IMPLEMENTATION OF SIMPLE ONE-STEP STOOL TESTING TO DIAGNOSE TUBERCULOSIS IN CHILDREN AGED 0-14 YEARS IN UGANDA USING XPERT MTB/RIF ULTRA

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Lastly, all staff of NTLP and NTRL who contributed in one way or the other but have not been specifically mentioned are recognized and appreciated.

FOREWORD

The global commitment to end tuberculosis (TB) by 2030, as articulated in the WHO END-TB Strategy, necessitates a robust diagnostic infrastructure, particularly for vulnerable populations such as children and adolescents. The United Nations has underscored the critical need for effective diagnostic tests, aiming for all notified TB patients to be tested with a WHO-recommended rapid diagnostic test (WRD) by 2025. Despite these goals, diagnostic testing remains a significant challenge in the continuum of TB care, with only 47% of cases worldwide being tested with a WRD as an initial test in 2022.

One of the major barriers to effective TB diagnosis in children, especially those under five years old, is the difficulty in obtaining sputum samples. Traditional sample collection methods like sputum induction, nasopharyngeal aspiration, and laryngeal aspiration are invasive and require specialized skills and equipment that are often unavailable in many healthcare settings.

In response to these challenges, the World Health Organization (WHO) has recommended the use of stool as an alternative sample for TB confirmation in children. This approach, leveraging the GeneXpert platform, provides a non-invasive, easily obtainable sample, enabling bacteriological confirmation of TB in children under 14 years. This is a pivotal development, ensuring that children receive the appropriate treatment regimen and facilitating early initiation of therapy.

In Uganda, the adoption of the Simple One Step (SOS) technique for stool-based TB testing has been a significant advancement. This technique aligns with the current TB testing protocols and requires no additional materials, simplifying the process for healthcare providers.

The JSI Research & Training Institute, Inc. (JSI), through the National TB Reference Laboratory under the National TB and Leprosy Control Program, was awarded a TB commitment grant. This grant, provided as an in-kind sub-award under the United States Agency for International Development (USAID) Tuberculosis Implementation Framework Agreement (TIFA), supports the enhancement of childhood TB case finding through the implementation of the SOS stool-based TB testing using Xpert MTB/RIF Ultra.

This report outlines the key aspects of the project implementation, activities, and achievements. It reflects our collective effort to improve TB diagnosis in children, showcasing the progress made and the potential impact on public health.

We are optimistic that the findings and strategies detailed in this report will contribute significantly to the ongoing efforts to eradicate TB in children and pave the way for innovative approaches to TB diagnosis and treatment globally.

By addressing the diagnostic challenges faced by healthcare providers and ensuring the implementation of non-invasive, efficient testing methods, we move closer to realizing the goal of ending TB in children by 2030.

Prof. Moses Joloba,

Head NTRL/SRL-UGANDA, Ministry of Health

ABBREVIATIONS

SOS	Simple one step
HIV	human immunodeficiency virus
LMICs	Low- and middle-income countries
PBC	Pulmonary bacteriologically confirmed
ART	Antiretroviral therapy
BCG	Bacille Calmette-Guérin
aNAAT	Automated nucleic acid amplification test
DST	drug-susceptibility testing
EQA	external quality assessment
MoH	Ministry of Health
MTBC	Mycobacterium tuberculosis complex bacteria (e.g. M. tuberculosis or M. bovis bacteria)
mWRD	Molecular WHO-recommended rapid diagnostic test
NAAT	Nucleic acid amplification test
	Pulmonary clinically confirmed
TB	Tuberculosis
NTLP	National Tuberculosis and Leprosy Program
NTRL	National Tuberculosis Reference Laboratory
USAID	United States Agency for International Development.
JSI	John Snow, Inc.
MDR/RR-TB	Multidrug-resistant or rifampicin-resistant tuberculosis
TIFA	Tuberculosis Implementation Framework Agreement
SOP	Standard operating procedure
SRL	Supranational reference laboratory
SRLN	Supranational Reference Laboratory Network
WHO	World Health Organization
XDR	extensively drug-resistant TB

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DEFINITIONS

Term	Definition
Child	A person aged less than 15 years (0 – 14 years)
Bacteriologically confirmed TB case.	A person from whom a biological specimen is positive by smear microscopy, or culture or WHO-Approved Rapid Diagnostics (such as GeneXpert or Xpert MTB/ RIF).
Infant	A child under 1 year of age
Neonate (or newborn)	An infant under 28 days of age
Clinically diagnosed TB case	A person who does not fulfill the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. Includes X-ray and histological diagnosis.
Contact person	Any person who was exposed to a person with TB.
Index patient (index case) of TB	The initially identified person with TB disease in a specific household or other comparable setting in which others may have been exposed. An index patient is a person on whom a contact investigation is centered but who is not necessarily the original source of an outbreak of TB.
A person with presumptive TB	A patient who presents with symptoms and signs suggestive of TB
Lost to follow-up (previously known as defaulter)	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more
Multidrug Resistant TB	Resistance to Rifampicin and Isoniazid
New patient	A person who has never been treated for TB or has taken anti-TB medicines for less than 1 month
Previously treated patient	A person who has received 1 month or more of anti- TB medicines in the past.
Pulmonary Tuberculosis	Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.
Relapse patient	A patient who has previously been treated for TB was declared cured or treatment completed at the end of their most recent course of treatment and is now diagnosed with a recurrent episode of TB
Screening	The systematic identification of people at risk for TB disease in a predetermined target group by clinical examination, assessing symptoms and using tests (sputum-smear microscopy, LF-LAM, C-reactive protein), or other procedures (e.g. chest radiography). For those who screen positive, the diagnosis should be established by one or more diagnostic tests (e.g. mWRD, culture). This term is sometimes used interchangeably with “active tuberculosis case-finding”.
Source case	A person with infectious TB (usually bacteriologically confirmed) who transmits infection to one or more other individuals.
TB infection	A state of persistent immune response to stimulation by M. tuberculosis antigens with no evidence of the clinical manifestations of TB disease. This is also at times referred to as “latent TB infection”. There is no gold standard test for direct identification of M. tuberculosis infection in humans. Most infected people have no signs or symptoms of TB but are at risk for progression to active TB disease.
TB disease (Active TB)	Refers to illness that occurs in someone infected with Mycobacterium tuberculosis and is characterized by clinical signs and symptoms, with or without laboratory or radiographic evidence.

EXECUTIVE SUMMARY

Each year, 1.1 million children globally fall ill with tuberculosis (TB), of whom only 400,000 are notified; with the case detection gap being highest in children aged under 5 years. In 2022, globally 1.25 million children (0- 14 years) developed TB accounting for 12% with 214,000 children dying due to the disease. Obtaining bacteriological confirmation of TB is challenging in children because of the frequent paucibacillary presentation of the disease. Diagnostic tests are central to obtaining timely and accurate TB diagnosis in children but this is complicated by difficulty in obtaining a quality specimen in this age category due to hardship to effectively expectorate and produce a sputum sample and the invasiveness of other procedures such as sputum induction or gastric aspiration among others.

In 2021, the World Health Organization (WHO) recommended stool as an alternative specimen type for TB diagnosis for both Xpert MTB/RIF and Xpert Ultra as the initial diagnostic test for TB and the detection of rifampicin resistance in children aged under 10 years with signs and symptoms of pulmonary TB. A systematic review and meta-analysis of Xpert Ultra data for stool testing found a sensitivity of 53% (95% CI: 35–70) and a specificity of 98% (95% CI: 93–99) closing the gap for childhood TB diagnosis by increasing diagnosis accuracy, reduce the time to treatment initiation, impact patient-important outcomes, and being cost-effective.

To introduce stool testing in Uganda a phased early implementation approach was adopted from August 2023 to May 2024. These efforts saw 56 sites trained under the original grant funding. By the ninth month of implementation, the national TB program had mobilized other partner resources to facilitate training of 64 additional GeneXpert testing sites and 113 non-GeneXpert testing sites that routinely refer samples. Stool testing led to bacteriological confirmation of 124 patients giving a yield of 2.9% during this implementation period. All SOS-negative patients were further assessed clinically. Clinical diagnosis contributed 88.5% (971/1097) of the total TB patients notified among children who received a stool test at the trained facilities,

The introduction of simple one-step stool testing led to an increase in the number of bacteriologically confirmed TB cases among children and proved to be effectively feasible to provide a definitive diagnosis in even children below one year. Scale-up and integration of the SOS technique within the routine diagnostic program of TB among children across all the DTUs country-wide is required to sustain and ensure universal access among all children in Uganda.

1. BACKGROUND

Globally, an estimated 10.6 million people developed TB with 1.3 million TB deaths registered in 2022 and 1.25 million children (0- 14 years) developed TB accounting for 12% with 214,000 children dying due to the disease, accounting for 16% of all TB deaths. (WHO 2023). Uganda is among the 30 high-burden TB and TB/HIV countries with an estimated 94,000 people with TB in 2022 and 14,182 incident TB cases aged 0-14 years were notified out of the expected 13,622.

The overall goal of the **2020/21 – 2024/25** national TB and leprosy strategic plan is to increase the proportion of notified new and relapse TB cases with bacteriological confirmation from 53% to 80% and increase the current proportion of TB cases notified for children to 15% of all notified cases by 2024/25 and also have the childhood TB treatment coverage increased from 64% to >90%. This translated to a TB treatment coverage of 104.1% above the NSP target of 90%. (NTLP 2022/2023). In 2023, Uganda notified 11,919 childhood incident TB cases and 37% were bacteriologically confirmed whereas 55% were clinically diagnosed showing an increase in bacteriological confirmation from 2022 (57% being clinically diagnosed and 35% being bacteriologically confirmed) Additionally, for the same period, 633 DR-TB cases were registered with 4% being children aged 0-14 years.

As part of the global targets set in 2018 at the UN high-level meeting on TB, the target for the number of people with TB treated in five years between 2018- 2022 is 40 million including 3.5 million children and 1.5 million people with DR TB including 115,000 children. Of the 1.2 million children who developed TB in 2022 only 42% among children aged 0-4 years and 55% among children aged 5-14 years were reported hence a case detection gap of 58% and 45 % respectively. (WHO 2023).

By 2022, in Uganda, an estimated 36% of children with TB remained undiagnosed and unreported as of 2021, putting them at risk of severe complications and even death. The NTLP recommends that healthcare providers obtain a sample for bacteriologic confirmation of TB in children and adolescents who have presumptive TB. % (NTLP 2022/2023).

The clinical presentation of TB in children is nonspecific and similar to other respiratory conditions and this creates high chances of missed diagnosis. Obtaining bacteriological confirmation of TB is challenging in children because of the frequent paucibacillary presentation

of the disease. Diagnostic specimens have a low bacterial load, which decreases diagnostic test sensitivity. Diagnosis is further complicated by the fact that obtaining a sufficient volume of specimens from children can be difficult. Children, especially young children (0-5 years), generally cannot effectively cough out a sputum sample. Additionally, there is inadequate knowledge, specialized skills and access to equipment and supplies required for sample collection in children using sputum-based invasive procedures such as sputum induction. Limited access to care is also experienced as a result of the failure of the caretakers to recognize the symptoms of TB and seek care.

Rationale for Introducing stool as an alternative sample for TB diagnosis in children

Diagnostic tests are central to meeting the goal of ending TB in children and adolescents by 2030 as set by the United Nations in the WHO END-TB Strategy. The goal is that by 2025, all notified TB patients will be tested using a WHO-recommended rapid diagnostic test (WRD) as an initial test, including the use of the GeneXpert platform, but diagnostic tests remain a weak link in the continuum of care with only 47% being tested with a WRD as an initial test worldwide in 2022. More often, healthcare providers lack the skills to obtain sputum samples from children especially those < 5 years. The recommended sample collection methods such as sputum induction, nasopharyngeal aspiration, and laryngeal aspiration are considered invasive methods and require specialized skill and equipment which are not routinely available in our context.

The recommendation by WHO to use the stool as an alternative sample for TB confirmation allows children < 15 years to get an opportunity for bacteriological confirmation of TB using the GeneXpert platform, an important step in determining the appropriate treatment regimen and early initiation. In addition, stool collection is non-invasive and it is easy to obtain a sample for bacteriological confirmation in children. Uganda adopted the SOS technique given the simplicity of performing the test with no extra materials needed from what is currently used in routine TB testing.

JSI Research & Training Institute, Inc ("JSI") awarded the National TB Reference Laboratory under the National TB and Leprosy- Control Program a TB commitment grant as an in-kind sub-award issued under the United States Agency for International Development (USAID) Tuberculosis Implementation Framework Agreement (TIFA) to support the improvement of childhood TB case finding through the implementation of the Simple One Step (SOS) stool-based

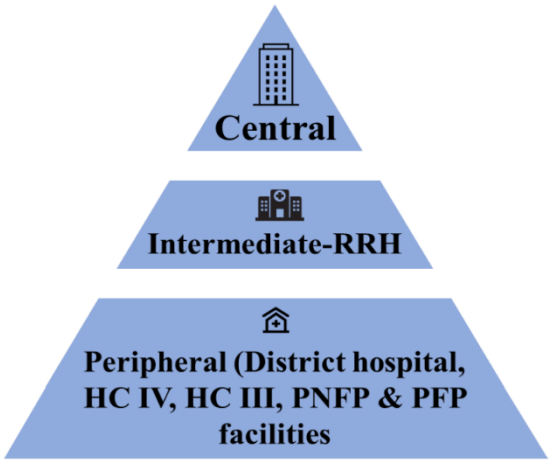
TB testing using Xpert MTB/RIF Ultra. The following report highlights key aspects of the project implementation processes, activities and achievements.

OBJECTIVES

1. To introduce the simple one-step (SOS) stool-based TB testing for TB diagnosis among children using Xpert MTB/RIF Ultra in Uganda.
2. To adopt guidelines and monitoring tools on simple one-step (SOS) stool-based TB testing for TB in children using Xpert MTB/RIF Ultra in Uganda.
3. Early implementation of the simple one-step (SOS) stool-based TB testing using Xpert MTB/RIF Ultra testing among children with presumptive TB in Uganda.

2. IMPLEMENTATION APPROACH

A phased early implementation approach was adopted in the introduction of the SOS technique in Uganda from August 2023 to May 2024. The project targeted 56 health facilities (17 Regional Referral Hospital, 5 national Referrals, and 34 General hospitals) across the country. The facilities were selected based on the level within the current tiered TB laboratory network in the country *(figure 1*) that would subsequently facilitate effective scale-up of the technique to lower facilities. All the selected facilities were functional GeneXpert sites and fulfilled the minimum biosafety requirements to implement the SOS technique. The implementation approach involved the following activities:



Development of SOS training materials

The TB program adapted key training materials, including KNCV SOS Toolbox, WHO Guidelines, Global Laboratory Initiative tools, and Uganda NTLP guidelines, SOPs, job aids, plus exercises and developed 13 standardized training modules to be utilized while conducting training of health workers on the SOS stool processing technique across Uganda.

Stakeholder engagement meetings

The TB program conducted two stakeholder engagement meetings with; the Ministry of Health, development partners, implementing partners, adolescents and school health advisors, academia, Health caregivers, caretakers of children affected by TB, WHO, and The Union against TB and Lung Disease, Civil Society Organizations. The main purpose of the stakeholder engagement meeting was to review and endorse the SOS early implementation plan, training materials, SOPs and job aids.

Training of Trainers (TOT) workshops

Training of Trainers (TOT) workshop targeted 44 personnel from 5 national and 17 regional referral hospitals, 1 health center IV and 1 health Centre III, and were conducted across the country. Each national and regional referral hospital selected one laboratory personnel and one clinician (Pediatrician or Medical Officer/Clinician) to attend the five-day training workshop. Participants developed regional and health facility-specific plans to cascade SOS training to two (2) general hospitals with high numbers of pulmonary clinically diagnosed TB(PCD) cases in the previous year. For effective follow-up after training, a WhatsApp group for all the trained personnel was formed to facilitate effective communication, updates, and experience sharing among the trained personnel.

On-site training

A two-day onsite training for 34 selected facilities was conducted in all regions per facility. At each facility, theoretical and practical sessions were conducted for atleast 10 health workers that included nurses, laboratorians, clinicians and TB linkage facilitators. As a result, a pool of 56 facilities with the capacity to subsequently cascade the SOS method to other facilities was obtained. With support from partners, an additional 192 health facilities were trained on SOS by May 2024 of which 79 were GeneXpert and 113 non GeneXpert testing sites. The districts and partners also mentored lower facilities on stool sample collection and referral to GeneXpert sites.

Support supervisions

Three (03) rounds of bi-monthly support supervision visits were conducted targeting the trained health facilities to follow-up implementation at all enrolled sites, assess utilization of SOS services as per set TB diagnostic algorithm, linkage to care, address facility-specific challenges and data

collection on the progress of the implementation. Data collected from facilities was discussed during the NTRL and NTLP performance review meetings for planning and decision-making.

Virtual learning sessions

Two virtual learning sessions were conducted during the period of implementation to share experiences, challenges and lessons learned during the implementation of SOS. These learning sessions guided the support offered to regions, districts and facilities and identified areas for more focus during subsequent support supervisions.

Digitalization of the SOS training Course

The audiovisual-assisted learning platform was also developed to aid health workers in further cascading the SOS technology to other health facilities within the network as well as providing guidance and reference during the implementation of the SOS technology at health facilities. https://youtu.be/99x19cJ5vrM?si=o9ReDryYjULEL7li

Data collection methods

A mixed method approach was utilized in the collection of data quarterly. Quantitative data was collected using a controlled data collection tool that focused on the following key indicators:

I. Number of children screened for TB.
II. Number of children presumed for TB
III. Number of stool samples tested and rejected
IV. Number of MTB detected from SOS samples
V. Number of RIF resistance detected from SOS samples
VI. Number initiated on treatment clinically but with negative SOS results
VII. GeneXpert Error rates attributed to stool samples

Qualitative data was collected by administering standardized support supervision checklists to obtain the perceptions and impact of the SOS technology within the community.

Collaborations and partnerships

Advocacy meetings with regional TB and HIV/TB implementing partners across the country were conducted to advocate for the scale-up of SOS technology to facilities not reached under the SOS TIFA grant. NTLP collaborated with Partners (WHO Uganda, USAID, CDC & DOD partners, and

District Local Government) to scale up SOS. Plans are underway to finalize the national rollout by conducting training in the remaining regions.

Quality Assurance

Quality assurance checks were incorporated at all stages of project planning and implementation mainly focusing on the following areas;

- comprehensive project work plan
- staff training and competency
- support supervision and follow-up assessments
- recording and reporting
- maintenance of equipment
- Performance review meetings.

3. RESULTS

OBJECTIVE 1

To introduce the simple one-step (SOS) stool-based TB testing for TB diagnosis among children using Xpert MTB/RIF Ultra at NTRL Uganda.

Catalytic implementation of SOS stool processing and testing in Uganda led to the development of a 3-unit (3-CU) course with 13 peer-reviewed modules. Initial SOS training created a pool of both clinical and laboratory SOS implementation experts as shown in table 1 below.

Table 1: SOS knowledge and skills training

Category of Experts	Number trained	level of implementation
Master trainers	10	Central
National and Regional trainers	44	Intermediate facilities
Health workers	186	Peripheral facilities

The first training involved 10 master trainers who were personnel with diverse expertise that included pediatricians, laboratorians, and M&E specialists. These subsequently trained national and regional trainers during a 5-days workshop, who later conducted two-day onsite training to at least 5 health workers at each site.

These efforts saw 56 sites trained under the original grant funding. By the end of May 2024, the national TB program had mobilized other partner resources to facilitate training of 64 additional GeneXpert testing sites and 113 non-GeneXpert testing sites that routinely refer samples as shown in Table 2 below.

Table 2: Sites trained following SOS stool testing for TB rollout in Uganda

Funding source	Number of GeneXpert testing health facilities trained	Number of non-GeneXpert testing health facilities trained
TIFA	56	
other funding sources from implementing partners	79	113

These collaborative efforts underscore the impact of IPs that led to the increment of SOS rollout from 18.9% (56/297) within two months to 45.5% (155/297) across GeneXpert sites within nine months after initial SOS training.

Indicators	Number	Proportion
Children screened for TB	406,436	
Children with presumptive TB	24,554	6.0%
SOS tests done	4,397	17.9%
Children detected with MTB via stool testing	126	2.9%
MDR	2	1.6%
Errors/invalid/no results	351	8.0%
Number of samples rejected	73	1.7%

The introduction efforts led to the development of an open-source video that captures aspects of WHO & country guidelines on Implementation aspects of SOS stool testing for TB among Children. The video is available online and can be routinely accessed by health workers. **https://youtu.be/99x19cJ5vrM?si=o9ReDryYjULEL7li**

OBJECTIVE 2

Adopt guidelines and monitoring tools on simple one-step (SOS) stool-based TB testing for TB in children using Xpert MTB/RIF Ultra in Uganda.

Stool testing has been incorporated in routine data capture tools that include the HMIS TB 013-Presumptive register, HMIS TB 010 -TB laboratory register, and HMIS 105-monthly data tool collection and HMIS 106a quarterly data collection tool that have been reviewed as observed in annex 1 attached. The national guidelines on the management of TB in children and adolescents have been revised to capture stool testing in the section on Laboratory diagnosis of TB in children and adolescents.

OBJECTIVE 3

Early implementation of using the simple one-step (SOS) stool-based TB testing using Xpert MTB/RIF Ultra testing among children with presumptive TB in Uganda.

Monitoring uptake of SOS stool testing for TB included collection of data on the number: (I) screened, (II) presumed, (III) tested using SOS, (IV) positivity rate, (V) error and rejection rate as shown in Table 3 below.

Table 3: SOS testing cascade from August 2023 to April 2024.

NB: 24.3% of the presumptive children were tested on GeneXpert using other samples other than Stool. This put the overall testing using a WRD at 42.2% which left the rest of the presumed patients without a documented laboratory test done.

SOS PERFORMANCE PER REGION BETWEEN AUG 2023 TO APRIL 2024

By the end of August 2023, all 15 regions across the country had at least three facilities conducting SOS stool testing for TB among children using Xpert MTB/RIF assay. By May 2024, the regions of Karamoja, Busoga, Kampala, Wakiso, Mukono, Acholi and Kigezi had all the Xpert sites trained in their respective regions. A total of 104 primary GeneXpert testing healthcare facilities reported data during the 9-month implementation period. Sites not yet reporting included those that had not yet implemented for at least a month since the time of training.

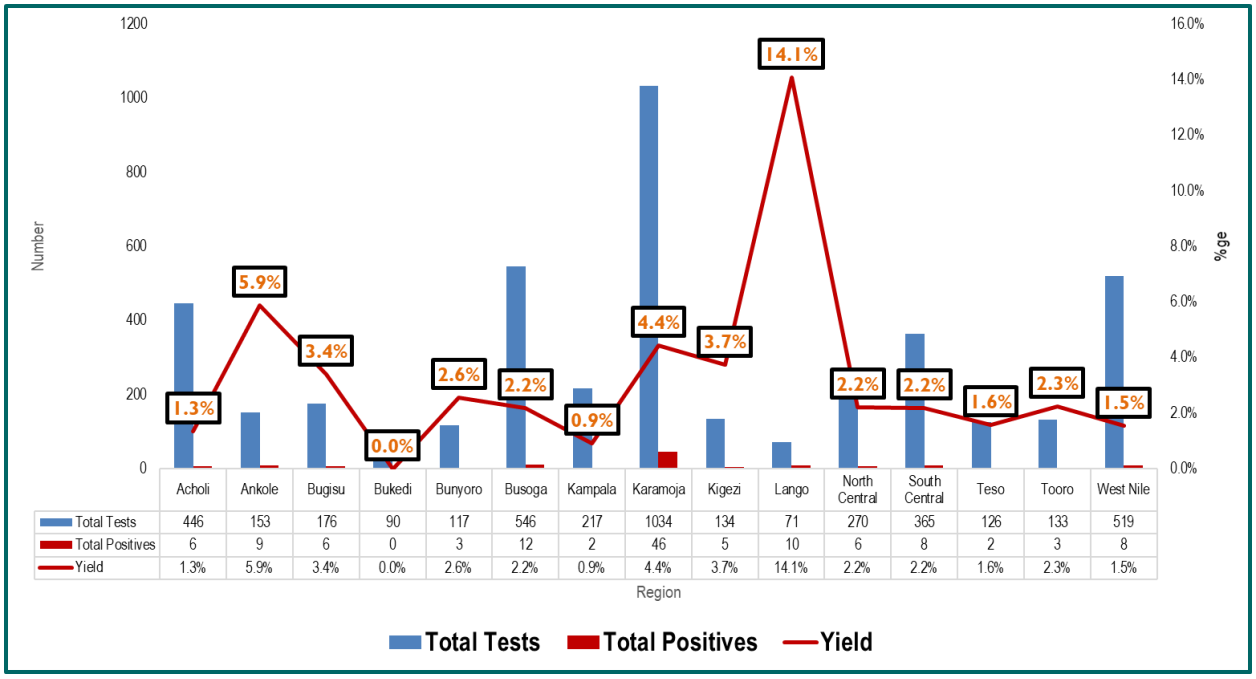
Table 4: SOS TB testing cascade per region from August 2023 to April 2024.

Region	Screened	Presumptive TB	Stool samples tested	MTB Detected	MTB Not detected	Yield
Acholi	20,531	1,038	446	6	419	1.3%
Ankole	1,271	1,271	153	9	136	5.9%
Bugisu	3,186	959	176	6	162	3.4%
Bukedi	8,242	482	90	0	89	0.0%
Bunyoro	6,331	471	117	3	111	2.6%
Busoga	73,375	2,639	546	12	522	2.2%
Kampala	42,152	1,900	217	2	213	0.9%
Karamoja	9,632	1,239	1,034	46	944	4.4%
Kigezi	14,396	672	134	5	126	3.7%
Lango	16,793	1,449	71	10	35	14.1%
N.Central	69,016	2,670	270	6	255	2.2%
S.Central	55,516	2,678	365	8	342	2.2%
Teso	426	298	126	2	73	1.6%
Tooro	26,280	750	133	3	128	2.3%
West Nile	59,289	6,038	519	8	365	1.5%
Grand Total	406,436	24,554	4,397	126	3,920	2.9%

Overall, a total of 406,436 children aged 0 -14 years were screened at the 104 reporting sites of which 6.0% (24,554) had presumptive TB. Of all the children with presumptive TB, 17.9% (4,397/24,554) had a stool sample tested for bacteriological confirmation and 126 had a positive Xpert MTB/RIF giving a yield of 2.9%. This yield is two times higher than some earlier SOS pilot implementers such as Zambia which had a positivity rate of 1.2%, and Zimbabwe at 1.7% while

lower than DR. Congo whose pilot led to a 16% positivity yield. From Table 4 above, regions with all GeneXpert sites trained in the early months of implementation reported the highest number of tests done (1st-Karamoja, Busoga 3rd) and highest PBCs. (1st-Karamoja, Busoga 2nd).

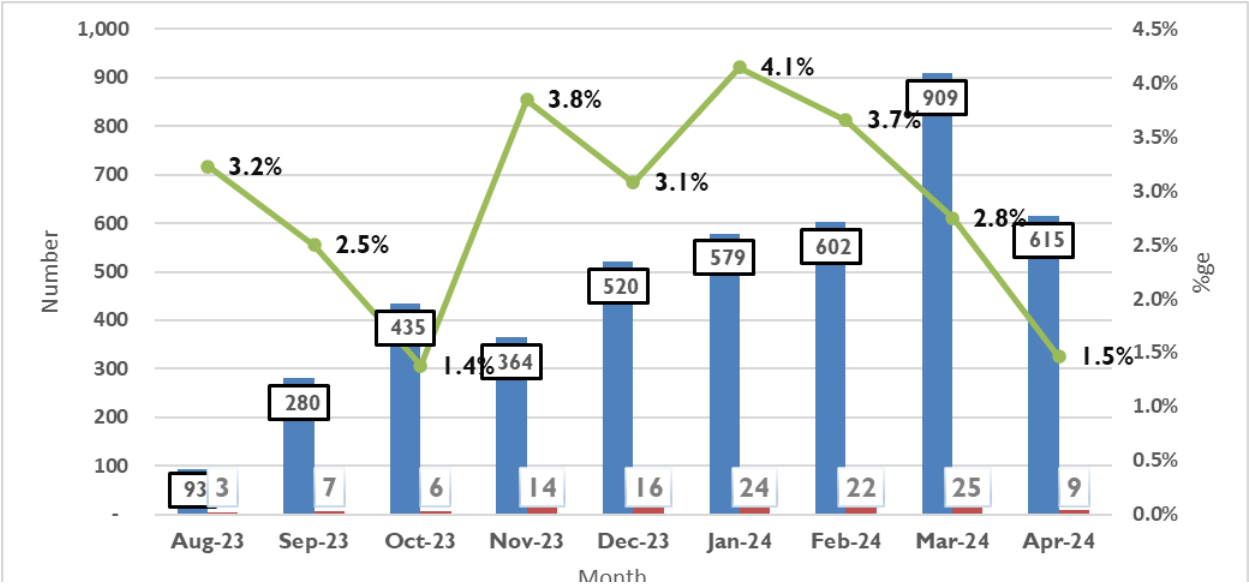
Graph 1: SOS testing and yield per region from August 2023 to April 2024.



	Acholi	Ankole	Bugisu	Bukedi	Bunyoro	Busoga	Kampala	Karamoja	Kigezi	Lango	North Central	South Central	Teso	Tooro	West Nile
Total Tests	446	153	176	90	117	546	217	1034	134	71	270	365	126	133	519
Total Positives	6	9	6	0	3	12	2	46	5	10	6	8	2	3	8
Yield	1.3%	5.9%	3.4%	0.0%	2.6%	2.2%	0.9%	4.4%	3.7%	14.1%	2.2%	2.2%	1.6%	2.3%	1.5%

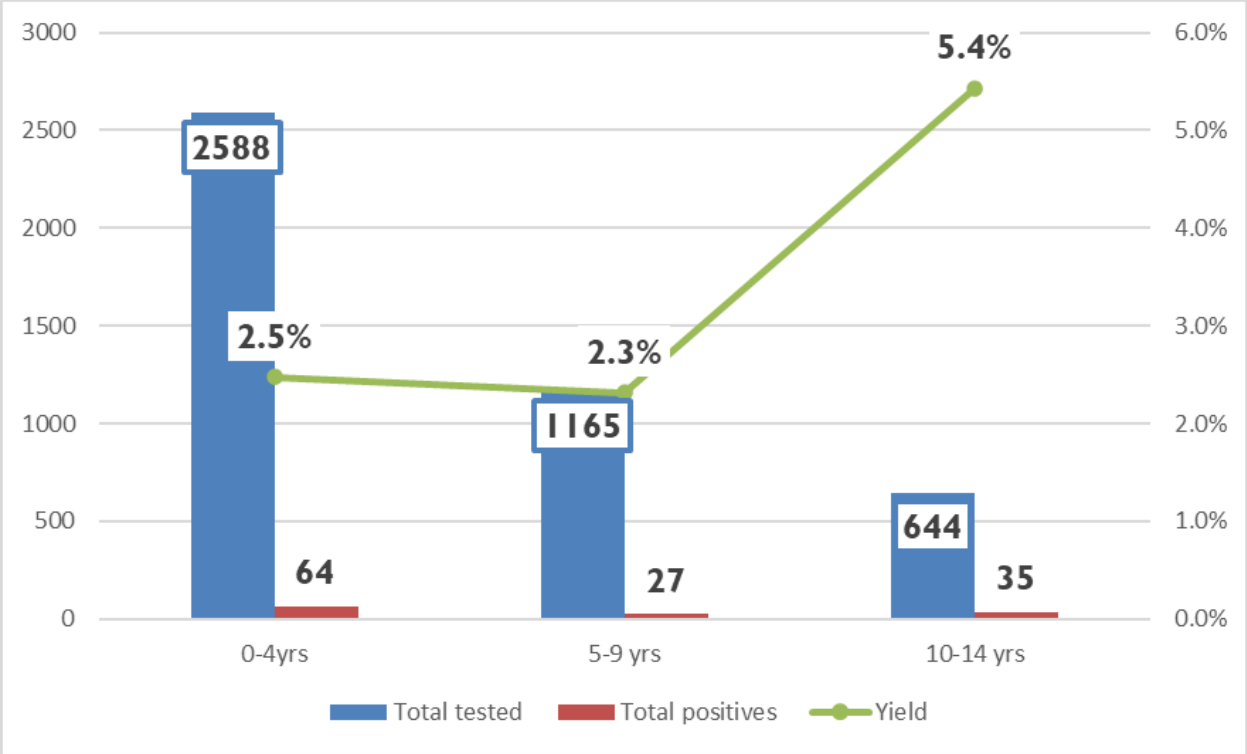
The yield varied across the different regions of the country with the highest rate of 14.1% (10/71) registered in the Lango region nonetheless having tested the fewest samples while the lowest rate was noted in Bukedi which has not registered any positive since implementation and notably also with a low suspicion index. To understand the trend of SOS implementation this data was plotted across the different months of implementation as shown in graph 2 below.

Graph 2: SOS testing and yield per month



The data above represents an overall report from 82 facilities during the implementation time of nine months. It should be noted that between August-October 2023, only 59 sites had started testing and the number of testing sites increased as training was cascaded to other facilities. The implementation has generally seen an increasing trend of stool samples tested although with a fluctuating yield that climaxed in January at 4.1% and lowest in April at 1.5%. The overall proportion of SOS PBCs from the implementation time stood at 2.9%. The absolute number as seen in graph 2 above shows an increasing trend of positives as more samples were increasingly getting tested due to an increase in the number of testing sites. This can be attributed to several factors that include increasing competence of health workers for intensified case finding among children and also performing SOS technique.

Graph 3: SOS testing and yield per Age group from Aug 2023 to April 2024.

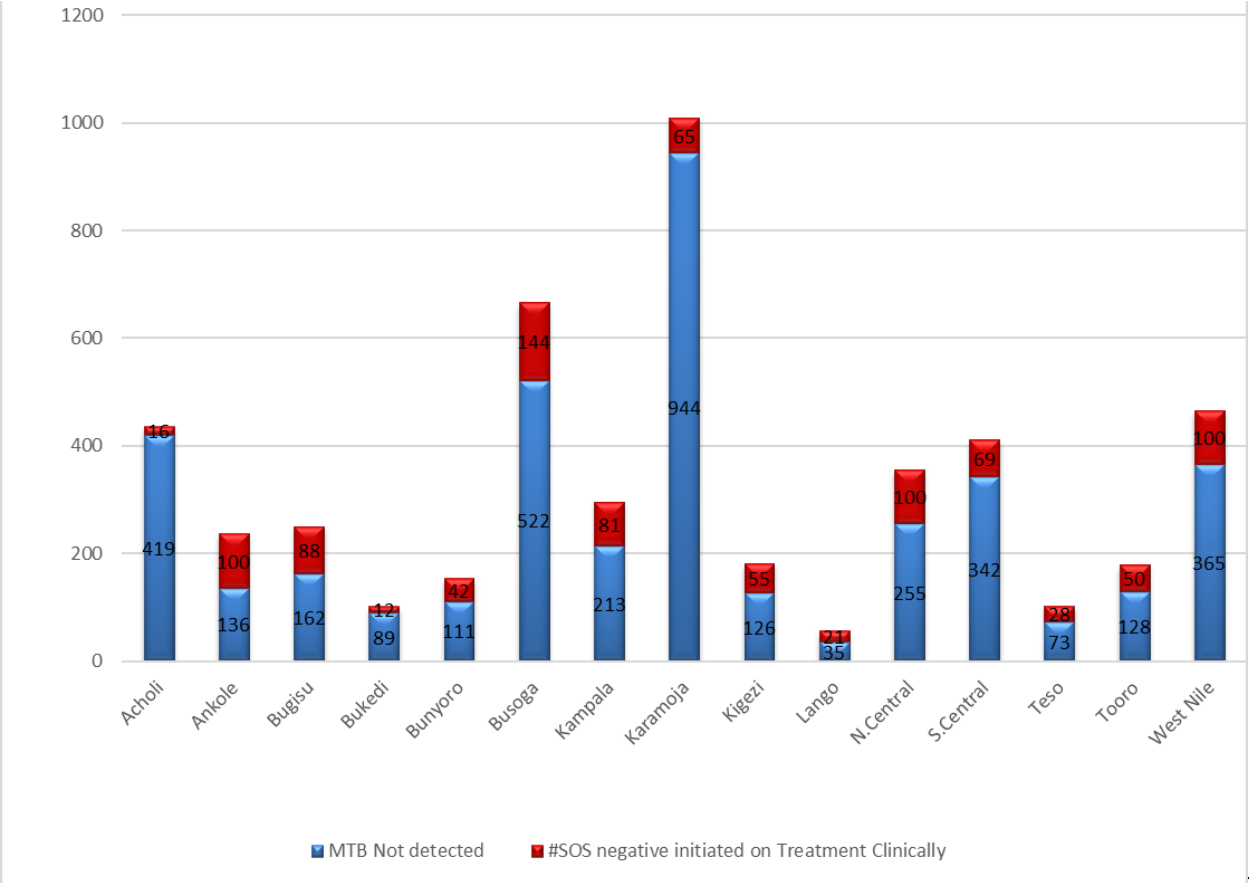


Age categorization was key in data collection to establish the usage of SOS across the different ages as shown in graph 3 above. It can be noted that stool testing was used two times more for the age category 0-4 years as compared to all other age categories although this category had a lower proportion of positives reported compared to the other categories. The TB yield was highest in the 10 - 14-year age group at 5.4% a similar situation in other countries where SOS has been piloted such as in Zambia which had a yield of three times more in critically ill adults compared to children under 10 years.

Implication of Negative SOS results.

Following a negative SOS stool test on Xpert MTB/RIF Ultra, patients were further assessed to rule out TB disease**.** This ultimately underscored the impact of clinical knowledge and skills gained following the SOS training. Clinical decision was thereby taken following an informed view and those deemed with TB disease were initiated on Treatment and routinely monitored to assess treatment response. This increased the number of PCDs among children compared to the period before implementation in these facilities. The graph below shows the magnitude of this intervention.

Graph 4: Number initiated on treatment clinically per region from August 2023 to April 2024 following negative SOS result.



All SOS-negative patients were further assessed clinically. Clinical diagnosis contributed 88.5% (971/1097) of the total TB patients notified among those who received stool testing. All SOS-negative patients were further screened clinically and those with all signs and symptoms suggestive of TB were started on childhood-friendly formulations putting 22.1% (971/4397) of the total number of children who received stool testing as clinically diagnosed patients.

4. IMPACT OF SOS STOOL TESTING

Region	% Coverage Apr to Jun 2023	% Coverage Jul to Sep 2023	% Coverage Oct to Dec 2023	% Coverage Jan to Mar 2024	Trend Line
Acholi	31%	45%	26%	39%	
Ankole	0%	16%	14%	17%	
Bugisu	29%	29%	35%	23%	
Bukedi	32%	33%	60%	38%	
Bunyoro	12%	25%	36%	41%	
Busoga	23%	13%	25%	27%	
Kampala	26%	21%	15%	16%	
Karamoja	16%	21%	30%	26%	
Kigezi	17%	0%	10%	3%	
Lango	81%	76%	77%	54%	
North Central	34%	28%	35%	28%	
South Central	10%	37%	44%	19%	
Teso	7%	39%	25%	11%	
Tooro	40%	59%	29%	22%	
West Nile	28%	15%	28%	34%	
Grand Total	**24%**	**24%**	**30%**	**26%**	

The implementation of SOS stool testing across different regions has had a fluctuating impact on the number of bacteriologically confirmed TB patients. There is a grand increase in the number of pediatric PBCs diagnosed among all the SOS implementing sites by 6% after SOS was introduced between the periods of Jul-Sep 2023 to Oct-Dec 2023. Regions of Bunyoro, Busoga, Ankole and West Nile have seen a positive trend of PBCs diagnosed. All regions showed an immediate increase in PBCs immediately after the introduction of SOS although a decline has been observed in some regions such as Teso during the second quarter of implementation. The decline in some regions can be attributed to the low suspicion index for pediatrics in these specific regions and quarters, and the slow uptake of SOS technique among the trained facilities, among others. The reasons for a decline in the last quarter of implementation are not well understood at the time of closure of this project implementation.

Role of stool testing in DR-TB diagnosis.

Bacteriological confirmation of multi-drug resistant TB in children has always remained a hurdle with clinical diagnosis as the only option available leading to blind initiation of children especially 0-5 years on imprecise medication. The introduction of SOS has led to the timely identification of two MDR-TB patients in the regions of West Nile and Karamoja respectively. This early MDR-TB detection and treatment with appropriate anti-tuberculosis drugs has the ultimate potential to reduce the duration of infection in the community, thereby decreasing the number of new children exposed and infected. This underscores the role of stool testing in ensuring universal access to DST testing among all presumed TB patients.

A Clinician's Perspective

"With the introduction of the SOS stool testing technique in the country, many missed opportunities of delayed TB diagnosis in children due to challenges in sample collection have significantly reduced. Previously invasive procedures like nasopharyngeal aspiration and gastric aspiration were used to obtain an appropriate sample for TB diagnosis in children who could not expectorate. These procedures required expertise and very few healthcare providers were able to perform them. With the coming of SOS stool testing for TB that is noninvasive and user-friendly, sample collection has become easier, hence early diagnosis and detection of drug-resistant TB and as health workers, we can make quick treatment decisions. This has reduced the hospital stay and improved the prognosis with better treatment outcomes for children with TB, and ultimately reduced the burden on the health system and the community at large *"Dr. Nakayenga Aminah-Medical officer Mbarara Regional Referral Hospital)*

SOS SUCCESS STORY: CASE STUDY

On 20/11/23, a clinician at Buyamba HC III (Non-GeneXpert site) screened SD, a male of 7 years at OPD, he presented with chest pain, cough, night sweats and low weight for his age. SD was presumed to have had PTB. The clinician presumed SD to be suffering from TB and requested stool GeneXpert who was referred to Rakai Hospital for SOS stool testing. The DTLS had earlier disseminated SOS stool testing information to this peripheral site following an onsite training that was conducted in September 2023. On 21/11/23 Rakai Hospital lab tested and reported through lab expert SMS system to the clinician in buyamba HC III that SD had MTB detected Low RIF resistance not detected. SD was started on TB treatment. SD was unable to produce sputum for follow-up at 2,5, and 6 months, the clinician monitored him based on clinical evaluation and successfully completed his treatment on 22/5/24.

5. CHALLENGES ENCOUNTERED

Several challenges have been identified during implementation and these included:

- Notable gaps were observed in recording and reporting procedures in some facilities as evidenced by partially completed registers at some sites and the absence of registers at key entry points. To address this gap, recommendations were made, such as CMEs and refresher training for health care providers.

- There was also low uptake of the technique as observed in some facilities following the first support supervision. However, this improved over time in the subsequent support supervision. Some of the anecdotal reasons raised included, caregivers being skeptical to consent for stool collection to test for TB which is primarily a respiratory disease.; slow information dissemination to all health workers in charge of patient screening.
- Inability to obtain accurate data of the screened vs presumed cases given that some facilities were using electronic systems that do not capture such details.
- Stock out of essential supplies at some facilities e.g. cartridges, was a notable challenge.
- Some Caregivers have not fully appreciated the role of stool sample collection in childhood TB testing and diagnosis and thus there was stigma associated with the sample collection in some regions.
- The inability of the Labxpert connectivity system to transmit SOS data to the central monitoring team at NTLP. I think the software developers can be engaged to have the data capture age and sample type specifications.

6. LESSONS LEARNT.

- ✓ Stakeholder engagement consultations conducted during the early implementation phase provided a platform for reviewing and endorsing the implementation plan that enhanced the uptake of the SOS- technology countrywide.
- ✓ Scale-up of the SOS technique to additional DTUs during the implementation phase with support from local partners is a lesson that further rollout of the technique would require consolidated efforts from various stakeholders including but not limited to the local implementing partners, District health teams and CSOs.
- ✓ Peripheral facilities without a Molecular WRD should be targeted for capacity building on the SOS technique to further improve the utilization of the SOS technique across the TB laboratory network in the country.

- ✓ Addressing gaps related to data capture and reporting experienced during the implementation phase should be best addressed through a comprehensive review of HMIS tools to allow provisions for the capture of data related to the SOS technique and also integrated within the routine national reporting mechanisms.
- ✓ The project has clearly demonstrated that TB in children can be diagnosed with molecular WRD using simple stool processing methods.

7. RECOMMENDATIONS

Successful implementation of the year-long project allowed the NTLP/ NTRL to develop a comprehensive way forward with the following recommendations;

To continuously achieve the milestone of SOS, further resourcing to support SOS testing scale-up efforts is a top priority and the areas below are the key recommendations to prioritize.

1. To scale up SOS testing to all facilities in the country network
2. Onsite orientation on SOS among specialized pediatric clinics and hospitals. Several such facilities (mainly private and other non-government entities) are managing a high volume of children and do not have GeneXpert machines onsite hence would highly benefit from TB referral services if fully engaged in the SOS stool testing method.
3. Dissemination of IEC materials and community engagement. Print and distribute IEC materials to increase awareness and encourage the adoption of SOS testing at various entry points in all TB testing facilities.
4. To ensure continued monitoring of childhood TB indicators at all levels of the health care system.
5. To ensure continued engagement of regional Implementing partners (IPs) and local district technical officers (clinical and laboratory personnel). This support will capacitate the sub-national teams and IPs to subsequently support their respective sites (both Xpert and non-Xpert sites) in their region and scale up SOS testing. This will ease technical collaboration between the IPs and the TOTs at regional referral hospital
6. LabXpert software developers and NTLP to engage Cepheid to allow data capture for age and sample type specifications to track SOS indicators.

7. SUSTAINABILITY

The subsequent implementation of SOS stool testing in children will require the strategies below to ensure implementation beyond the pilot phase.

- Inclusion for discussion of the SOS implementation activities in the performance review meetings held at the district and regional level quarterly
- Consideration for the increase in the number of supplies during the quantification of essential supplies and commodities including GeneXpert cartridges.
- Data management tools DHIS2 and ECBss have been revised to capture and monitor childhood TB indicators obtained from stool-based testing and this provides a sustainable approach to decision-making.
- Incorporate SOS testing in existing NTP initiatives like CAST TB campaigns, refresher training, mentorships and support supervision.

Area of intervention	**Approach**
Capacity Building	The SOS training course will be integrated into continuous training programs at NTLP and SRL-Uganda training curriculum programs and training tracked on the (tbmis.net) platform and pre-service curriculum for health training institutions. SOS training SOS should be included in the pre-service curriculum for health training institutions. Strengthen the capacity of the centers of excellence for pediatric TB diagnosis in regional and district hospitals.
Community Engagement and Awareness	Strengthen the existing and ongoing community awareness programs emphasizing the importance of stool testing for TB in children with mentorship to village health teams routinely.
Financial Sustainability	Advocate for continued and improved funding to national TB health budgets by both government and international organizations like the Global Fund, USAID, and WHO. Integrate TB testing into national health insurance schemes.
Advocacy and Policy Support	The NTLP shall continuously engage implementing partners to develop and implement policies supporting routine TB stool testing in children. Strengthen the existing stakeholders (healthcare providers, researchers, NGOs, patient advocacy groups, CSOs) coalition to advocate for funding to support the TB program.

Technological Innovation	Staying informed about new technologies (e.g., TrueNat) that improve TB stool testing efficiency and accessibility, and strengthen the utilization of mobile health (mHealth) solutions for appointment reminders and follow-ups of patients under-care
Data collection	A variable of use of stool samples has been included in the primary data collection tools and will be regularly monitored

8. CONCLUSION

The National and Leprosy TB program with support from its partners has successfully introduced and implemented the SOS technique across all 15 health regions in Uganda. However, further scale-up and integration of the SOS technique within the routine diagnostic program of TB among children across all the DTUs country-wide is still required. This will ensure optimization of the impact of SOS towards achieving both the pediatric national strategic plan targets as well as the END TB strategy target of ending TB in children and adolescents by 2030. Therefore, this calls for a consolidated effort from all key stakeholders to sustain and expand on the early implementation milestones that have been achieved in the roll-out of pediatric TB diagnosis using stool in Uganda.

This report was drafted and finalized by the Uganda NTLP and NTRL

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