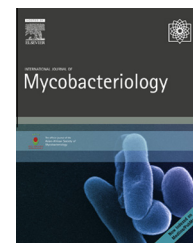


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## Does intensified case finding increase tuberculosis case notification among children in resource-poor settings? A report from Nigeria



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### ARTICLE INFO

#### Article history:

Received 12 October 2015

Accepted 31 October 2015

Available online 20 November 2015

#### Keywords:

Childhood tuberculosis

Intensified case finding

Nigeria tuberculosis

### ABSTRACT

**Objective/Background:** Tuberculosis (TB) is a major cause of morbidity and mortality in developing countries. Passive case detection in national TB programmes is associated with low case notification, especially in children. This study was undertaken to improve detection of childhood TB in resource-poor settings through intensified case-finding strategies. **Methods:** A community-based intervention was carried out in six states in Nigeria. The creation of TB awareness was undertaken, and work aids, guidelines, and diagnostic charts were produced, distributed, and used. Various cadres of health workers and ad hoc project staff were trained. Child contacts with TB patients were screened in their homes, and children presenting at various hospital units were screened for TB. Baseline and intervention data were collected for evaluation populations and control populations.

**Results:** Detection of childhood TB increased in the evaluation population during the intervention, with a mean quarterly increase of 4.0% [new smear positive (NSP), although the increasing trend was not statistically significant ( $\chi^2 = 1.8$ ;  $p < .179$ )]. Additionally, there was a mean quarterly increase of 3% for all forms of TB, although the trend was not statistically significant ( $\chi^2 = 1.48$ ;  $p < .224$ ). Conversely, there was a decrease in case notification in the control population, with a mean decline of 3% (all forms). Compared to the baseline, there was an increase of 31% (all forms) and 22% (NSP) in the evaluation population.

**Conclusion:** Intensified case finding combined with capacity building, provision of work aids/guidelines, and TB health education can improve childhood-TB notification.

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Peer review under responsibility of Asian African Society for Mycobacteriology.

<http://dx.doi.org/10.1016/j.ijmyco.2015.10.007>

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## Introduction

Tuberculosis is arguably one of the major deadly diseases affecting children in developing countries, causing the death of approximately >80,000 children annually, and with over 500,000 new cases each year, reflecting ongoing transmission within communities [1–4]. Although TB causes large morbidity and mortality rates among children in developing countries, it continues to suffer neglect from programme planners [1,2,5,6]. It is estimated that children younger than 15 years constitute ~6–11% of all forms of TB cases [2], with this percentage even higher in developing countries with high TB burden and reaching as high as 40% of all new TB cases [7,8].

Children are more susceptible to developing active TB compared with adults, and acquire the infection mostly from adults within their household, including their parents [5,9]. This intra-household transmission appears to be aggravated by the parents/caregivers suffering from TB, and is worse in instances where the household member also lives with human immunodeficiency virus (HIV) [10,11]. This is perturbing in the Nigerian context, where the national TB/HIV coinfection rate is 23% [12].

There is a growing body of evidence that suggests that childhood tuberculosis is underdiagnosed in many countries with high TB burden [2,6,7,13,14]. In Nigeria, where children account for more than 40% of the population and it is estimated that childhood TB may be over 10% of all cases, only 5.8% of the notified cases in 2013 were in children [14]. The situation prior to this was not much better. Specifically, from 2008 to 2010, childhood TB constituted only ~2% of annual smear-positive TB cases found in the country. At a regional level, a retrospective review of 12-year data from 14 states in southern Nigeria showed that the percentage of children among notified cases ranged from 1% to 5% [6]. A recent review of childhood TB in Lagos State in southern Nigeria showed an increasing trend in notification of childhood TB, from 5.9% in 2011 to 7.6% in 2014 [15]. This, however, still falls short of the World Health Organization (WHO) estimate for the country.

Studies containing disaggregated data on childhood TB are scarce, however, emerging evidence from Lagos State, Nigeria, shows a slight preponderance of infected females (54%) as compared to males (46%) [15]. These results are a reversal of the global pattern of the female:male ratio of TB notified cases, which is usually about 1–1.5:2.1 [16]. The Lagos study also found that new smear-positive (NSP) cases notified between 2011 and 2014 ranged from 16.3% to 20%, new smear-negative (NSN) cases notified during the same period ranged from 68.2% to 74.6%, and that extrapulmonary TB (EPTB) notification during this period ranged from 6.7% to 10.6% [15].

Factors that contribute to low case detection among children include inability of children to produce sputum. Even when sputum is produced by a child, cheap diagnostic tests, such as smear microscopy, can only accurately detect ~30% of the cases [7,14,17]. Other factors include low capability among healthcare staff to diagnose childhood TB, reliance on smear microscopy as the primary method of TB detection, ineffective family-centred contact tracing, paucity of printed

workers aid/guidelines, dearth of adequate training on childhood TB screening and diagnosis [13,18], and lack of data-capturing tools [15].

Little is known about the effectiveness of implementing intensified TB case finding (ICF) among children living in high-burden, resource-poor settings, despite the fact that ICF seems to be promoted as the solution to the low-case findings associated with passive case finding. This intervention, therefore, sought to determine the effectiveness of intensified TB case-finding strategies in southern Nigeria. This study also sought to assess the characteristics of childhood TB cases detected through ICF intervention.

## Materials and methods

### Intervention design

A prospective, community-based intervention was carried out in six states in southern Nigeria from 1st July 2013 to 30th June 2014.

### Intervention setting

The states in southern Nigeria were stratified according to three geopolitical zones, namely south–south, southeast, and southwest zones. The states included Akwa Ibom and Rivers (south–south), Enugu and Ebonyi (southeast), and Ogun and Lagos (southwest). Two states were randomly selected from each of the zones. To select the “control” states, the states were stratified into the same three geopolitical zones, and then two states were selected from each zone. As a community-based intervention, control states were selected to match the intervention states in most respects, except for the intervention. The control states were Cross River and Edo (south–south), Anambra and Imo (southeast), and Ondo and Ekiti (southwest). In each intervention state, all tertiary and secondary healthcare facilities were selected.

### Target population

The target population consisted of children younger than 15 years in the intervention states. These included 2,133,036 children, 1,155,418 children, 2,020,671 children, 4,866,546 children, 1,745,071 children, and 2,821,443 children for Akwa Ibom, Ebonyi, Ogun, Lagos, Enugu, and Rivers, respectively, giving a total of 14,742,185 children. This accounted for 47.6% of the total population within the intervention areas. To obtain baseline data that included complete cohort reports of all children treated for TB in the intervention and control states at the time the research protocol was developed in 2012 (Table 1), the data for 2011 were used as the baseline. For comparison, the proportions of children younger than 15 years in the six control states were computed (Table 2).

All children (<15 years old) who presented with signs and symptoms of TB at the participating health facilities were eligible for inclusion in the study. All children (<15 years old) living with a confirmed smear-positive TB patient (whether HIV positive or negative) at the time of treatment were also included in the study.

**Table 1 – TB cases (all forms) in children (<15 years) as a proportion of total cases notified in six intervention states in 2011.**

State	Total population	Total population of (<15 years)	Total TB cases (all forms)	Total TB in children (all forms)	TB in children (%)
Akwa Ibom	4,481,168	2,133,036	2723	140	5.1
Ebonyi	2,427,349	1,155,418	1619	51	3.2
Ogun	4,245,107	2,020,670	2521	123	4.9
Lagos	10,223,836	4,866,546	8653	518	6
Enugu	3,666,118	1,745,071	1672	76	4.5
Rivers	5,927,443	2,821,443	2313	159	6.9
Total	30,971,021	14,742,185	19,501	1067	5.4

Note: TB = tuberculosis.

**Table 2 – TB cases (all forms) in children (<15 years) as a proportion of total cases notified in six control states, 2011.**

State	Total population	Total population (<15 years)	Total TB cases (all forms)	Total TB in children (all forms)	TB in children (%)
Ondo	3,872,903	1,808,646	1575	70	4.4
Anambra	4,670,462	2,181,106	1544	133	8.6
Edo	3,580,244	1,671,974	1887	61	3.2
Ekiti	2,693,888	1,258,046	680	26	3.8
Imo	4,463,262	2,084,343	1401	53	3.7
Cross River	3,238,948	1,512,588	2079	140	6.7
Total	22,519,707	10,516,703	9166	483	5.3

Note: TB = tuberculosis.

### Healthcare facilities

Each of the intervention states had an array of healthcare facilities, including publicly-owned healthcare facilities, faith-based non-profit-oriented healthcare facilities, and for-profit private healthcare facilities. These facilities fall into primary, secondary, and tertiary levels. The study was designed to take place in both healthcare facilities and in the homes of registered smear-positive TB patients who were receiving treatment and had children residing in same households.

Five healthcare facilities were purposely selected to include facilities that attend to the highest number of children in each state. Thus, a total of 30 healthcare facilities were selected. Within each facility, the intervention was undertaken in every unit where children were attended to, including the children outpatient clinic, children emergency room (CHER), general outpatient department (GOPD), anti-retroviral (ART) clinic, and the TB directly observed treatment, short-course (DOTS) clinic.

### Intervention strategies

The intervention was divided into two main phases: the preparatory phase and the ICF and treatment phase. During the preparatory phase, advocacy meetings were held with key stakeholders, including the National Coordinator of the National Tuberculosis and Leprosy Control Programme (NTBLCP), the State TB and Leprosy Control Officers of the selected states, heads of healthcare facilities/paediatricians in the selected hospitals, and heads of state school health

boards. To increase awareness of childhood TB among community members and healthcare workers, 6000 handbills were produced and distributed to parents of children accessing care in hospitals, school children, and community members. A total of 1500 posters were also produced and distributed in the communities, healthcare facilities, schools, and markets. Over 20 visits were carried out to primary schools in order to provide health education concerning TB. One thousand copies of flip charts (work aids) were produced and distributed to the healthcare workers. Other work aids produced and distributed were 600 copies of flowcharts and 6000 copies of growth-monitoring charts. Additionally, 5000 units of purified protein derivative for tuberculin skin testing (TST) were procured and distributed.

Training was done to improve the knowledge and skills of healthcare workers in identifying presumptive childhood TB cases, appropriately diagnosing and treating confirmed cases. Key healthcare workers who were trained included 120 medical officers/paediatricians and 150 nurses other general health workers (GHWs). The training also included how to use various tools, including WHO score charts, flip charts, flowcharts, and growth-monitoring charts. To complement the job of the healthcare workers in the intervention, 38 ad hoc workers were recruited, trained, and posted to the selected healthcare facilities. Their training included how to use the screening form to verbally assess if a child had any of the symptoms and signs of TB. Given the ubiquitous presence of patent medicine vendors (PMVs) and the anecdotal evidence indicating that they are usually the first point where community members seek care, they were also integrated into this intervention. Thus, 90 PMVs were trained to identify

presumptive child TB cases and instructed in the appropriate use of tools given to them.

In the ICF phase, three ICF strategies were used: ICF at outpatient clinics, ICF through contact tracing, and ICF at ART clinics. Nurses/GHWs and ad hoc workers used the screening forms to identify presumptive TB cases. The screening form contained seven features (symptoms and signs) of childhood TB, including, fever for  $\geq 2$  weeks, weight loss/failure to thrive, cough of  $\geq 2$  weeks, night sweats, swelling of the lymph nodes, abdominal/bone/joint swelling, and swelling of the back/angular deformity. The presence of any feature carried a score of 1. A score of  $\geq 1$  suggested that a child was a presumptive TB case and therefore required further assessment by a nurse or medical officer/paediatrician. In the TB DOTS clinics, GHWs and TB supervisors provided health education to registered cases with co-resident child (ren) younger than 15 years. Those who gave consent were visited at home, where screening forms were used to assess for symptoms and signs of TB. Again, a score of  $\geq 1$  identified a child as a presumptive TB case needing diagnostic attention.

In summary, three key ICF strategies were used: ICF at outpatient clinics (screening of children at various outpatient clinics), ICF through contact tracing (screening of children coresident with known TB cases in their homes), and ICF at ART clinics (screening of children living with HIV at ART clinics).

Identified presumptive cases capable of producing sputum samples were guided on sputum production. However, with the permission of the NTBLCP, only two samples produced at least 1-h apart were used. The samples were processed using Ziehl–Neelsen smear/alcohol-fast bacilli microscopy.

Diagnosis of TB in children who could not produce sputum or who presented with features of EPTB was challenging. To help overcome this challenge, clinicians used the Keith Edwards child TB score chart (adopted by WHO in 1996). The score chart is a diagnostic tool that takes into consideration a combination of clinical and investigative characteristics in order to arrive at a diagnosis by assigning numerical scores to the absence or presence and degree of severity of clinical characteristics. These characteristics include duration of illness, nutritional status of the child, family history of TB, TST, unexplained fever and night sweats, lymphadenopathy, joint/bone swelling, abdominal mass or ascites, central nervous systems affection, and angle deformity of the spine. Children who scored  $\geq 7$  were further evaluated by a paediatrician or experienced medical officer trained in TB diagnosis. All investigations, including smear microscopy, X-rays, and TST, were provided at no cost to the children. Apart from children who were screened for TB at the ART clinics, since their HIV status was already known, other presumptive TB cases were offered HIV counselling and testing, alongside their parents/caregivers.

#### *Tuberculosis treatment*

Children who were confirmed as having TB were initiated on a full course of anti-TB drugs under full observation of their treatment. They were monitored and followed up in line with NTBLCP guidelines. Children who tested HIV positive were

referred to the ART clinic for HIV care, treatment, and support.

#### *Data collection*

Tools were developed for the monthly collection of data at the facility and local government levels. Each unit in the intervention hospitals was also provided with standardised registers, which were filled with data from the screening forms. Ad hoc staff and nurses/GHWs also retrieved relevant data from the hospital case folders and updated the screening forms and registers at their units. On a monthly basis, they collated their data and completed the monthly reporting forms. These were validated by the local government TB and Leprosy supervisors, who then sent the reports to the State TB and Leprosy Control Programme (STBLCP) office, where the STBLCP Monitoring and Evaluation (M&E) team carried out further data validation.

#### *Statistical analysis*

Data were double-entered into the database and cross-checked by two independent M&E officers. Data analysis was done using Epi-Info version 3.4.1 (Centres for Diseases Control and Prevention, Atlanta, GA, USA).

Descriptive statistics were used to compute the sociodemographic and clinical characteristics of the detected cases, as well as targets, indicators, and yields of each of the key case-finding strategies. Further analyses were done using the chi-square test to compare proportions. A trend analysis was undertaken to demonstrate the pattern of changes in case detection in the 3 years before and during the intervention in both the intervention (evaluation population) and control states (control population).

#### *Ethical approval*

The study complies with international guidelines for research and was approved by the Ethics and Research Advisory Committee of the State Tuberculosis Control Programme, Ministry of Health, Ebonyi State, Nigeria. The intervention was also approved by the Central Unit of the National Tuberculosis Control Programme, Federal Ministry of Health, Abuja, Nigeria. Approval was also obtained from the management of each of the healthcare facilities where the intervention was implemented. Every participant gave an informed consent, with the parents/care-givers represented the children. Every activity conformed to the international ethics of clinical management of TB in children. Anonymous data were collected without personal identifiers.

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## **Results**

### *Sociodemographic and clinical characteristics of detected childhood TB cases*

A total of 1590 childhood TB cases (all forms) were detected during intervention, with 830 of the cases female and 760 male. Age differentiation showed that children in the age

range of 0–4 years constituted 39.2% (623 cases), while those between 5 years and 14 years accounted for 60.8% (967 cases). Approximately 86% (1373 cases) were NSP/bacteriologically confirmed cases. Most of the cases (97.2%) were new cases (Table 3).

### Case-finding strategies and their outputs

In the ICF among children attending outpatient clinics in healthcare facilities, the target population comprised children brought to the GOPD, CHER, and other outpatient clinics. As shown in Table 4, 36,214 children were screened, with 9257 children identified as presumptive TB cases, yielding 648 TB cases (all forms). The percentage of confirmed cases among the number screened was 1.8% for all forms and 0.3% for NSP cases. The percentage of confirmed cases among the number tested was 19.1% (all forms) and 6.9% (NSP).

Through tracing of child contacts of smear-positive patients on treatment in TB DOTS clinics, 1303 children were screened. Among the screened children, 318 children had TB symptoms. Twenty-five cases were confirmed (all forms), with none being NSP. The percentage of confirmed cases among the number screened was 1.9% (all forms), with 0% NSP, while the percentage of confirmed cases among the number tested was 11.5% (all forms), with 0% NSP (Table 4).

In the ICF among children living with HIV (CLHIV) attending ART clinics, 2686 children were screened, with 561 identified as presumptive TB cases. Out of 159 suspects examined through smear microscopy, 45 were confirmed as smear positive. The percentage of confirmed cases among the number screened was 5.0% (all forms), with 1.7% NSP (Table 4).

Comparing the cases detected during the 12 months of intervention to the baseline (the 12 months immediately before the intervention), 1590 TB cases (all forms) and 307 cases (NSP) were found, as compared to the historical baseline of 1210 (all forms) and 252 NSP cases. Thus, the unadjusted additional cases (additionality) recorded during the period were 380 (all forms) and 55 (NSP). The percentage change from historical baseline was 31% for all forms and 22% for NSP/bacteriologically confirmed TB cases.

“Additionality” was used as a measure of the effectiveness of the intervention in detecting cases that would have been missed had the intervention not occurred.

The results of trend analysis showed that although smear-positive case notification per quarter varied during the period of the study, the number of cases increased from 75 in Q3 2013 to 86 in Q2 2014, with a mean quarterly increase of 4.0% (Fig. 1). The upward trend remained consistent after the first quarter of project implementation, although the increasing trend was not statistically significant ( $\chi^2 = 1.8$ ;  $p < .179$ ).

Similarly, for all forms, the number detected initially varied by quarter, with a mean quarterly increase of 3.0% during the period. The number of all forms of TB cases notified increased from 366 in Q3 2013 to 461 in Q2 2014, though the increasing trend was not statistically significant ( $\chi^2 = 1.48$ ;  $p < .224$ ). Conversely, in the control population, TB notification decreased during this period, with a mean quarterly decline of 3% percent for all forms of TB (Fig. 2).

## Discussion

The findings of this study suggested that ICF for TB could be useful in improving case finding in resource-poor settings, such as Nigeria, where advanced techniques for detection of TB in children may not be easily available. The findings also highlighted preliminary measures that should be taken before commencement of an ICF for TB among children, especially given that awareness, knowledge, and skills in TB detection in children are usually low among healthcare workers in settings like Nigeria. These findings are similar to a report from Bangladesh, which suggested that measures to improve awareness, knowledge, and skills in the diagnosis of childhood TB need to be put into place before such interventions [13]. The findings also present a challenge to national TB programmes and healthcare facilities, because the use of only healthcare workers to routinely screen children for TB could prove difficult.

The detection of TB in more females as compared to males in this study, though similar to the Bangladesh study [18], as well as the report from Lagos State [15], was different from the usually reported gender patterns associated with case notification. The reported global epidemiological gender ratio is usually ~1–1.5:2.1 [16]. Here, children 0–4-years old accounted for 39.2% (623 cases) of TB cases (all forms), similar to the 39.7% obtained in a retrospective review of case notification from 2011 to 2014 in Lagos State [15]. Children aged 5–14 years accounted for 60.8% (967 cases) among all forms of TB, also similar to the results from the Lagos State study (60.3%) [15]. In our study, only 217 of 1590 cases (13.6%) were EPTB, similar to the 9.2% reported in the Lagos State study [15], but slightly more than twice the proportion (6.3%) found in Bangladesh [18].

Findings from trend analysis indicated that while case findings increased in the evaluation population during the intervention period, there was no commensurate increase in cases detected in the control population. There was a mean quarterly increase of 4.0% over the implementation period, starting with 75 in Q3 2013 and increasing up to 86 in Q2 2014. By contrast, case detection decreased in the control

**Table 3 – Demographic and clinical characteristics of detected childhood TB cases (n = 1590).**

Category	n (%)
Gender	
Female	830 (52.2)
Male	760 (47.8)
Age (years)	
0–4	623 (39.2)
5–14	967 (60.8)
TB type	
Pulmonary	1373 (86.4)
Extrapulmonary	217 (13.6)
Case registration	
New cases	1546 (97.2)
Retreatment cases	44 (2.8)

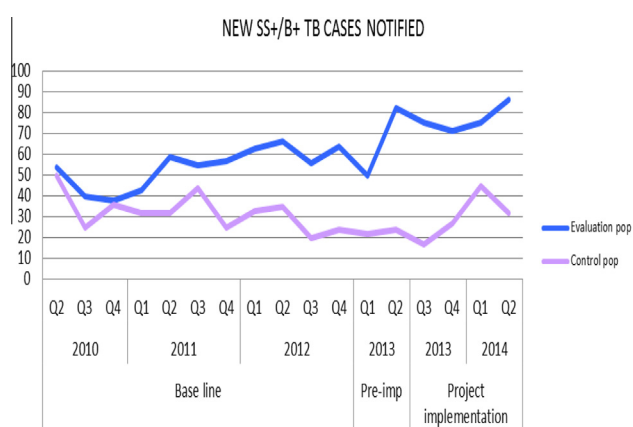
Note: TB = tuberculosis.



**Table 4 – Clinical characteristics of childhood TB cases detected through the three key intensified case finding strategies.**

Clinical characteristics	Key case-finding strategy			
	ICF at outpatient clinics	ICF through contact tracing	ICF at ART clinics	Total
No. of children screened	36,214	1303	2686	40,203
Presumptive TB cases identified	9257	318	561	10,136
No. examined with smear microscopy	1310	38	159	1507
No. confirmed new smear/ bacteriological positive (NSP)	91	0	45	136
All forms of TB cases confirmed	648	25	133	806
All forms as % of numbers screened	1.8	1.9	5	2
NSP as % of numbers screened	0.3	0	1.7	0.34
All forms as % of presumptive cases	7	7.9	23.7	7.96
NSP as % of presumptive cases	1	0	8	1.34

Note: TB = Tuberculosis; ICF = Intensified case finding; ART = Anti-retroviral treatment; NSP = New smear positive.

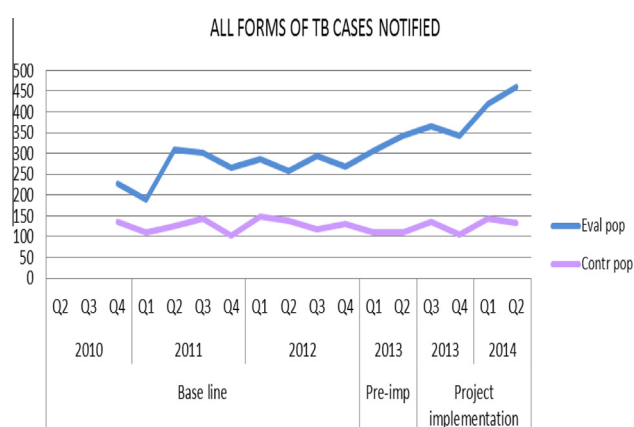


**Fig. 1 – Trend of new SS+/B+ TB cases notified in evaluation and control populations from 2010 to 2014. Baseline data consisted of TB cases notified in 2011. Note: Control pop = control population; Evaluation pop = evaluation population; NSP = new smear positive; Pre-imp = pre-implementation period, referring to the two quarters immediately before intervention; SS+/B+ TB = sputum smear-positive/bacteriological-positive tuberculosis, which was used synonymously with NSP in this study; TB = tuberculosis.**

population, except for transient increases in Q4 2013 and Q1 2014 after which it dipped again. The Bangladesh study also reported similar findings for its intervention (evaluation) population, but, unlike our study, case notification also increased in their control population [13,18].

A similar trend was observed for detection of all TB cases, with a mean quarterly increase of 3.0% in the evaluation population during the intervention. There was an increase from 366 in Q3 2013 to 461 in Q2 2014. By contrast, in the control population, TB case detection decreased during the period, with a mean quarterly decline of 3% for all forms of TB.

While the three case-finding strategies were associated with increases in case finding, larger numbers of children were screened using two strategies, namely ICF among children attending outpatient clinics and ICF among CLHIV attending ART clinics. In these two strategies, ad hoc staff



**Fig. 2 – Trend of all forms of TB cases notified in evaluation and control populations. Baseline data consisted of TB cases notified in 2011. Note: Contr pop = control population; Eval pop = evaluation population; Pre-imp = pre-implementation period, referring to the two quarters immediately before intervention; TB = tuberculosis.**

were recruited to complement full-time employees of the healthcare facilities because the full-time healthcare staff were finding it challenging to combine their routine clinical duties with the screening of children for TB. While in some settings using healthcare staff only to carry out screening may be effective, our findings indicated that this proved challenging in the Nigerian context. One plausible explanation might be the weak health system, characterised by an ageing workforce that is continually diminished through retirement, resignations, and death, with no commensurate recruitment of staff. Thus, healthcare staff often find themselves overburdened with duties. In ICF through contact tracing, screening was done by local government tuberculosis supervisor and TB DOT clinic staff.

However, in terms of yields as a proportion of numbers screened, ICF among CLHIV attending ART clinics seemed to be most effective. This was likely due to immunosuppression among such children and their increased susceptibility to TB.

The strength of this intervention was that it piloted the detection of TB in children using intensified TB case-finding

strategies in an under-resourced setting with a weak health system and a high burden of TB. Furthermore, it improved the capacity of the health facilities for TB care, and data quality was ensured, as the data collected were validated in order to avoid errors and ensure consistency.

The intervention had some inherent limitations. First, it was designed to include performance of nasogastric/nasopharyngeal intubation for collection of specimens. This was, however, not done due to various reasons, including the negative attitude of health workers toward the procedure. Second, it was not possible to carry out GeneXpert MTB Rif tests due to constraints with the transport of specimens.

In conclusion, the project was successful in increasing notification of childhood TB cases during the intervention period as compared with the baseline in the evaluation population, while TB case notification actually decreased during the same period in the control population.

### Conflicts of interest

The authors declare no conflicts of interest.

### Acknowledgements

We acknowledge all the all health workers, programme, and ad hoc project staff who participated in the meticulous data collection and reporting for their support and contributions. This intervention was funded as a TBREACH Wave 3 project through the StopTB Partnership by the Canadian International Development Agency (CIDA).

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