decision in September 2010. It would consolidate eight implementing *partner*-operated laboratories into *one public EID laboratory* based at the Central Public Health Laboratories (CPHL) in Kampala, to be operated by the MoH. Members also discussed options for sample transport and for improvements in clinical care, including PMTCT.

The MoH had *no* money to overhaul the laboratory and DBS transportation infrastructure. It decided to seek equipment donations first, hoping to convince additional partners to support transformation of all aspects of the EID program. The CHAI staff in Uganda, through their global lab team, contacted Roche Diagnostics South Africa. Roche agreed to provide two automated Ampliprep–Taqman analyzers with an understanding that the MoH would buy increasing quantities of Roche's reagents. UNITAID, through CHAI, had already been procuring EID

reagents, consumables, and DBS collection bundles for Uganda's eight testing laboratories and would continue to do so after lab consolidation. The US Centers for Disease Control program in Uganda provided startup funds: paying for renovation of the lab space, addition of personnel, and other recurrent costs.

The Kampala laboratory, depending on sample transport to improve efficiency, began operations in July 2011 and a National Sample and Results Transport Network (NSRTN) later that year.[30] Local networks based at hospitals serve as *hubs* for all health facilities within a defined catchment area (30–40 km radius). The MoH allotted each hub a motorbike and funds to employ a rider to make (at least) weekly scheduled sample pickups from all its facilities. The transport network assured rapid delivery of samples to the high-tech EID laboratory from every health facility in the county.[30–32]

Evaluating Achievements and Challenges in 2012

In December 2012, our team (from MoH and CHAI) conducted a post-intervention study. To optimize design of DNA PCR testing in Uganda, we wanted to understand the cost of operating Uganda's EID program, and in particular, of a consolidated centralized laboratory versus the eight partner-run EID laboratories.

We designed a cross-sectional retrospective study to compare costs, TAT, and patient retention before and after lab consolidation. We drew data from the EID database, patient chart reviews, program work plans, and bills from EID testing labs before lab consolidation. The MoH's EID recorded information on the facility and the patient that had been sent to testing laboratories with each DBS sample – dates of sample collection and time to initiating return of results plus the date they were received back at the health facility. We then calculated the TAT for three periods: before lab consolidation (July 2010 – June 2011 with 53 440 entries), after lab consolidation but before sample transport (July 2011 – December 2011 with 18 878 entries) and with both lab consolidation and the new sample transport network from the initial 19 sample transport hubs (March 2012 – December 2012 with 46 476 entries).

We chose *turnaround time* to measure results – defined as days for processing the DBS sample between sample collection and return of DNA PCR results to the facility. After cleaning data and exporting it into the SSPP 10 statistical software, we analyzed the data. All tests were two-sided

and statistical significance was set at *P*-value <0.05. We estimated odds ratios along with 95 per cent confidence intervals for each time period.

We compared recurrent costs at the eight-lab network and the consolidated laboratory for personnel, lab space, power and water, service and maintenance, and administration. As CHAI donated reagents and consumables, we did not include them. As we had no startup cost information for the eight laboratories, we did not include one-time startup costs for renovation of the lab space or procurement of equipment (refrigerators, freezers, biosafety hoods, thermo-mixers and so on) for lab consolidation in 2011.

We also analyzed how improved laboratory function and timely return of test results correlated with increasing participation of babies and mothers in ART. We compared patient retention under the eight-laboratory network (February – September 2009) and the consolidated laboratory (January – December 2012).

Results

Recurrent lab costs: During the first year of consolidation, from 1 July 2011 to 30 June 2012, the MoH ran 57 513 tests from over 800 health facilities and paid $290 000 for recurrent costs ~$5 average cost per test – compared to $22.2 recurrent cost per test charged by the eight-lab network. The redesigned EID program saved ~$17 per test.

Laboratory consolidation and TAT: Laboratory TAT came down from a 25-day average in the eight-lab network, to 2 days. When combining *laboratory TAT* with transport times to the consolidated Kampala MoH laboratory (using the National Sample Referral Transport Network, NSRTN), TAT from sample collection to result return decreased from 49 to under 14 days Figure 5.

HIV+ infants lost to care: For the pre-EID redesign period, we tracked retrospectively a cohort of 244 HIV+ infants. We learned that 39 per cent (94) never received test results from clinicians; of the 150 who received results, 35 per cent (52) never had a clinician enroll them in *pre-ART care*; of the 98 who were enrolled in pre-ART, 42 per cent (41) were lost before starting ART. This amounted to a total loss to follow-up of 77 per cent.

One year after redesigning of EID services (July 2011 – July 2012), we retrospectively tracked a cohort of 1472 HIV+ infants: 22 per cent (322) never received their test results; of the 1150 who received results, 19 per

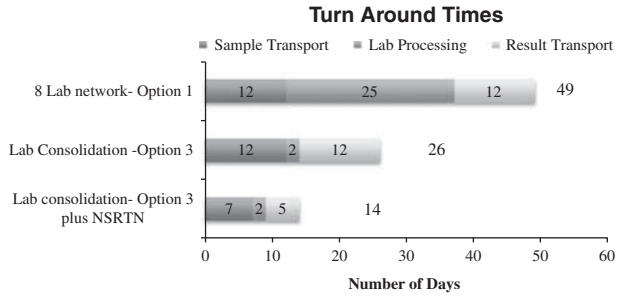

Figure 5: Turnaround times (TAT) for (1) Sample Transport (2) Laboratory Analysis, and (3) Result Transportation times.
Source: Uganda's National EID Database: 2009, 2011, 2012.
Note: Because we changed the system, data were not available for same period for each option, thus we used those available as follows: for 2009, full calendar year data for the eight-lab system; for 2011, data from 1 July to 31 December 2011 for post-EID redesign (without transport); and again the full calendar year in 2012 for post-EID redesign (including transport).

cent (222) were not enrolled in pre-ART. Of the 928 who enrolled in pre-ART, only 11 per cent (106) did not start ART. Overall, loss in this period amounted to 43 per cent.

Overall, patient retention rose from 23 per cent in the eight-laboratory network to 57 per cent in the centralized laboratory network; laboratory consolidation and associated EID system-strengthening initiatives reduced loss to follow-up by 34 per cent.

More Gains and Broadening Use of EID Model after the Study: 2012–2014

With improved information and systems, we have been able to upgrade the program further, track additional gains, and identify challenges. Improvements in data collection, management, and delivery anchor all other gains. In response to early successes and our request, in 2012 Hewlett-Packard attached high-capacity servers to the consolidated laboratory for enhanced data storage, management and analysis, and communication.

Integration of data entry and testing processes reduced transcription errors and saved time. In 2013, at each of 78 DBS sample transport hubs (up from 19 in 2012), the EID program installed *GSM printers* that transmit results from the consolidated lab to the hub in real time. Each facility reports all infant ART starts and whether the infant returns for

subsequent ART clinical visits through the GSM printers. Internet links these printers to the central EID database at CPHL in Kampala. The EID program rapidly transmits results from the database through the GSM printers, irrespective of distance. TAT dropped to between 4 and 7 days from 14 days. In 2014, 2206 facilities contributed dried blood samples for EID analysis – up from 1700 in 2011. In 2014, the consolidated laboratory ran more than 8100 tests/month, with a laboratory TAT of 2 days.

For routine, real-time monitoring, the EID program posts summary program data to a Web-based *dashboard*. The MoH is now extending this system to TB, Malaria, Surveillance and Outbreaks, and pathology programs, routing results through the EID servers to GSM printers for real-time printing at the hubs.

The EID consolidated laboratory has attracted funding for additional lab services using the same model – neonatal sickle cell screening, and viral load monitoring for all ART patients. The GSM printers helped monitoring retention and ART initiation for HIV+ infants and we expect similar improvement in other MoH programs that depend on sample transport.

Achievements Introduce New Challenges and Offer Lessons

Overall, the biggest challenge has been funding: the consolidated laboratory and the transportation network remain heavily dependent on donors. Any problem at the one laboratory could halt service. Bad terrain and poor roads cause frequent motorbike breakdown, high maintenance and replacement costs, and frequent motorbike accidents. We will need new bikes.

EID program reductions in recurrent costs exceeded those projected using benchmark data from other sub-Saharan countries (CHAI, 2010, internal document not published). The eight labs running DNA PCR tests on which Uganda's EID program first depended had been designed to meet *research* needs of the implementing partners rather than routine public health objectives of the MoH. Thus, the MoH had paid for additional expenses, inflating routine testing costs. The centralized laboratory is efficient because it receives sufficient samples to run daily and as data are always available, reports are easily generated.

Health workers and patients report great relief that prompt results mean fewer repeat visits to obtain delayed results – probably a key reason for improved retention. Even so, our challenge is to engage the

remaining 40 per cent of clients who do not collect their infants' results. Persistent loss to follow-up means we may need to complement centralized testing with point-of-care (on-site) molecular tests when they become available, especially in hard-to-reach areas.

Conclusion

Uganda has transformed its fragmented EID laboratory network into a single entity, for which the MoH bears total responsibility. Our analyses disproved the common belief that government-run programs can never be efficient and cost-effective. We believe laboratory consolidation into the MoH has increased substantially the sustainability of HIV testing for infants. Institutionalization of this laboratory within the MoH also promises gains for controlling other diseases including tuberculosis and malaria.

Acknowledgements

EID testing services are currently offered to patients free of charge. All testing reagents and laboratory consumables are donated to the MoH by UNITAID (through CHAI), and all overhead costs are funded directly by PEPFAR through USAID and CDC. We thank the Joint Clinical Research Center (JCRC) Laboratories that managed the eight-lab network, the hub coordinators, and the bike riders of all hubs involved in this analysis. The technical team at CPHL, notably Mr Guma Guspard, the chief technologist, Mr Amato Ojwiya Menya, and Mr Steven Aisu, the Head of CPHL. Thanks to the EID administrator Ms Rebecca Nakidde and the administrators at CPHL: Mr Sulaiman Ikoba and his team; and Diana Kamusiime, Susan Namboozo, and Rita Eragu.

About the Authors

Charles Kiyaga, BS, MSc (Biomedical Sciences and Management), is completing an MPhil in Medical Science at the University of Cambridge. He is the National Coordinator of the EID Program and Director of the EID laboratory at the Central Public Health Laboratories Ministry of Health.

Hakim Sendagire, MD, PhD, is a technical advisor to the Ugandan MoH on laboratory services.

Eleanor Joseph worked with the Clinton Health Access Initiative (CHAI) in Uganda as its Laboratory Program Manager.

Jeff Grosz, MBA, is the Country Director of Clinton Health Access (CHAI).

Ian McConnell was the previous Country Manager of CHAI from 2008 to 2011 and currently studies medicine at Yale University.

Vijay Narayan, MPH, was a Program Manager with the Clinton Health Access Initiative for health system strengthening for PMTCT, EID, and Pediatric HIV services.

Godfrey Esiru, MBCHB and M. Med (OBGY), is Uganda's National PMTCT Coordinator at the Ministry of Health.

Peter Elyanu, MBCHB and M. Med (Pediatrics), oversees Pediatric and Adolescent HIV Care and Treatment at the Ugandan Ministry of Health.

Zainab Akol, MBCHB and MPH, managed the AIDS Control Program at the Ministry of Health when EID services were redesigned.

Wellford Kirungi, MBCHB and MSc (Epidemiology), is project manager of MOH/CDC Cooperative agreement through which the AIDS Control Program is funded.

Joshua Musinguzi, MBCHB, MSc (Epidemiology and Biostatistics), manages the Ugandan MoH AIDS Control Program.

Alex Opio, MSc, MS, PHD, is the Commissioner of Uganda's National Disease Control Department at the Ministry of Health.

References

1. Hay Burgess, D.C., Wasserman, J. and Dahl, C.A. (2006) Global health diagnostics. *Nature* 444(Suppl 1): 1–2.

2. Girosi, F. *et al* (2006) Developing and interpreting models to improve diagnostics in developing countries. *Nature* 444(Suppl 1): 3–8.
3. Okero, A.F., Aceng, E., Madraa, E., Namagala, E. and Serutoke, J. (2003) Scaling up antiretroviral therapy: Experience in Uganda, perspectives and practices in antiretroviral treatment, http://www.who.int/hiv/amds/case3.pdf, accessed 15 December 2014.
4. World Health Organization Report. (2003) 3 by 5 initiative; Treating 3 million with HIV/AIDS by 2005, http://www.who.int/3by5/en/, accessed 15 December 2014.
5. *Ministry of Health report, Kampala, Uganda*. (2005) Uganda HIV/AIDS sero-behavioural survey report 2004, dhsprogram.com/pubs/pdf/AIS2/AIS2.pdf, accessed 15 December 2014.
6. *Ministry of Health report, Kampala, Uganda*. (2012) HIV/AIDS indicator survey report 2011, health.go.ug/docs/UAIS_2011_KEY_FINDINGS.pdf, accessed 15 December 2014.
7. World Health Organization Guidelines. (2010) Antiretroviral therapy for HIV infection in infants and children: Towards universal access: Recommendations for a public health approach, www.who.int/hiv/pub/guidelines/art/en/, accessed 15 December 2014.
8. Violari, A. *et al* (2008) Early antiretroviral therapy and mortality among HIV-infected infants. *New England Journal of Medicine* 359(21): 2233–2244.
9. World Health Organization Guidelines. (2014) Algorithm for early infant diagnosis, http://www.who.int/hiv/pub/guidelines/arv2013/annexes/WHO_CG_annex_5.pdf.
10. Barker, P.M., Mphatswe, W. and Rollins, N. (2011) Antiretroviral drugs in the cupboard are not enough: The impact of health systems' performance on mother-to-child transmission of HIV. *Journal of Acquired Immune Deficiency Syndrome* 56(2): e45–e48, doi:10.1097/QAI.0b013e3181fdbf20.
11. Ghadrshenas, A. *et al* (2013) Improved access to early infant diagnosis is a critical part of a child-centric prevention of mother-to-child transmission agenda. *AIDS* 27(Suppl 2): S197–205.
12. Aledort, J.E. *et al* (2006) Reducing the burden of HIV/AIDS in infants: The contribution of improved diagnostics. *Nature* 444(Suppl 1): 19–28.
13. *UNAIDS* Report. (2011) Count down to zero: Global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive 2011–2015, http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/unaidspublication/2011/20110609_JC2137_Global-Plan-Elmination-HIV-Children_en-1.pdf" \t "_blank" www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/unaidspublication/2011/20110609_JC2137_Global-Plan-Elmination-HIV-Children_en-1.pdf, accessed 15 December 2014.
14. Mahy, M., Stover, J., Stanecki, K., Stoneburner, R. and Tassie, J.M. (2010) Estimating the impact of antiretroviral therapy: Regional and global estimates of life-years gained among adults. *Sexually Transmitted Infections* 86(Suppl 2): ii67–ii71.
15. WHO report. (2013) Global update on HIV treatment 2013: Results, impact and opportunities, http://www.who.int/hiv/pub/progressreports/update2013/en/, accessed 15 December 2014.
16. Petti, C.A., Polage, C.R., Quinn, T.C., Ronald, A.R. and Sande, M.A. (2006) Laboratory medicine in Africa: A barrier to effective health care. *Clinical Infectious Diseases* 42(3): 377–382.
17. Tanyanyiwa, D.M. (2010) Cost challenges for laboratory medicine automation in Africa. *Pan African Medical Journal* 6: 22.
18. Adebimpe, W.O. (2013) Challenges facing early infant diagnosis of HIV among infants in resource poor settings. *African Journal of Reproductive Health* 17(1): 122–129.
19. Dube, Q. *et al* (2012) Implementing early infant diagnosis of HIV infection at the primary care level: Experiences and challenges in Malawi. *Bulletin of the World Health Organization* 90(9): 699–704.
20. Braun, M. *et al* (2011) Inadequate coordination of maternal and infant HIV services detrimentally affects early infant diagnosis outcomes in Lilongwe, Malawi. *Journal of Acquired Immune Deficiency Syndromes* 56(5): e122–e128.

21. Binagwaho, A. *et al* (2013) Scaling up early infant diagnosis of HIV in Rwanda, 2008–2010. *Journal of Public Health Policy* 34(1): 2–16.
22. Creek, T.L. *et al* (2007) Infant human immunodeficiency virus diagnosis in resource-limited settings: Issues, technologies, and country experiences. *American Journal of Obstetrics and Gynecology* 197(3 Suppl): S64–S71.
23. Olmsted, S.S. *et al* (2010) Strengthening laboratory systems in resource-limited settings. *American Journal of Clinical Pathology* 134(3): 374–380.
24. Roberts, L. and Jasny, B. (2008) HIV/AIDS: Money matters. *Science* 321(5888): 511.
25. Cohen, J. (2008) HIV/AIDS: The great funding surge. *Science* 321(5888): 512–519.
26. Charles Kiyaga, I.M. *et al* (2010) Uganda's innovative efforts to improve testing, retention, and care of HIV-exposed infants. *International AIDS Conference*, Vienna Abstract book 2.
27. Ciaranello, A.L., Park, J.E., Ramirez-Avila, L., Freedberg, K.A., Walensky, R.P. and Leroy, V. (2011) Early infant HIV-1 diagnosis programs in resource-limited settings: Opportunities for improved outcomes and more cost-effective interventions. *BMC Medicine* 9(59): 59.
28. Mugambi, M.L., Deo, S., Kekitiinwa, A., Kiyaga, C. and Singer, M.E. (2013) Do diagnosis delays impact receipt of test results? Evidence from the HIV early infant diagnosis program in Uganda. *PLoS One* 8(11): e78891.
29. McCollum, E.D. *et al* (2012) Superior uptake and outcomes of early infant diagnosis of HIV services at an immunization clinic versus an 'under-five' general pediatric clinic in Malawi. *Journal of Acquired Immune Deficiency Syndromes* 60(4): e107–e110.
30. Kiyaga, C. *et al* (2013) Uganda's new national laboratory sample transport system: A successful model for improving access to diagnostic services for early infant HIV diagnosis and other programs. *PLoS One* 8: e78609.
31. Nuwagaba-Biribonwoha, H. *et al* (2010) Introducing a multi-site program for early diagnosis of HIV infection among HIV-exposed infants in Tanzania. *BMC Pediatrics* 10(44).
32. Chiduo, M.G. *et al* (2013) Early infant diagnosis of HIV in three regions in Tanzania: Successes and challenges. *BMC Public Health* 13(910).