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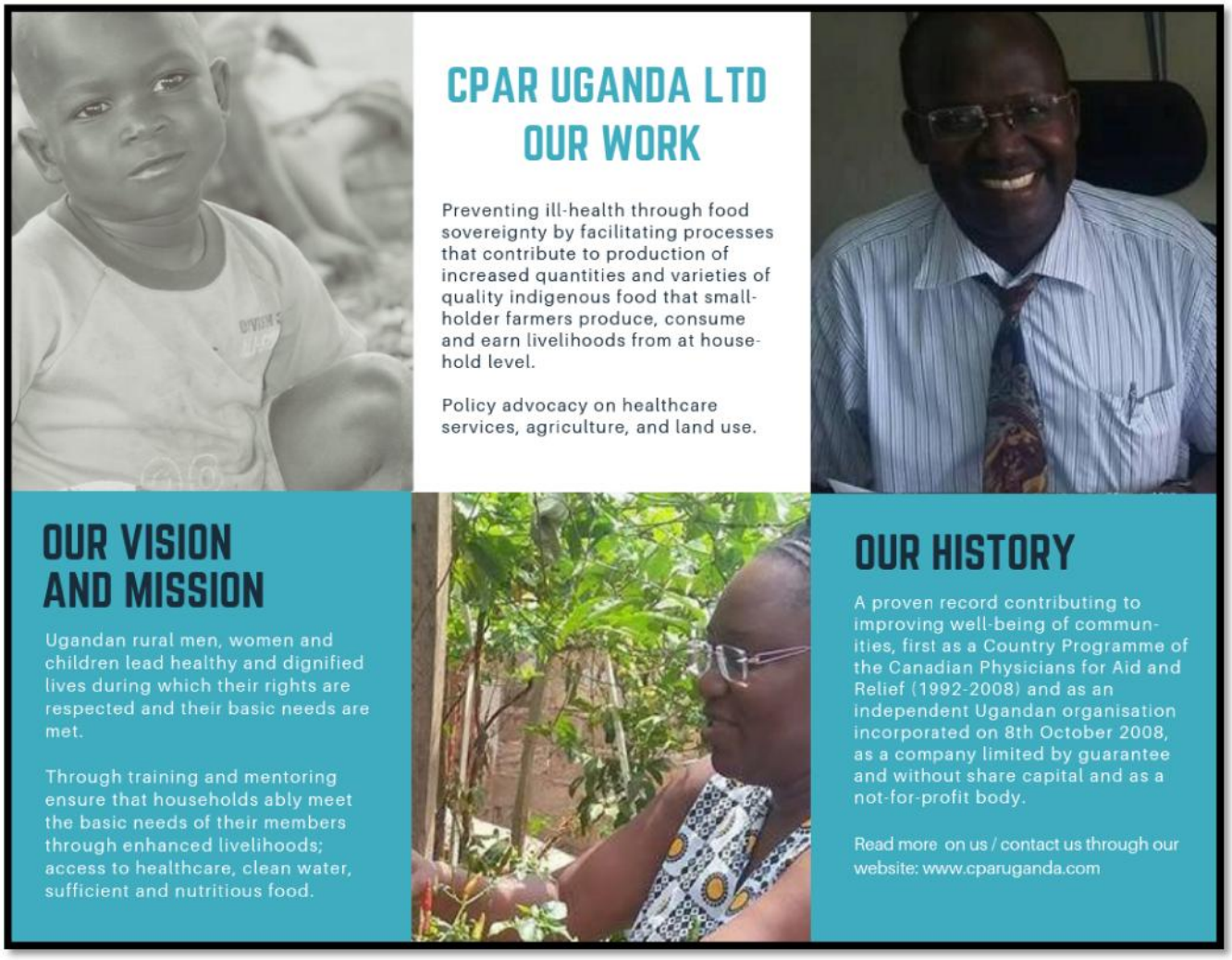
Discussion of Research Findings on the Use of GeneXpert Technology in Greater Northern Uganda



Contact Us:
Plot 5 Makerere Road, Lira Municipality
P.O. Box 820, Lira
Email: info@cparuganda.com

Introduction

The "***gold standard has to be the GeneXpert"*** asserted respondents in CPAR Uganda's qualitative investigation into pulmonary tuberculosis (TB)[1]. GeneXpert machines facilitate diagnosis of TB for, as described by WHO (World Health Organisation 2016), they are used to run ***"automated, cartridge-based nucleic acid amplification tests (that are) performed directly on sputum and other specimens from adults and children."*** As of 2010, in fact, GeneXpert is a WHO recommended technology for detecting TB. The Uganda National TB and Leprosy Control Programme (NTLP), in its current strategic plan (2017), recommend the use of GeneXpert machines, if available, as ***"the test of first choice for all presumptive TB cases."***

CPAR Uganda, indeed, explored the use of GeneXpert technology in Uganda; however, this discussion only covers its findings for Uganda's Greater Northern Region, the region; and thus the un-credited quotes in this discussion are of the region's respondents. The region hosts 21 percent of Uganda's population, about 7.2 million people; and it covers 42 percent (84,194.8 km^2) of Uganda's land area[2], including: Karamoja, Lango, Acholi and West Nile.

Uganda's Greater Northern Region				
Region / # districts / km^2			**Population # / density**	
Karamoja	07	27,528.0	965,008	35
Lango	08	12,793.7	2,061,694	161
Acholi	07	28,019.7	1,500,770	54
West Nile	08	15,593.1	2,660,667	171
Northern	**30**	**83,934.5**	**7,188,139**	**86**
Uganda	**112**	**200,203.3**	**34,634,650**	**173**

The region shares borders with the Democratic Republic of the Congo in the west, the Republic of South Sudan in the north, and the Republic of Kenya in the east. Each of these three countries has experienced unrest in the recent past; unrest that necessitated a significant number of their citizens to flee their homelands and to seek refuge in Uganda. The region, therefore, hosts a significant number of refugees – living in refugee camps and others living within communities as ordinary Ugandans do.

The Latent GeneXpert Capacity

There were at least 20 GeneXpert machines in the region in 2017; which were located in 17 districts, spread over the region's four sub-regions; and which were confirmed existent as follows:

- Through respondents' testimonies[3] the physical presence of eight machines located in six districts in two sub-regions was known.

- A report by researchers (Karamagi, et al. 2017) affiliated with a project of the United States Agency for International Development (USAID), Apply Science to Strengthen and Improve Systems (ASSIST), confirmed the physical presence of five GeneXpert machines, that were located in five districts in two sub-regions. However, one of the machines evaluated by USAID ASSIST seems among the ones known through respondents.

- In addition, an NTLP generated Uganda map showing the distribution of GeneXpert machines, which is published in an NTLP Bulletin, as part of a report (Nyombi 2018), ***"Updates on GeneXpert network,"*** confirmed eight machines located in seven districts in two sub-regions.

Latent GeneXpert Capacity and the Population

Uganda's target national ratio for GeneXpert machines to the population, in 2017, was 1:101,291. This is derived from the NTLP strategic plan which stipulates 344 as the total number of machines that the country needs, in order to ***"ensure 100 percent coverage of Hubs and districts"*** (Nyombi 2018); and by assuming a population of 34.6 million people.

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[1] *Details on the CPAR Uganda qualitative investigation into TB are contained in its two reports titled:* ***"Research Activity Report on Qualitative Investigation into Tuberculosis in Uganda (2017)"****, and* ***"Findings of Qualitative Investigation into Pulmonary Tuberculosis in the Greater Northern Region of Uganda (2018)."*** *PDFs of both reports are available to download free from the* ***"Tuberculosis page"*** *on its website www.cparuganda.com*

[2] *Uganda population and area statistics in this discussion are from the Uganda Bureau of Statistics from the most recent population census* (The National Population and Housing Census 2014 - Main Report 2016) .

[3] *CPAR Uganda's briefing on research findings containing its qualitative data-set on the* ***"Capacity to Test for Tuberculosis Uganda's Greater Northern Region"*** *is available to download free from its website.*

Assuming 20 machines serving a population of 7.2 million, the regional GeneXpert machine to population ratio was 1:359,407. Within the region, however, West Nile, with the highest ratio of 1:532,133, was comparatively the least served sub-region. While Acholi was the best served, since it had the lowest ratio in the region of 1:250,128, followed by Karamoja with a ratio of 1:321,669 and Lango with a ratio of 1:343,616.

2017 GeneXpert Machine Population Coverage

Region	Population	Units	Cover
Karamoja	965,008	03	1:321,669
Lango	2,061,694	06	1:343,616
Acholi	1,500,770	06	1:250,128
West Nile	2,660,667	05	1:532,133
Northern	**7,188,139**	**20**	**1:359,407**
Uganda	**34,634,650**	**344**	**1:101,291**

Even though Acholi covers 28,019.7 km^2 and Karamoja 27,528 km^2; each covering a wider area than West Nile, which covers 15,593.1 km^2; West Nile was still the least served. This is because both Acholi and Karamoja with population densities of 54 and 35, respectively, are significantly less populated than West Nile, which has the highest population density of 171 in the region.

Similarly, even though Lango covers 12,793.7 km^2 and has a population density of 161, it is less populated than West Nile.

Latent GeneXpert Capacity and the Districts

2017 GeneXpert Machine District Coverage

Region	Districts	Units	Cover
Karamoja	07	03	43%
Lango	08	06	75%
Acholi	07	06	86%
West Nile	08	05	63%
Northern	**30**	**20**	**57%**
Uganda	**112**	**344**	**100%**

Only 57 percent of districts in the region had at least one GeneXpert machine located within their geography. Acholi with 86 percent district coverage was the best served. Lango with 75 percent and West Nile with 63 percent were comparatively better served than Karamoja with 43 percent coverage.

The Functional GeneXpert Capacity

GeneXpert machines that are available in the region are of the same type - "***the one with four modules. If you go to all these government hospitals which have them, you will get the same thing.***" This means that "***if you are working on standard procedure from 8:00 a.m. to 5:00 p.m., you only have to run 16 samples per day - you run four samples, you remove. It takes two hours, and so on.***"

An NTLP analysis (Nyombi 2018), which includes four machines from the region indicates 16 samples as the expected maximum for the machines to run per day. USAID ASSIST researchers, as well, noted that of the machines they reviewed ***"all five GeneXpert machines can run up to four samples every two hours."***

Actual GeneXpert Performance in the Region

"***Weekly data showed that about five samples were being run each day"*** per machine, the USAID ASSIT researchers found of the machines they reviewed. Similarly, the four machines in the region which were included in the NTLP analysis were indicated as running below 10 samples per day – ranging from five samples to nine samples per day; meaning that on average the NTLP reviewed machines were running seven samples per day.

Of the respondents who discussed GeneXpert machines, 86 percent indicated that, since installation, each of the eight machines that they were familiar with had had a period in which it malfunctioned or was not functioning at all, and that the episodes lasted from minutes to months; and for various reasons:

Unit 1 ***"No funds for servicing the machine. Had to have the module replaced, it took over a year because the owners of the machine - the company is called CEPHEID they are the ones with the service contract. There was a delay in giving them a new service contract. They took a while to replace it and within that time the machine produces errors." "Challenge has been power. The service contractor has delayed to repair the power system. Need a stable power backup system. The batteries are dead, the system is actually not working. It works on direct power, but if power goes, it will black out."***

Unit 2	***"Lack certain things like fridges to keep samples." "Power - they are still using solar. On a rainy day, it gets down."***
Unit 3	***"Problem with the power. Six months they have been disconnected."***
Unit 4	***"It is only one module working – it runs one sample after two hours."***
Unit 5	***"They were just handwriting the results." "No regular servicing by the service provider. You inform them, they take long – after two months or three months."***
Unit 6	***"Ran out of cartridges. Informed National TB Reference Lab and up to now (time of interview, days later) they have not sent any cartridges." "CPU had problems. Took it to Kampala and it took almost a month."***
Unit 7 and 8	GeneXpert machines confirmed non-functional. Healthcare facilities sending samples to other facilities for testing.

It would, in fact, seem that, at any one time during 2017, the real GeneXpert functional capacity in the region could have been the equivalent of one functional machine per sub-region; which is 13 percent district coverage (four machines serving 30 districts). This means also that the coverage of the population could more likely have been a ratio of over 1:1,800,000 of GeneXpert machine to population.

A real functional capacity of four machines serving the region's population of 7.2 million people is feasible. After all, 86 percent of respondents who discussed GeneXpert machines talked about machine downtime; 57 percent of them talked about supplies out of stock and 43 percent of them talked about inadequate machine servicing.

The Cost of Malfunctioning GeneXpert Machines

Malfunctioning GeneXpert machines are costly, because of the losses the machines occasion. Losses, for example, caused because of aborted tests due to power outage while machines are connected directly to the national power grid and not through power backup systems.

"Remember, these cartridges, each one of them is 17 dollars (about 61,000 shillings). You have gloves you will have used; you have pipettes; and my time you would have lost it. Yes, remember, even the hub rider who is going down to the community to pick that sample is paid. The fuel he is using is paid, the motorcycle it is to be repaired, all those are costs. You will have lost 50 dollars (about 179,000 shillings) per sample."

An analysis (Hsiang, et al. 2017), which included a machine that is located in the region, found that the mean unit cost for a GeneXpert test in Uganda was US$ 21 (about 74,000 shillings) – including costs of overhead, building space, equipment, staff, reagents and consumables.

On average, the respondents' estimates and those of Hsiang et al give an indicative cost of testing one sample in the region as 126,000 shillings. Using this indicative average cost, the total loss per session would have been more than half a million shillings each time the power went off, while a machine was connected direct to the national grid, and the four samples in the running test session were aborted.

Malfunctioning machines, furthermore, caused long delays between the time a sample was taken from a patient and the time that the patient received the results. Case in point, using the hub system, it meant that presumptive cases had to wait for multiple weeks before getting their test results. This is because:

"The hub rider goes once to a facility in a week. So if you go this time you find a patient and he gives you a sample, he is waiting for results next week. If next week you go with the results showing error and maybe even the patient does not have transport to get back to the facility, this patient will have to take quite a while in the community out there before he chances to get the right diagnosis."

Testing ***"error might not happen only once, twice, thrice;"*** therefore, it is no wonder, that the experience of TB patients accessing diagnostics was difficult. "***It was not very easy for them to detect what was happening to me. I went all round the government hospitals and there were no proper gadgets for testing TB,"*** a TB survivor among the respondents, for example, shared. And another explained that: "***finally they found I had TB, It took me some lump sum money. It cost me like 800,000 shillings. I paid for the testing."***

Respondents' testimonies validate findings of a study (Hanrahan, et al. 2016) which included a GeneXpert machine in the region, that: ***"GeneXpert was underutilised in Uganda and did not significantly increase the number of patients starting treatment for TB."*** Obviously, it follows that delayed testing of presumptive TB cases, prevents the individuals and the medical personnel from knowing and confirming their status and, therefore, it delays the start of treatment.

Financing GeneXpert Machines

Machines malfunctioning and going into downtime is a symptom of how TB management in Uganda is grossly underfunded[4], ***"right from the budget of Ministry of Health to the budget of the hospitals, the funds are insufficient."*** NTLP annual budgets for the five years 2013-2017, as published in the WHO annual ***"Global Tuberculosis Report",*** show that on average the annual NTLP budget was US$ 34.2 million (about 123 billion shillings).

NTLP Budgets 2013 – 2017

Period	Budget (US$)	Funded (US$)	%
FY 2013	31,000,000	21,500,000	69
FY 2014	24,000,000	7,500,000	31
FY 2015	24,000,000	19,400,000	81
FY 2016	38,000,000	25,700,000	68
FY 2017	54,000,000	15,660,000	29
Totals US$	**171,000,000**	**89,760,000**	**52**
Totals Ug.shs	**614,000,000,000**	**322,080,000,000**	**52**

Not only were the NTLP budget allocations insufficient, they were consistently not fully funded. Taken together, only 52 percent of the budgets for the five year period were funded; and, moreover, only 10 percent were covered from domestic funds. The NTLP budget for the financial year 2017, with only 29 percent of it funded, was the least covered within the five year period. The budget for the year 2014 was also significantly not funded with only 31 percent covered. For the other years, even though the budgets were not fully funded, they were at least covered above 60 percent.

Conclusion and Recommendations

There is insufficient GeneXpert capacity in the region – whether it is latent or real. Appreciating the high TB prevalence rates in the region[5], action should urgently be taken in order to increase GeneXpert capacity in the region. There are two ways in which this could be done.

The first, and the more practical way in terms of achievability in the short term, is ensuring the effective use of existing GeneXpert machines. The reasons for machine downtime and malfunctioning are within the means of the Government to eradicate, through the provision of finances in order to ensure that the machines are well maintained – serviced regularly and as scheduled, as well as repaired promptly when the need arises.

It is also within the Government's means to make provisions for constant and adequate power supply, either through the national grid and/or through installation of backup power supply sources – installation of solar panels and generators at all healthcare facilities hosting GeneXpert machines, for example.

Issues related with stock-outs of supplies and materials, such as cartridges, can also be easily resolved by the Government through more efficient monitoring of supplies and the distribution system. Certainly, the current centralised distribution system needs to be reviewed and the option to replace it with regional or even district level distribution systems should be considered.

The second option, procurement and installation of additional GeneXpert machines, is the more costly, but which could be achieved in the longer-term if Government would take seriously the provision of adequate financing for TB management in Uganda.

Yes, GeneXpert machines are very expensive. For example, the 29 GeneXpert machines that were donated to Uganda by the U.S. Government (U.S. Mission Uganda 2017) reportedly (Namagembe 2017) cost US$ 17,000 (about 61 million shillings) each.

[4] *CPAR Uganda's briefing on research findings containing its qualitative data-set on the* ***"Tuberculosis economics in Uganda's Greater Northern Region"*** *is available to download free from its website.*

[5] *Available to download free from its website are CPAR Uganda's two analyses:* ***"Tuberculosis the silent epidemic in Uganda's Greater Northern Region,"*** *and "****Discussion of research findings on prevalence of pulmonary tuberculosis in Greater Northern Uganda."***

Add to that the installation costs per machine, which can range from as low as 9.4 million shillings, if laboratory space and electricity are available at the health facility; to 25.4 million shillings, if space and power are not available. These installation costs estimates are derived from calculations of researchers (Abdurrahman, et al. 2014) in the context of Nigeria, but are applicable to Uganda as well. If these cost estimates hold true in the context of Uganda, then it means that the cost for one fully installed GeneXpert machine would be a minimum of 70 million shillings.

Implementing the second option requires strategic thinking in determining the location of the machines. Population size and density should be factored in, and West Nile region should be given higher priority to have more machines installed.

It is important to first try to install new GeneXpert machines in health facilities which have laboratory space and electricity. However, in cases when it is not feasible, and the installations are done in facilities needing space and electricity, it is prudent and frugal for the Government to make sure that the requisite laboratory space, the equipment such as fridges, and the constant electricity power supply which is need are provided as part of the installation.

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About the author

Ms. Norah Owaraga is the Managing Director (MD) of CPAR Uganda and on its behalf she authored this discussion. Owaraga is a cultural anthropologist, in which capacity she functioned as the Social Scientist for the ***"Tuberculosis: Working to Empower the Nation's Diagnostic Efforts (TWENDE)"*** Consortium, under which CPAR Uganda conducted its investigation. She holds a Master of Science Degree in Development Management from the Open University UK and a Bachelor of Arts degree in Communication Studies from Queen Margaret University, Edinburgh, Scotland.

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