

Decentralisation and integration of paediatric tuberculosis services to primary healthcare facilities as an approach to optimise management in Cameroon and Kenya: a descriptive cohort study

Rose Masaba ¹, Nicole Herrera,² Boris Tchounga ³, Stephen Siamba,¹ Millicent Ouma,¹ Gordon Okomo,⁴ Patrice Tchendjou,³ John Ditekemena,⁵ Anne-Cecile Zoung-Kanyi Bissek,⁶ Martina Casenghi,⁷ Rhoderick Machezano,² Appolinaire Tiam,^{2,8} Lise Denoeud-Ndam ⁷

To cite: Masaba R, Herrera N, Tchounga B, *et al.* Decentralisation and integration of paediatric tuberculosis services to primary healthcare facilities as an approach to optimise management in Cameroon and Kenya: a descriptive cohort study. *BMJ Public Health* 2024;**2**:e001005. doi:10.1136/bmjph-2024-001005

► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/bmjph-2024-001005>).

Received 1 February 2024
Accepted 9 July 2024



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Dr Rose Masaba;
rmasaba@pedaids.org

ABSTRACT

Introduction Tuberculosis (TB) remains a major cause of morbidity and mortality for children less than 5 years. Diagnosis and treatment of children with active TB is often centralised in district hospital settings due to poor public health infrastructure and lack of diagnostic capabilities in primary healthcare (PHC) facilities. This analysis aims to evaluate TB case detection and treatment outcomes by comparing district hospitals and PHC facilities.

Methods To increase paediatric TB case detection, an intervention was designed to decentralise and integrate paediatric TB diagnosis and management into PHC facilities. Between May 2019 and March 2021, we screened and enrolled children under age 5 years with presumptive TB at different entry points in 32 study facilities in Kenya and Cameroon. TB services were described by level of care. Fischer's exact test was used to determine significance when comparing categorical variables and a Wilcoxon-Mann-Whitney test was used to test for significance of continuous variables.

Results A total of 610 children were enrolled; 481 (79%) had received services at the district hospitals and 129 (21%) at the PHC facilities. The median age was 15.4 (IQR: 6.1–36.0) months; 59% were children below age 2 years, 53% were male and 5% were HIV coinfecting. A total of 74 (12%) children were diagnosed with TB, 19 (15%) in PHC and 55 (11%) in district facilities, 11 (15%) with a bacteriological confirmation. The time from TB symptom onset to TB diagnosis was significantly shorter in the PHC (1.0 month (IQR: 0.1–2.1)) than district hospitals, (1.8 months (0.8–4.4), $p=0.043$). The proportion of lost to follow-up was higher in district hospitals (15.8%) than in PHC (1.8%, $p=0.05$). Mortality (overall 1.4%) did not significantly differ by setting.

Discussion Decentralisation of TB screening and diagnosis at the PHC level was feasible and significantly shortened the time from the onset of symptoms to TB diagnosis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Tuberculosis (TB) is a major cause of morbidity and mortality in children in low-income and middle-income countries.
- ⇒ Children usually access primary healthcare (PHC) or child health services in facilities where the capacity to diagnose TB in children is often limited.

WHAT THIS STUDY ADDS

- ⇒ Our study demonstrates that decentralised paediatric case identification and other TB services to PHC facilities, following healthcare worker training to diagnose and treat TB, is feasible and significantly shortened the time from the onset of symptoms to TB diagnosis.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Our findings emphasise the need to decentralise paediatric TB services and include them as part of the PHC package to reduce delays in TB diagnosis.
- ⇒ Better tracking and documentation of patients, specimens and X-ray referrals will be key factors to successfully decentralise TB services.

Trial registration number [NCT03862261](https://clinicaltrials.gov/ct2/show/study/NCT03862261).

INTRODUCTION

Globally, in 2022, an estimated 10.6 million people were diagnosed with tuberculosis (TB). Africa, with only 14.7% of the global population, had 23% of the estimated number of individuals diagnosed with TB 12% of whom were children aged 0–14 years.¹ Children

aged 0–14 years accounted for 14% of the estimated 1.3 million deaths globally, making TB one of the leading causes of death in children. However, 55% of estimated TB cases among children are not reported to national TB programmes.¹ Although national TB programmes in the African region recognise children as a priority population, diagnosis and management of paediatric TB remains a significant challenge.² The high burden of TB in children and their poor outcomes are largely because of the difficulties in confirming TB diagnosis in children, arising from the non-specific nature of symptoms and signs of TB in children which overlap those of other common childhood diseases; the paucibacillary nature of childhood TB; the challenge of obtaining good-quality sputum samples, especially in young children; and difficulties in accessing health service.³ Additionally, children usually access primary healthcare (PHC) or child health services in facilities where the capacity to diagnose TB in children is often limited.⁴

In many sub-Saharan African countries, diagnosis and treatment of children with active TB are centralised at a high level of care and provided in separate TB clinics. This is mainly due to the poor public health infrastructure and lack of diagnostic capabilities in PHC facilities.^{5–7} This adds to the list of barriers to identification of cases and scale-up of treatment for children with TB disease. Paediatric services such as maternal, neonatal and child health (MNCH) services, outpatient clinics for children, paediatric antiretroviral therapy services and nutrition services may represent a first entry point for diagnosis of children with TB disease in many countries.⁸ Diagnosing TB in children requires access to specific diagnostic services such as radiography, sample collection procedures such as gastric aspiration, nasopharyngeal aspiration, induced sputum and experience in diagnosis of TB based on clinical signs and symptoms. However, such services are often concentrated in referral-level hospitals or specialised facilities. By contrast, children generally access the health system through outpatient or MCH clinics at primary care facilities or private general practitioners.⁹ To avoid missed or delayed opportunities for TB care, it is necessary to decentralise child-appropriate TB services by making these services available at the points of the health system where care is first sought. The Decentralise Tuberculosis services and Engage Communities to Transform lives of Children with Tuberculosis (DETECT Child TB) study in Uganda on decentralisation of child TB services showed that strengthening paediatric TB services at peripheral health facilities was associated with increased case finding, improved treatment outcomes and the successful implementation of contact screening and case management.¹⁰ Other studies have also shown that community outpatient-based treatment is associated with improved treatment outcomes, faster time to treatment initiation^{11 12} and reduced pretreatment lost to follow-up (LTFU).¹³ We aimed to evaluate and compare TB services and patient outcomes in children under age 5 years at different levels of healthcare following the

implementation of the Integrating Pediatric TB services into child healthcare services in Africa (INPUT) study.

MATERIALS AND METHODS

Study design and setting

This paper is a secondary analysis of data collected during the INPUT Study,¹⁴ a multicountry stepped-wedge cluster randomised trial which compared the standard of care where paediatric TB case detection and management were mainly conducted at district hospitals versus the intervention, where decentralised paediatric TB services were integrated into key child healthcare services. The study was conducted in 12 district-level hospitals (hubs) and their referral PHC facilities (spokes) for a total of 32 facilities in both Cameroon and Kenya. Hubs are higher-level facilities where samples or patients are referred for specialised management while spokes are PHC facilities that refer samples and patients to the hubs. Before the intervention, TB diagnostic procedures for children were mainly conducted at the hubs (district hospitals) by designated healthcare workers (HCWs) in both countries. The two countries purposively selected had the highest TB burden in their respective regions in sub-Saharan Africa. Facilities, which were purposively selected based on their TB case load, they all started under standard of care case management and were randomised to start the intervention at different time points.

Study population

The study population consisted of children aged less than 5 years of age who presented for care in the selected study district hospitals and their referral PHC facilities with signs and symptoms presumptive of TB. For this analysis, we considered children screened for TB, diagnosed with TB and followed up on TB treatment during the intervention period. Children enrolled on the study were followed up monthly while on treatment and after 2 months following completion of treatment for a maximum period of 14 months.

Data collection

Trained study nurses, who were deployed to each study cluster, collected data during screening, consenting, enrolment and follow-up of study participants. Children were prospectively enrolled and followed up from May 2019 to March 2021. Study nurses collected and entered data directly into a tablet using an electronic case report form on a CliniOps platform. Data collected included aggregate data from all entry points in the study facilities, data on children with presumptive diagnosis of TB, confirmation of TB diagnosis, treatment initiation and completion. Specifically, we collected site characteristics, sociodemographic characteristics such as place of residence, caregiver education, time it takes to get to facility, age, sex; and clinical characteristics such as HIV exposure status, HIV status, TB diagnostic procedures such as specimen collection and subsequent investigation (GeneXpert, sputum microscopy) and chest X-ray. Children with

presumptive TB at screening were treated with antibiotics and later reassessed for the persistence of signs and symptoms of TB before further diagnostic procedures. Reassessed children are those who came back to the facility for this reassessment. Those who were not reassessed are those who did not come back.

For this analysis, we only extracted from the main study database, data related to the intervention period, disaggregated by type of facility level: district hospitals and PHC facilities. Decentralised care for purposes of this manuscript is defined as care that is provided in non-specialised PHC facilities closer to where a patient lives, often by nurses or clinical officers.

Statistical analysis

Baseline categorical demographic and other characteristics of the population were described as frequency tables while continuous variables were summarised as medians and IQR. When comparing categorical variables, Fischer's exact test was used to determine significance while a Wilcoxon-Mann-Whitney test was used to test for significance of continuous variables. Data analysis was conducted by using SAS software V.9.4 (SAS Institute).

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination of our research.

RESULTS

During the intervention period, 109 614 children under age 5 years visited the 12 study clusters for services, 69 592 (63.5%) in the district hospitals and 40 022 (36.5%) in the PHC facilities. A total of 1150 (1.0%) screened positive for TB signs and symptoms, 836 (72.6%) in district hospitals and 314 (27.3%) in PHC facilities. Following symptom screening, some of the children received a course of antibiotics and other diseases were ruled out before assessing eligibility based on persistence of TB presumption. Of those who initially screened positive for TB signs and symptoms, 715 (62.2%) were reassessed for study eligibility; 610 (85.3%) were eligible for the study and enrolled (figure 1).

Table 1 summarises the baseline characteristics of children enrolled in the study and investigated for TB according to level of care. Of the 610 children enrolled, 481 (79%) received services at district hospitals and 129 (21%) at PHC facilities. A higher proportion of the children were from Cameroon compared with Kenya, 469 (76.9%) and 141 (23.1%), respectively. The median age was 15.4 (IQR: 6.1–36.0) months. Children in the district hospitals were older than those in PHC facilities (median age of 19.6 months (IQR: 10.3–35.1) in the district hospitals vs 15.7 months (IQR: 8.2–28.9) in the PHC facilities). A total of 273 (56.8%) and 87 (67.4%) of the children were under 2 years

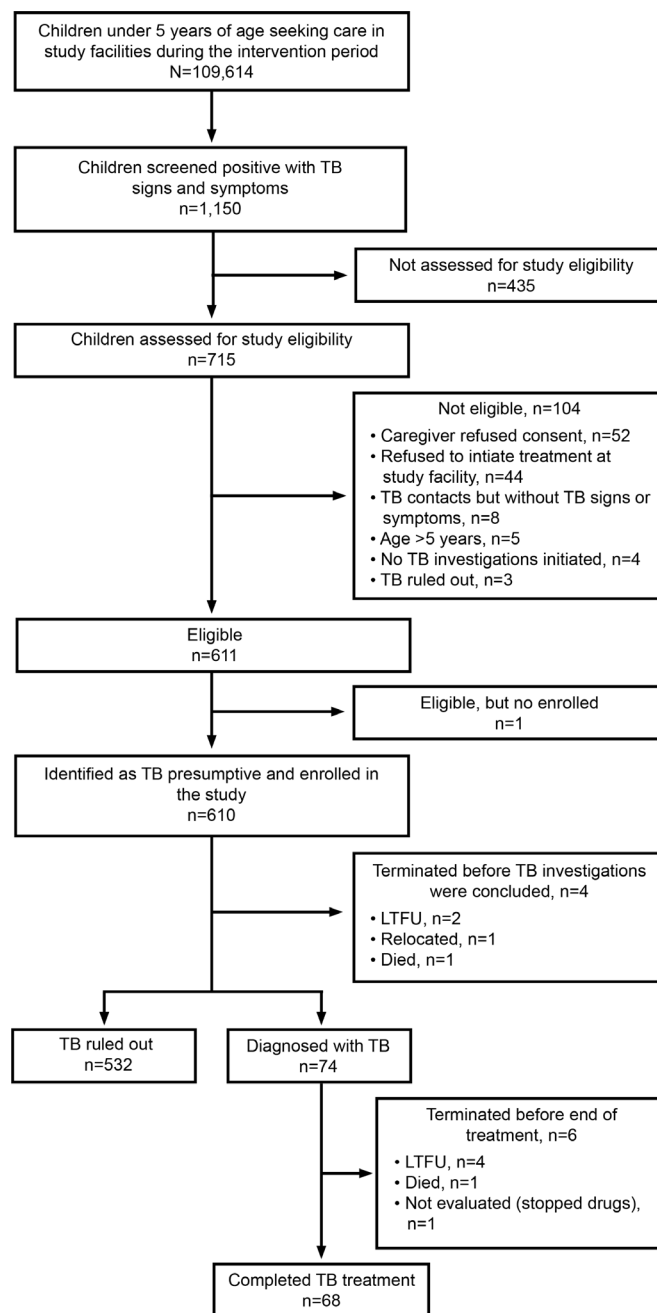


Figure 1 Study flow chart that shows the cascade of care of children under 5 years seeking care in study facilities during the intervention period. LTFU, loss to follow-up; TB, tuberculosis.

of age in district hospitals and PHC facilities respectively, $p=0.03$. Males accounted for 254/481 (52.8%) and 75/129 (58.1%) in the district hospitals and PHC, respectively. In district hospitals, children were more likely to be seen at the outpatient department (OPD) (49.1%), inpatient department (IPD) (17.3%), chest clinic (15.6%) and MNCH (10.0%) while in PHC facilities, children were more likely to be seen at the OPD (72.1%), MNCH (15.5%), IPD (3.9%) and chest clinic (3.9%). Children seeking services in the PHC facilities were more likely to be seen in the OPD compared with district hospitals, 72.1% vs 49.1%, $p<0.0001$. However,

Table 1 Baseline characteristics of children enrolled with presumptive TB and investigated for TB according to level of care in study facilities during the intervention period

| Variable | District hospitals N=481; n (%) | PHC facilities N=129; n (%) | Overall N=610, n (%) |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|--------------------------------|-------------------------|
| Site characteristics | | | |
| Country | | | |
| Cameroon | 360 (74.8) | 109 (84.5) | 469 (76.9) |
| Kenya | 121 (25.2) | 20 (15.5) | 141 (23.1) |
| Service point | | | |
| OPD | 236 (49.1) | 93 (72.1) | 329 (53.9) |
| IPD | 83 (17.3) | 5 (3.9) | 88 (14.4) |
| Chest/TB clinic | 75 (15.6) | 5 (3.9) | 80 (13.1) |
| MCH/PMTCT | 48 (10.0) | 20 (15.5) | 68 (11.2) |
| HIV/CCC | 26 (5.4) | 4 (3.1) | 30 (4.9) |
| Emergency room | 7 (1.5) | 0 (0) | 7 (1.2) |
| Other | 5 (1.0) | 0 (0) | 5 (0.8) |
| Nutrition | 1 (0.2) | 2 (1.6) | 3 (0.5) |
| Demographic characteristics | | | |
| Gender | | | |
| Male | 254 (52.8) | 75 (58.1) | 329 (53.9) |
| Female | 227 (47.2) | 54 (41.9) | 281 (46.1) |
| Median age in months (IQR) | 19.6 (10.3–35.1) | 15.7 (8.2–28.9) | 15.4 (6.1–36.0) |
| Age under 2 years | 273 (56.8) | 87 (67.4) | 360 (59.0) |
| Place of residence | | | |
| Rural | 193 (40.1) | 56 (43.4) | 249 (40.8) |
| Urban | 288 (59.9) | 73 (57.0) | 361 (59.2) |
| Travel time to facility <1 hour (N=585) | 354 (77.5) | 99 (77.3) | 453 (77.4) |
| Caregiver's highest level of education | | | |
| Unknown/never attended/primary | 138 (28.7) | 43 (33.3) | 181 (29.7) |
| Secondary school and above | 343 (71.3) | 86 (66.7) | 429 (70.3) |
| Medical history and comorbidities | | | |
| HIV-exposed infants | 55 (11.4) | 10 (7.8) | 65 (10.7) |
| Child HIV Status | | | |
| Negative | 180 (37.4) | 40 (31.0) | 220 (36.1) |
| Unknown | 273 (56.8) | 84 (65.1) | 357 (58.5) |
| Positive | 28 (5.8) | 5 (3.9) | 33 (5.4) |
| Positive and on ART | 20 (71.4) | 4 (80.0) | 24 (72.7) |
| History of asthma or chronic lung disease | 34 (7.1) | 4 (3.1) | 38 (6.2) |
| Malnutrition | | | |
| Moderate acute malnutrition | 19 (4.0) | 6 (4.7) | 25 (4.1) |
| Severe acute malnutrition | 31 (6.4) | 5 (3.9) | 36 (5.9) |
| TB contact history | | | |
| Household contact diagnosed with TB | 83 (17.2) | 6 (4.6) | 89 (14.6) |
| Of whom, on TB treatment | 70 (84.3) | 6 (100.0) | 76 (85.4) |
| ART, antiretroviral therapy; CCC, comprehensive care clinic; IPD, inpatient department; MCH, maternal and child health; OPD, outpatient department; PHC, primary healthcare; PMTCT, prevention of mother-to-child HIV transmission; TB, tuberculosis. | | | |

a higher proportion of children were screened for TB symptoms and signs in the district hospitals in IPD and chest clinics. The proportions of children in rural versus urban sites and those spending less than an hour to get to the facility were similar between the district hospitals and PHC facilities. The majority of caregivers (70.3%) had secondary education. Based on hospital records, 5.8% of children in district hospitals and 3.9% at PHC level had a known HIV infection at enrolment. The proportion of children with moderate to severe

malnutrition was higher in the district hospital (10.4%) compared with PHC facilities (8.5%), $p=0.001$.

A larger proportion of study children were household contacts of a TB case in district hospitals (83/481, 17.2%) compared with primary-level facilities (6/129, 4.6%), $p=0.004$.

TB diagnostic procedures and outcomes

TB diagnostic procedures conducted for children during the intervention period in the district and PHC facilities

Table 2 TB investigations overall and by level of care

| | District hospitals N=481, n (%) | PHC facilities N=129, n (%) | P value | Overall N=610, n (%) |
|-------------------------------------------------------------------------|------------------------------------|--------------------------------|-------------------|-------------------------|
| Place where the specimen was collected | n=430 | n=105 | 0.014 | N=535 (87.7) |
| Site of screening | 411 (95.6) | 92 (87.6) | | 503 (94.0) |
| Site of referral | 16 (3.7) | 10 (9.5) | 0.007 | 26 (4.9) |
| Other | 3 (0.7) | 3 (2.9) | | 6 (1.1) |
| Time from specimen collection to date of results (days) n, median (IQR) | 418, 2.0 (1.0–5.0) | 103, 1.0 (0.0–4.0) | 0.133 | 521, 2.0 (1.0–5.0) |
| Place where specimen was processed (n=534) | | | | |
| Site of screening | 123 (28.7) | 6 (5.7) | | 129 (24.2) |
| Site of referral | 233 (54.3) | 89 (84.8) | <0.0001 | 322 (60.3) |
| Other | 73 (17.0) | 10 (9.5) | | 83 (15.5) |
| Specimen type (n=535) | | | | |
| Gastric aspirate | 304 (70.7) | 97 (92.4) | <0.0001 | 401 (75.0) |
| Nasopharyngeal aspirate | 97 (22.6) | 3 (2.9) | | 100 (18.7) |
| Sputum | 17 (4.0) | 2 (1.9) | | 19 (3.6) |
| Induced sputum | 8 (1.9) | – | | 8 (1.5) |
| Other | 4 (0.9) | 3 (2.9) | | 7 (1.3) |
| Xpert assay performed | 408 (84.8) | 102 (79.1) | 0.117 | 510 (83.6) |
| Xpert assay result (n=509) | | | | |
| Positive | 9 (2.2) | 2 (2.0) | 0.871 | 11 (2.2) |
| Negative | 397 (97.5) | 100 (98.0) | | 497 (97.6) |
| Indeterminate | 1 (0.3) | – | | 1 (0.2) |
| Missing | 1 | – | | 1 |
| Smear microscopy performed | 101 (21.0) | 23 (17.8) | 0.427 | 124 (20.3) |
| Smear microscopy result | | | | |
| Positive | – | – | | 0 |
| Negative | 101 (100) | 23 (100) | | 124 (100) |
| Indeterminate | – | – | | 0 |
| X-ray performed | 246 (51.1) | 62 (48.1) | 0.534 | 308 (50.5) |
| X-ray result | | | | |
| Normal | 118 (48.0) | 24 (38.7) | <0.0001 | 142 (46.1) |
| Abnormal, consistent with TB | 35 (14.2) | 6 (9.7) | | 41 (13.3) |
| Abnormal, not consistent with TB | 88 (35.8) | 21 (33.9) | | 109 (35.4) |
| Unknown | 5 (2.0) | 11 (17.7) | | 16 (5.2) |

Significant p-values are in bold.

PHC, primary healthcare; TB, tuberculosis.

are shown in [table 2](#). Overall, 535 (87.7%) children had a specimen collected, 89.4% among those identified at district hospitals and 81.4% at PHC facilities, $p=0.014$. The proportion of children referred for sample collection was higher at PHC facilities (9.5% vs 3.7%; $p=0.007$), however, even at PHC facilities, 87.6% of children had their sample collected on-site. The proportion of samples that were referred for processing was higher at PHC facilities (84.8% vs 54.3%; $p<0.0001$). The time taken from when the specimen was collected to receipt of results in the facility was shorter in PHC facilities (1.0 day (IQR:0.0–4.0) vs 2.0 days (IQR:1.0–5.0), $p=0.133$). The difference was, however, not statistically significant. Most specimens collected were gastric aspirates, followed by nasopharyngeal aspirate. The proportion of children who had gastric aspirate obtained was significantly higher in PHC than in district facilities (92.4% vs 70.7%; $p\leq 0.0001$).

There was no significant difference in Xpert MTB/RIF testing for children in district hospitals compared with PHC facilities (84.8% vs 79.1%, $p=0.12$). Of all Xpert tests performed, 11 (2.2%) were positive 9 (2.2%) in district hospitals and 2 (2.0%) in PHCs. Half of the children had a chest X-ray done with 14.2% and 9.7% of the chest X-rays showing abnormal images that were consistent with TB in district hospitals and PHC facilities, respectively. The proportion of chest X-rays with unknown results was higher in the PHC facilities compared with

district hospitals (17.7% vs 2.0%, $p<0.0001$). A total of 74 (13.8%) children were diagnosed with TB, 11 (14.9%) by GeneXpert, 41 (55.4%) by chest X-ray (three children diagnosed by both GeneXpert and chest X-ray) and 25 (33.8%) based on clinical signs only. 11 children (14.9%) had bacteriological confirmation of TB disease (not shown). In total, 19/129 (14.7%) were diagnosed with TB in PHC facilities and 55/481 (11.4%) were diagnosed in district hospitals, $p=0.309$ (not shown).

[Table 3](#) and online supplemental figure S1 compare the TB screening and diagnosis cascade for district hospitals and PHC facilities. The proportion of children identified with TB signs and symptoms and among those, the proportion of children reassessed for signs and symptoms of TB afterwards were significantly higher in the district hospitals, respectively, 1.2% vs 0.8% and 67.5% vs 48.1%; $p<0.001$. However, among those reassessed for the persistence of signs and symptoms of TB, the proportion with presumptive TB was similar between district hospitals and PHC facilities, 85.3% vs 85.4%; $p=0.964$. The time from TB symptom onset to TB diagnosis was significantly shorter in PHC facilities compared with district hospitals, 1.0 month (IQR: 0.1–2.1) vs 1.8 months (IQR:0.8–4.4); $p=0.043$. Time from TB diagnosis to TB treatment initiation was less than a day and this was the same in district and PHC facilities. The proportion of children with presumptive TB who were later confirmed

Table 3 Comparison of TB screening and diagnosis cascade at district hospitals and primary healthcare facilities

| | District hospitals n (%) | PHC facilities n (%) | P value |
|----------------------------------------------------------------------------------|--------------------------|----------------------|-------------------|
| Under-5 year attendees seen | 69 592 (63.5) | 40 022 (36.5) | N/A |
| Patients identified with signs and symptoms of TB | 836 (1.2) | 314 (0.8) | <0.001* |
| Of those identified, proportion reassessed for signs and symptoms of TB (N=1150) | 564/836 (67.5) | 151/314 (48.1) | <0.001* |
| Presumptive of TB who underwent TB investigations, among the reassessed, all | 481/564 (85.3%) | 129/151 (85.4%) | 0.964* |
| Confirmed with TB among the presumptive (N=610) | 55/481 (11.4) | 19/129 (14.7) | 0.309* |
| Proportion confirmed with TB among those initially screened presumptive of TB | 55/836 (6.6) | 19/314 (6.1) | 0.745* |
| Time from TB symptom onset to TB diagnosis, month, median (IQR) | 1.8 (0.8–4.4) | 1.0 (0.1–2.1) | 0.043† |
| Time from TB diagnosis to TB treatment initiation, days | 0 (0, 0) | 0 (0, 0) | 0.939† |
| Treatment outcome | n=55 | n=19 | |
| Cured | 5 (9.1) | 0 (0) | 0.319† |
| Completed treatment | 49 (89.1) | 14 (73.7) | 0.136† |
| Died | 0 (0) | 1 (5.3) | 0.257† |
| LTFU | 1 (1.8) | 3 (15.8) | 0.05† |
| Not evaluated | 0 (0) | 1 (5.3) | 1† |
| Favourable treatment outcome‡ | 54 (98.2) | 14 (73.7) | 0.001† |

Significant p-values are in bold

*Pearson's χ^2 test.

†Wilcoxon-Mann-Whitney test.

‡Favorable treatment outcome=cured and treatment completed versus other outcomes.

ARV, antiretroviral; LTFU, loss to follow-up; N/A, not applicable; TB, tuberculosis.

with a TB diagnosis was similar at both levels of care. Overall, 68/74 (91.9%) participants had a favourable treatment outcome (98.2% were cured or completed treatment in district hospital and 73.7% in PHC facilities, $p=0.001$). The proportion of LTFU was higher in PHC facilities (3/19, 15.8% vs 1/55, 1.8% in district hospitals, $p=0.05$), however, the proportion of deaths was not statistically different (1/19, 5.3% in PHC facilities vs 0/55, 0% in district hospitals, $p=0.257$).

DISCUSSION

In this study, we demonstrated that implementing an intervention offering paediatric TB services integrated into key child healthcare services to decentralise services and address key barriers to case detection and management of TB is a feasible strategy. PHC facilities are likely to be the first point of contact children infected with TB have with the health system. Patients are more likely to access care in the PHC facilities first and go to district hospitals more often when they are referred. Overall, 12% of children enrolled in the study were diagnosed with TB. The proportion of those diagnosed with TB was comparable between PHC facilities and district hospitals. TB diagnostic procedures for children were mainly conducted at the district hospitals by designated HCWs before the study. This created barriers to access for diagnostic services. A number of studies whose strategies focused on increasing childhood TB case detection at PHC facilities have shown that increasing case identification at PHC level is associated with a sustained improvement of childhood TB diagnosis overall.^{10 15–17} This is also similar to the DETECT study that showed that decentralisation and strengthening of child TB services were associated with a significant increase in case notifications for the TB programme.¹⁰ These studies did not, however, compare case detection rates between district hospitals and PHC facilities.

We also found that the median time from TB symptom onset to TB diagnosis was significantly shorter in the PHC facilities compared with district hospitals. There were more referrals for sample processing and testing at PHC facilities; however, sample referral was not associated with more missing results or with a longer time to receive the test results. This indicates that sample referral is an efficient system with no added delays in receiving results at PHC facilities. These findings differ from a study conducted by Maior *et al*, who found that at PHC facilities, the median time from symptom onset to the initiation of treatment of pulmonary TB was 11 (6–24) weeks in Brazil, which was longer than reported in our study.¹⁸ Studies in Bangladesh, Nigeria and Ethiopia reported a median time of 7–11 weeks from symptom onset to diagnosis of TB,^{19–21} and a systematic review reported a wide range of 25–185 days total time to diagnosis of pulmonary TB.²² The shorter time to diagnosis in PHC facilities in our study is most likely due to the capacity building of the PHC staff, who performed timely collection of

specimens to send to the referral laboratories. Furthermore, specimens were sent to the laboratories through an existing sample networking system and results were received through the same system, thereby eliminating delays. Where diagnostic services are not decentralised, there is a need to establish effective systems to ensure the referral of patients and specimens to capitalise on the diagnostic capacity of district hospitals. In our study, the referral system worked well, and referral was not associated with additional diagnostic delays. These results show that decentralised services in this study did not lengthen the time to receive results at the PHC facilities or increase the probability of having missing results.

The intervention further strengthened decentralisation of TB diagnosis by making Xpert MTB/RIF testing available and using chest X-rays for children seen at PHC facilities. The intervention ensured a strong referral system to facilities that had Xpert MTB/RIF and chest X-ray machines. Our results show that coverage for both Xpert testing and chest X-ray was similar between the district hospitals and PHC facilities. However, almost 20% of those in the PHC did not receive their chest X-ray results. Similar challenges have been reported in a study in Kenya, which noted that there are few radiologists which leads to a delayed delivery time for paper reports.²³ This may have led to underdiagnosis of cases. Generally, most TB cases in children are clinically diagnosed and a chest X-ray suggestive of TB is one of the main criteria required to make a clinical diagnosis.¹⁵ By making chest X-ray readily available, clinicians have more information to either diagnose or exclude TB in children. Other studies report limited access to chest X-rays in public health facilities and patients may also lack money to pay for transportation to access chest X-rays in district hospitals.^{23 24} Our study provided transportation vouchers for participants referred for chest X-ray. Receiving chest X-ray results at PHC seems more challenging, so this gap needs to be addressed when services are to be decentralised. This can be improved through the introduction of digital X-rays such as Computer-Aided Detection for TB (CAD4TB), which can easily transmit images and reports, therefore, eliminating the need for patients to physically carry their reports back to their clinicians. CAD4TB, which has been shown to have similar performance to that of clinicians in assessing abnormalities indicative of TB, has the potential to be used as a point-of-care decision tool, which can assist human readers in identifying subjects who require further testing.²⁵ Such innovations support a more consolidated approach, which will be critical to improve TB case detection in children at decentralised levels.

We also found that more children identified as having presumptive TB were household contacts of a TB case at district hospitals compared with PHC facilities. This lower frequency of identifying children through contact tracing indicates a necessity to enhance decentralisation of contact tracing efforts at PHC facilities.

Our study demonstrates that gastric aspirate is a feasible diagnostic procedure in PHC facilities,

especially after the capacity strengthening of staff in the conduct of this method of sample collection. The majority of specimens collected in PHC facilities were gastric aspirates. Since the process of obtaining a gastric aspirate is generally not an aerosol-generating procedure and young children are also at low risk of transmitting infection, gastric aspiration can be considered a low-risk procedure for TB transmission and can safely be performed at the child's bedside or in a routine procedure room.¹⁵ Therefore, this procedure can be conducted at any level of healthcare, as shown in the DETECT study.¹⁰ By strengthening HCW capacity and the availability of relevant commodities, gastric aspiration is easier to perform than nasopharyngeal aspirate and is a more feasible diagnostic procedure at the PHC level. A higher proportion of children with TB signs and symptoms in PHC facilities were not reassessed for TB as they did not return to the facility. It is possible some TB diagnoses were missed because children did not come back. It is also very likely that children with a cough at PHC went directly to the district hospital if the cough was prolonged after the initial treatment given at PHC facilities. Since children often present sooner for care at PHC facilities, it is important to create a pathway for rapid delivery of TB services there. While there may be greater challenges with TB diagnosis and treatment at PHC facilities compared with district hospitals, strengthening TB diagnostic capacity and HCW capacity in paediatric TB detection, diagnosis and management at PHC facilities could lead to earlier paediatric TB screening, diagnosis and treatment. Where referrals are needed for diagnostic testing, the referral and documentation systems must be strengthened. In our study, we showed that decentralisation was successful in bringing TB care 'closer' to children. This result indicates that with appropriate capacity building, HCWs at PHC facilities are equally capable of screening and diagnosing TB in children. Developing and strengthening the decentralisation of child TB services will provide important opportunities to improve TB case detection.

The overall favourable treatment outcome of 91.9% (98.2% in district hospitals and 73.7% in PHC facilities) in this study is higher than rates reported in other studies in the African region, namely; Cameroon (68%), Ethiopia (74.8%) and Nigeria (74%).^{26–28} This is also higher than the WHO treatment target of 90%.²⁹ The highly favourable treatment outcome in the district hospitals compared with PHC facilities was primarily driven by the higher LTFU observed in the PHC facilities. Death and LTFU during treatment in our study were 1.4% and 5.4%, respectively. The LTFU is consistent with previous reports of paediatric TB treatment in Nigeria, Ethiopia and South Africa.^{28 30 31} The mortality in our study is higher than reported in South Africa (<1%),³⁰ similar to studies in Ethiopia (1.8%),³² but lower than what has been reported in Botswana (3.4%), Tanzania (10.9%) and Ghana (17.4%).^{33–35} This wide

range is reflective of differences in settings as well as the dates when the study was conducted. The proportion of LTFU was higher at PHC facilities. It is likely that some of the LTFU observed at PHC level were rather referrals to a higher level of care that were not accurately documented. We cannot exclude however that some of the LTFU were true LTFU associated with treatment interruption or death which the health system needs to capture and address. Altogether, decentralisation models require the adoption of strong systems to track referrals at different levels of the health system and to trace the clients who are defaulting care.

Our study had a number of limitations that should be considered when interpreting these results. There is a scarcity of TB-specific care-seeking data. We used data for care-seeking for general illnesses as a proxy indicator. However, patients who seek care for a general illness may behave differently from those who seek care for TB or for respiratory symptoms specifically. Another limitation of this study was the onset of the COVID-19 pandemic during the study period. Enrolment of study participants was stopped for 4 months due to the COVID-19 pandemic and related Ministry of Health recommendations leading to fewer participants being enrolled. Second with the shift in focus on management of COVID-19, it is possible that participants were more likely to be diagnosed and managed as COVID-19 cases hence the fewer TB case detection. The small numbers of children enrolled and diagnosed with TB especially at PHC facilities resulted in limited power to measure a difference in the proportion diagnosed with TB at the different levels of care. Moreover, this low number of children diagnosed with TB and hence evaluated for TB outcomes was insufficient to provide adequate power to conduct a multivariable analysis of outcomes. There was also uncertainty about the accuracy of diagnosis in one-third of the patients who were diagnosed only on the basis of clinical signs and symptoms (no chest X-ray nor laboratory result were available). We did not identify other published studies comparing district hospitals and PHC facilities for diagnosis and management of TB in children. The study also engaged and trained additional staff as first screeners which might not be possible to duplicate in similar PHC settings due to resource constraints. However, we obtained valuable experience and provided evidence for the effectiveness of decentralising and integrating TB services in both district hospitals and PHC facilities to aid implementation of similar models. The involvement of all facility levels of care is essential for the effective control of TB in children under age 5 years.

In conclusion, our study shows that decentralisation of TB screening and diagnosis is feasible and can shorten the time to TB diagnosis. Strengthening HCW capacity in TB diagnosis and management and facilitating referral systems for patients and samples led to the diagnosis of a significant proportion of children with TB at the PHC facilities. A better tracking

and documentation systems for patients specimens and X-ray referrals will be key to improving the decentralisation system. Additionally, decentralising contact tracing more efficiently could be beneficial.

Author affiliations

- ¹Elizabeth Glaser Pediatric AIDS Foundation, Nairobi, Kenya
²Elizabeth Glaser Pediatric AIDS Foundation, Washington, District of Columbia, USA
³Elizabeth Glaser Pediatric AIDS Foundation, Yaoundé, Cameroon
⁴Department of Health, Homa Bay County Government, Homa Bay, Kenya
⁵Elizabeth Glaser Pediatric AIDS Foundation, Kinshasa, Democratic Republic of Congo
⁶Operational Research in Health Department, Ministry of Public Health, Yaounde, Cameroon
⁷Elizabeth Glaser Pediatric AIDS Foundation, Geneva, Switzerland
⁸George Washington University Milken Institute School of Public Health, Washington, District of Columbia, USA

X Rose Masaba @rose Masaba

Acknowledgements We acknowledge contribution of the INPUT study group collaborators, in Cameroon: Desire A Cheugoue, Loic Feuzeu, Albert Kuate, Sandrine Kwedi, Muhamed Mbunka, Giscard N Nana, Ferdinand Ngong, Lucie Nguimbous, Bernadette Ngum, Pascal Nyamb, Pierrette Omgba, Yanique B Tchounga. In Kenya: Caren Asibitar, Nicholas E Ekuwom, Elvirah R Emuhaya, Linda A Haga, Bentar Liwan, Joy Lochu, Gilchrist Lokoel, James Losike, Elgiva Wanyama, Kennedy O Ojowi, Mercy A Ojwang. We also thank Lynne Mofenson for helpful input and Shannon Viana for final review and editing.

Contributors LD-N, RMasaba, RMachekano, BT, MC, AT conceptualised the study. MO, GO, PT, JD, A-CZ-KB, RMasaba, BT collected the data. NH, SS and LD-N validated the data. NH and RMachekano performed the statistical analysis. All authors contributed to the interpretation of data. RMasaba prepared the original draft and is the guarantor and is responsible for the overall content of this paper. All authors reviewed and edited the draft. RMasaba, BT, LD-N and AT administered the project. AT and MC acquired funding. All authors read and approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

Funding The INPUT study is funded by UNITAID. Grant ID: 2017-20-EGPAF-CAP-TB.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the protocol was reviewed and approved by the Cameroon National Ethics Committee for Research in Human Health (CNERSH), (number 2018/12/1131/CE/CNERSH/SP dated 14 December 2018) in Cameroon and the Kenyatta National Hospital University of Nairobi Ethical Review Committee (number KNH-ERC/A/44 dated 7 February 2019) in Kenya and Advarra Institutional Review Board in the US (Pro00029181 dated 6 September 2018) in the USA. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Rose Masaba <http://orcid.org/0000-0003-1801-7938>
 Boris Tchounga <http://orcid.org/0000-0002-8747-9610>
 Lise Denoëud-Ndam <http://orcid.org/0000-0002-9482-1461>

REFERENCES

- World Health Organization. Global TB report. 2022. Available: <https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022> [Accessed 2 Jun 2023].
- Maphalle LNF, Michniak-Kohn BB, Ogunrombi MO, *et al*. Pediatric tuberculosis management: a global challenge or breakthrough? *Children (Basel)* 2022;9:1120.
- Dodd PJ, Gardiner E, Coghlan R, *et al*. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health* 2014;2:e453–9.
- World Health Organization. African Union and WHO urge swift action against childhood tuberculosis. 2022. Available: <https://www.afro.who.int/news/african-union-and-who-urge-swift-action-against-childhood-tuberculosis> [Accessed 10 Jul 2023].
- Newton SM, Brent AJ, Anderson S, *et al*. Paediatric tuberculosis. *Lancet Infect Dis* 2008;8:498–510.
- Reuter A, Hughes J, Furin J. Challenges and controversies in childhood tuberculosis. *Lancet* 2019;394:967–78.
- Huynh J, Thwaites G, Marais BJ, *et al*. Tuberculosis treatment in children: the changing landscape. *Paediatr Respir Rev* 2020;36:33–43.
- Marais BJ, Graham SM, Maeurer M, *et al*. Progress and challenges in childhood tuberculosis. *Lancet Infect Dis* 2013;13:287–9.
- Snow KJ, Cruz AT, Seddon JA, *et al*. Adolescent tuberculosis. *Lancet Child Adolesc Health* 2020;4:68–79.
- Zawedde-Muyanja S, Nakanwagi A, Dongo JP, *et al*. Decentralisation of child tuberculosis services increases case finding and uptake of preventive therapy in Uganda. *Int J Tuberc Lung Dis* 2018;22:1314–21.
- Bassili A, Fitzpatrick C, Qadeer E, *et al*. A systematic review of the effectiveness of hospital- and ambulatory-based management of multidrug-resistant tuberculosis. *Am J Trop Med Hyg* 2013;89:271–80.
- Weiss P, Chen W, Cook VJ, *et al*. Treatment outcomes from community-based drug resistant tuberculosis treatment programs: a systematic review and meta-analysis. *BMC Infect Dis* 2014;14:333.
- Moore BK, Erasmus L, Ershova J, *et al*. Pre-treatment loss to follow-up among children with multidrug-resistant tuberculosis in South Africa, 2008–2010. *PLoS One* 2020;15:e0230504.
- Denoëud-Ndam L, Otieno-Masaba R, Tchounga B, *et al*. Integrating pediatric TB services into child healthcare services in Africa: study protocol for the INPUT cluster-randomized stepped wedge trial. *BMC Public Health* 2020;20:623.
- Kaguije M, Nyangu S, Maimbolwa MM, *et al*. Strategies to increase childhood tuberculosis case detection at the primary health care level: lessons from an active case finding study in Zambia. *PLoS One* 2023;18:e0288643.
- Malik AA, Amanullah F, Codlin AJ, *et al*. Improving childhood tuberculosis detection and treatment through facility-based screening in rural Pakistan. *Int J Tuberc Lung Dis* 2018;22:851–7.
- Talukder K, Salim MAH, Jerin I, *et al*. Intervention to increase detection of childhood tuberculosis in Bangladesh. *Int J Tuberc Lung Dis* 2012;16:70–5.
- Maior M de L, Guerra RL, Cailleaux-Cezar M, *et al*. Time from symptom onset to the initiation of treatment of pulmonary tuberculosis in a city with a high incidence of the disease. *J Bras Pneumol* 2012;38:202–9.
- Demissie M, Lindtjorn B, Berhane Y. Patient and health service delay in the diagnosis of pulmonary tuberculosis in Ethiopia. *BMC Public Health* 2002;2:23.
- Odusanya OO, Babafemi JO. Patterns of delays amongst pulmonary tuberculosis patients in Lagos, Nigeria. *BMC Public Health* 2004;4:18.
- Karim F, Islam MA, Chowdhury AMR, *et al*. Gender differences in delays in diagnosis and treatment of tuberculosis. *Health Policy Plan* 2007;22:329–34.
- Sreeramareddy CT, Panduru KV, Menten J, *et al*. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infect Dis* 2009;9:91.

- 23 Dhoot R, Humphrey JM, O'Meara P, *et al.* Implementing a mobile diagnostic unit to increase access to imaging and laboratory services in Western Kenya. *BMJ Glob Health* 2018;3:e000947.
- 24 Kawooya MG. Training for rural radiology and imaging in sub-Saharan Africa: addressing the mismatch between services and population. *J Clin Imaging Sci* 2012;2:37.
- 25 Maduskar P, Muyoyeta M, Ayles H, *et al.* Detection of tuberculosis using digital chest radiography: automated reading vs. interpretation by clinical officers. *Int J Tuberc Lung Dis* 2013;17:1613–20.
- 26 Pefura Yone EW, Kuaban C, Kengne AP. HIV testing, HIV status and outcomes of treatment for tuberculosis in a major diagnosis and treatment centre in Yaounde, Cameroon: a retrospective cohort study. *BMC Infect Dis* 2012;12:190.
- 27 Muñoz-Sellart M, Cuevas LE, Tumato M, *et al.* Factors associated with poor tuberculosis treatment outcome in the Southern Region of Ethiopia. *Int J Tuberc Lung Dis* 2010;14:973–9.
- 28 Adejumo OA, Daniel OJ, Adebayo BI, *et al.* Treatment outcomes of childhood TB in Lagos, Nigeria. *J Trop Pediatr* 2016;62:131–8.
- 29 World Health Organization. The end TB strategy. 2015. Available: <https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19> [Accessed 2 Jul 2023].
- 30 Hailu D, Abegaz WE, Belay M. Childhood tuberculosis and its treatment outcomes in Addis Ababa: a 5-years retrospective study. *BMC Pediatr* 2014;14:61.
- 31 Osman M, Lee K, Du Preez K, *et al.* Excellent treatment outcomes in children treated for tuberculosis under routine operational conditions in Cape Town, South Africa. *Clin Infect Dis* 2017;65:1444–52.
- 32 Tilahun G, Gebre-Selassie S. Treatment outcomes of childhood tuberculosis in Addis Ababa: a five-year retrospective analysis. *BMC Public Health* 2016;16:612.
- 33 Siamisang K, Rankgoane-Pono G, Madisa TM, *et al.* Pediatric tuberculosis outcomes and factors associated with unfavorable treatment outcomes in Botswana, 2008-2019: a retrospective analysis. *BMC Public Health* 2022;22:2020.
- 34 Mtabho CM, Irongo CF, Boeree MJ, *et al.* Childhood tuberculosis in the Kilimanjaro region: lessons from and for the TB programme. *Trop Med Int Health* 2010;15:496–501.
- 35 Afrane AKA, Alhassan Y, Ganu V, *et al.* Childhood tuberculosis and factors associated with mortality and loss to follow-up at a major paediatric treatment centre in Southern Ghana. *Pan Afr Med J* 2022;43:90.