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A yield and cost comparison of tuberculosis contact investigation and intensified case finding in Uganda

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Abstract

Introduction

Resource constraints in Low and Middle-Income Countries (LMICs) limit tuberculosis (TB) contact investigation despite evidence its benefits could outweigh costs, with increased efficiency when compared with intensified case finding (ICF). However, there is limited data on yield and cost per TB case identified. We compared yield and cost per TB case identified for ICF and Tuberculosis-Contact Investigation (TB-CI) in Uganda.

Methods

A retrospective cohort study based on data from 12 Ugandan hospitals was done between April and September 2017. Two methods of TB case finding (i.e. ICF and TB-CI) were compared. Regarding ICF, patients either self-reported their signs and symptoms or were prompted by health care workers, while TB-CI was done by home-visiting and screening contacts of TB patients. Patients who were presumed to have tuberculosis were requested to produce a sample for examination. TB yield was defined as a ratio of diagnoses to tests, and this was computed per method of diagnosis. The cost per TB case identified (medical, personnel, transportation and training) for each diagnosis method were computed using the activity-based approach, from the health care perspective. Cost data were analyzed using Windows Excel.

Results

454 index TB cases and 2,707 of their household contacts were investigated. Thirty-one per cent of contacts (840/2707) were found to be presumptive TB cases. A total of 7,685 tests were done, 6,967 for ICF and 718 for TB-CI. The yields were 18.62% (1297/6967) and 5.29% (38/718) for ICF and TB-CI, respectively. It cost US$ 120.60 to diagnose a case of TB using ICF compared to US$ 877.57 for TB-CI.

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Conclusion

The yield of TB-CI was found to be four-times lower and seven-times costlier compared to ICF. These findings suggest that ICF can improve TB case detection at a low cost, particularly in high TB prevalent settings.

Background

Household contacts of pulmonary bacteriologically-confirmed (PBC) tuberculosis (TB) patients have a high risk of becoming infected with *Mycobacterium tuberculosis* and developing active TB [1–4]. Investigation of these contacts for TB could lead to early detection and treatment of active TB as well as prophylactic treatment of persons with latent TB [5,6]. This has long been a priority intervention in most low-incidence countries to reduce TB incidence [7]. However, in low and middle-income countries (LMICs), home visits for TB contact investigation (TB-CI) are limited by the high workload of health workers, poor adherence to treatments for latent TB and resources [2,8]. In most cases, health workers use the Intensified Case Finding (ICF) modality when individuals with TB symptoms either self-report to health facilities or are assessed for TB using the Intensified Case Finding Tool. But the stagnating Case Detection Rates (CDR) in dual epidemic TB and HIV countries including Uganda, [9,10] and the increasing prevalence of drug-resistant TB have prompted a reassessment of the potential benefit of TB-CI [11].

A recent TB-CI review conducted in LMICs found a cumulative yield of 4.5% (95% CI 4.3%-4.8%) among household contacts, [8] suggesting's that it has a utility in detecting additional cases. Mathematical models have suggested that the benefits of TB-CI could out-weigh costs and even increase efficiency in the long-run when compared with passive case finding (PCF) [12,13]. With TB-CI, TB cases are likely to be detected early, thereby minimizing the likelihood of further complications and hospitalization [14]. It is also possible to assume that with early TB case detection, TB transmission is interrupted and further cases are prevented [15]. TB-CI also removes some barriers to health care since health workers reach out to potential TB patients in the community, removing the pre-treatment costs and increasing access to health services [16].

However, empirical evidence of the cost-effectiveness of implementing TB-CI in real-world settings is limited [10,17–21]. To-date, only Sekandi *et al.* [10] have evaluated the cost and yield of various TB case finding strategies in Africa. This study therefore compared TB yield and cost for ICF and TB-CI in an operational setting in Uganda- a high burden TB/HIV country in sub-Saharan Africa.

Methods

Study design and setting

This was a retrospective cohort study of TB-CI using data collected from 11 Regional Referral Hospitals and one district Hospital in Uganda (Table 1). By the Uganda Ministry of Health categorization, Regional Referral Hospitals (RRHs) serve a population of 3 million persons while General Hospitals (GHs) serve a population of 500,000 people [22].

Study population

The study population was pulmonary bacteriologically-confirmed (PBC) tuberculosis patients (aged 18+ years) that were diagnosed at the above-mentioned study sites between April and

Table 1. Description of the study sites.

Health facility	Bed capacity	Annual OPD# attendance (2017)	Distance & direction from Capital
Arua RRH	323	153,451	480 km NW
Gulu RRH	397	97,415	333.7 km N
Jinja RRH	408	165,573	87 km E
Hoima RRH	268	41,930	190 km W
Kabale RRH	226	63,266	426 km SW
Kawolo GH	106	51,946	48.5 km E
Lira RRH	346	95,695	340 km N
Masaka RRH	540	125,025	130.2 km SSW
Mbale RRH	355	56,539	244 km E
Moroto RRH	172	54,188	463 km NE
Mubende RRH	173	45,681	149.1 km WSW
Soroti RRH	251	90,818	298 km NNE

*RRH-Regional Referral Hospital, *GH-General Hospital,
#OPD-Out Patient Department.

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September 2017. All consented PBC TB patients were visited at home for TB-CI. A household contact was defined as an individual who had resided in the household of an index TB patient for at least 7 consecutive days during the 3 months before the diagnosis of TB in the index case.

TB diagnosis

TB case finding was conducted using two different methods; Intensified Case Finding (ICF) and TB contact investigation (TB-CI). These methods are described in detail below.

1. **Intensified case finding (ICF)**. Under ICF, individuals with TB symptoms who self-report to health facilities are assessed for TB using the Intensified Case Finding Tool. It assesses for a cough lasting for 2 or more weeks or any cough for people living with HIV (PLHIV) or any of these signs and symptoms (evening persistent fevers >2 weeks, excessive night sweats >3 weeks and noticeable weight loss) were presumed to have TB and were subjected to further investigations to ensure that a definitive diagnosis was done. TB was diagnosed on receiving a *Mycobacterium tuberculosis* detected test from the GeneXpert test.
2. **TB contact investigation (TB-CI)**. TB patients that consented to a home visit were visited by two health workers, a nurse and a community health worker. Upon reaching the home, the team offered health education to household members. After family members were screened for TB using the Intensified Case Finding (ICF) Tool as above, any household contact who reported any of the signs and symptoms in the ICF tool was categorized as a presumptive TB case. Individuals who were found to be coughing were requested to provide a sputum sample which was transported to the health facility and subjected to MTB RIF GeneXpert (Cepheid, Sunnyvale, CA, USA). The other presumptive TB cases were referred to the health facility for further clinical examinations.

Data collection methods and procedures

Intensified case finding data. Intensified case finding (ICF) data included the total number of cases, number of PBC cases, number of MTB/RIF GeneXpert tests done to detect those cases. These data were extracted from the program registers using an intensified case finding tool (S1 File) and placed in a database.

TB contact investigation (TB-CI) data. TB-CI data were extracted using a TB contact investigation tool (S2 File) from health facility program data. Variables extracted from the records included patient's TB numbers, age, sex, number of contacts, number of contacts presumed to have TB, number of contacts offered a definitive diagnostic test for TB, number of contacts with TB, number of contacts who had an HIV test, and number of patients found HIV positive. These data were then entered into a spreadsheet (Windows Excel 2013, Microsoft Corp., Redmond, WA) in preparation for analysis.

Costing data. Costing data were collected on program costs including personnel, transport and training costs, as described below. We did estimate the direct economic costs related to diagnosing a TB case using either ICF or TB-CI from a provider's perspective. Most of the information was extracted from program records, together with interviews with staff at the various health care facilities. Efforts were made to adhere to guidelines stipulated in the literature [23,24]. We were not able to estimate the overhead costs such as utilities, custodial services, buildings, office space, computers and maintenance of medical equipment. These costs were excluded because we could not tease them out of the costs associated with the provision of other health care services [25].

1. **Personnel costs**. Personnel costs were estimated per method of TB diagnosis, as described below.

   i). *Intensified case finding (ICF)*. We collected data on personnel time spent by Nurses, Nursing Assistants, Clinicians (Clinical Officers and Medical Officers) and Laboratory Technologists. Using a time-series, ten samples were done per carder per health facility and the average taken. The hourly rates were calculated from monthly salaries as paid by the government of Uganda in 2017 assuming 40 hours working week [26]. The total personnel costs were obtained by multiplying the hourly rate with the estimated patient contact time, the assumption was every presumptive TB case made it to the laboratory. Hence the number of tests done was used as a proxy for patients seen by the health care workers for TB case finding.

   ii). *TB contact investigation (TB-CI)*. A stop-clock was used to obtain the time it took health care workers to travel from the health facility to the patient's home, conduct contact investigation and back. To calculate the personnel cost for TB-CI the same method as above was used, factoring in the hourly pay and time for the activity. The other costs incurred were meals and incidental expenses for the persons who performed TB-CI. US$ 5.56 was given per day, per person when they did perform TB-CI activities as guided by the Office of the UN Resident Coordinator in Uganda. [27]

2. **Transportation costs**. Transportation costs were incurred when the health care workers went to perform contact investigation. The distance between the health facility and the index patient's home was calculated from the odometer of a motorbike or a motor vehicle which was used for transport. The health care worker and a community health worker were compensated with Uganda Shillings [UGX] 200 (US$ 0.056) per kilometre as per the above-mentioned guidance. [27]

3. **Training costs**. Twenty-four (24) health care workers were trained, 2 per health facility, a clinician and a nurse for 5 days. The costs incurred were their per diems and transport. The per diem was US$ 44.78 per participant and facilitator as directed by standing orders for the government of Uganda per night [27]. Transport allowance was by public means for the

participant and was calculated depending on the distance from the health facility where the participant is based on the training venue. The participant was compensated for UGX 200 (US$ 0.056) per kilometre. Other costs incurred included the cost of hiring the training venue, payment for meals and refreshments during training and fuel for facilitators. These were all computed to get the total training costs. To compute the unit cost for training per TB case diagnosed by contact investigation, we divided the total costs of the training by TB cases diagnosed by contact investigation. There were no training costs incurred for ICF.

4. **Medical costs**. Medical costs were defined as all costs incurred at the point where health care was delivered. This included GeneXpert MTB/RIF and all other consumables required. The unit cost of an MTB/RIF GeneXpert test per patient was obtained from the literature. A GeneXpert test was found to cost, on average, US$ 21 in Uganda [28]. The number of tests done under each approach was obtained from program data, and these were 6,967 tests for ICF and 718 for TB-CI. The costs of consumables were market-based and were obtained from the National Medicines Stores (NMS) catalogue [29]. NMS is a government of Uganda agency responsible for the supply of medicines and other related products throughout the country. The quantities of consumables were calculated based on what a health care worker would use for a single patient.

Study outcomes

The primary outcome was TB yield in contacts of PBC TB patients contacted at home compared with those who self-referred themselves to the health facilities. The secondary outcome was the cost per TB case diagnosed from TB-CI when compared with the cost per TB case diagnosed using ICF.

Data analysis

We exported data from a spreadsheet (Microsoft Excel version 2013) into Intercooled Stata version 13 (Stata-Corp, College Station, Texas, USA). We summarized demographic and outcome data into frequencies, percentages, and measures of central tendency, the median and mean. The yield of TB was obtained by dividing the number of TB cases from contact investigation divided by the number of tests done. The cost per TB case identified by TB-CI was calculated from the healthcare perspective. All the ingredients needed to diagnose a TB case, using either ICF or TB-CI, were considered. These were summed up to get the total cost of diagnosing a TB case by either ICF or TB-CI. To determine the unit cost of either diagnosing a TB case using either ICF or TB-CI, the total costs of either modality were divided by the TB cases obtained from each method either ICF or TB-CI. The costs were converted from Uganda Shillings to 2017 United States Dollars (US$) rate at an exchange rate of US$ 1 to UGX 3,595; there was no discounting since the duration was less than a year.

Ethical approval

ICF is part of routine clinical care, while TB-CI is a WHO/Ministry of Health in Uganda recommended strategy and does not require ethical approval for introduction into a program. The secondary analysis was done on aggregate and anonymous project data; therefore, there was no need for additional ethical clearance. But consent was sort from the patients before the home visit for contact investigation.

Table 2. Socio-demographic characteristics of index patients and their household contacts.

Index TB patients		
Number of Index TB Patients	Total	N = 454
Age	Average	33.6 (SD = 13.734)
	Median	32 (0–90)
Sex	Female	158 (34.80%)
	Male	296 (65.19%)
HIV Status	HIV-positive	170 (37.44%)
	HIV-negative	284 (62.55%)
Household contacts		
Number of contacts	Total	N = 2707
	Average	6.0 (SD = 8.703)
	Median	4.0 (0–125)
Age	Average	34.7 (SD-12.45)
	Median	31 (0–84)
Sex	Female	1327 (49.03%)
	Male	1380 (50.97%)
HIV status	HIV-positive	74 (2.73%)
	HIV-negative	1790 (66.12%)
	Unknown	843 (31.14%)

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Results

Participants' characteristics

Table 2 shows the characteristics of the 454 index TB patients. These patients had a total of 2,707 contacts, with an average household size of six members (SD: ±8.70). The mean age of index patients and contacts were not very different with 33.6 years and 34.7 years respectively. The index TB patients were most likely to be males (65.2%) while there was an equal distribution of sex among the contacts with 49% females and 51% males. Thirty-seven per cent (170/454) of the index patients had HIV while only 3.97% (74/1864) of the contacts had HIV.

TB case notification, cases traced at home and TB yield

Table 3 shows the number of patients notified, the cases investigated at home and TB yield at each study site. Overall, a total of 6,967 MTB RIF GeneXpert tests were done to diagnose 1,297 TB cases resulting in an ICF yield of 19% (1297/6967). Of the 1,295 Pulmonary Bacteriologically-Confirmed (PBC) TB cases, 454 (35.0%) had their contacts investigated for TB. Only 31.0% (840/2,707) were presumed to have TB. Of these, 85.5% (718/840) had their samples sent to the laboratory for a definitive diagnosis and 5.3% (38/718) (95% CI 3.8% -7.2%) were diagnosed with TB. Kabale regional referral hospital had the highest TB yield (25%) followed by Moroto regional referral hospital (10.8%) while Jinja, Hoima, Masaka and Mbale had the lowest TB yield with no patients diagnosed with TB during TB-CI.

Cost for identifying a TB case using different case-finding modalities

Table 4 shows the cost of finding a TB Case using either ICF or TB-CI. The total costs were US $ 156,416.62 and US$ 33,347.83 for ICF and TB-CI respectively, while the unit costs were US$

Table 3. Number of patients notified, cases traced at home and TB yield at each study site.

HEALTH FACILITY	NOTIFIED TB CASES (APRIL-SEPT'17)	MTB/RIF GeneXpert Tests-ICF	P-BCβ CASES (APRIL-SEPT'17)	TB Yield for ICF	INDEX Ptsγ	NUMBER OF HOUSEHOLD CONTACTS	PRESUMED TB	INVESTIGATED FOR TB	TB Ptsγ	TB Yield for HCI
Arua RRH*	353	561	168	30%	51	629	210	190	15	7.89%
Gulu RRH*	221	660	131	20%	24	140	12	12	1	8.33%
Hoima RRH*	273	1253	111	9%	26	69	12	12	0	0.00%
Jinja RRH*	342	404	84	21%	30	58	17	17	0	0.00%
Kabale RRH*	86	697	66	9%	20	69	4	4	1	25.00%
Kawolo GH#	110	314	45	14%	48	249	64	35	2	5.71%
Lira RRH*	271	669	178	27%	107	710	220	218	9	4.13%
Masaka RRH*	297	527	139	26%	18	72	5	4	0	0.00%
Mbale RRH*	180	611	104	17%	13	45	12	12	0	0.00%
Moroto RRH*	200	454	109	24%	23	114	38	37	4	10.81%
Mubende RRH*	137	569	96	17%	58	296	204	139	3	2.16%
Soroti RRH*	121	248	66	27%	36	256	42	38	3	7.89%
	2591	6967	1297	19%	454	2,707	840	718	38	5.29%

*RRH-Regional Referral Hospital,

GH-General Hospital,

βP-BC-Pulmonary Bacteriologically Confirmed,

γ Pts-Patients.

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Table 4. Cost of finding a TB case using either passive case finding (ICF) or TB contact investigation.

COST CATEGORY	CASE FINDING MODALITY			
	ICF*		TB-CI#	
PROGRAM COSTS	**Cost**	**% Cost**	**Cost**	**% Cost**
Personnel Costs				
Training	0	0.00%	10,242.16	30.71%
Salaries	5,980.99	3.82%	1,174.73	3.52%
Allowances & Transport Costs	0	0.00%	6,738.04	20.21%
Sub-Total-Personnel Costs	5,980.99	3.82%	18,154.93	54.44%
Medical Costs				
Supplies & Consumables	4,128.63	2.64%	114.9	0.34%
MTB RIF GeneXpert	146,307.00	93.54%	15,078.00	45.21%
Sub-Total-Medical Costs	150,435.63	96.18%	15,192.90	45.56%
TOTAL	**156,416.62**	**100.00%**	**33,347.83**	**100.00%**
Total TB Cases (PBC)	1,297.00		38	
Cost per case	**$120.60**		**$877.57**	

(*ICF-Intensified Case Finding, #TB-CI-TB Contact Investigation)

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120.60 for ICF and US$ 877.57 for TB-CI. Under ICF, 93.54% of the cost went to performing MTB/RIF GeneXpert Tests while 2.64% was to Consumables and Supplies and 3.82% went to salaries. The main driver of costs under TB-CI was training at 30.71%; GeneXpert tests at 45.21%; allowances & transport at 20.21%; and supplies and consumables at 0.34%.

Discussion

We found TB-CI had a yield four times lower than ICF (5.29% versus 18.61%), and it cost almost seven-times more (US$ 877.57 versus US$ 120.60) to diagnose a case of TB using TB-CI when compared to ICF, suggesting that use of ICF is a more cost-effective strategy in identifying new TB cases particularly in high TB prevalent settings such as Uganda.

Although the TB yield was four times lower in TB-CI than ICF, it is higher than the yield reported in previous studies [8, 30]. Uganda is one of the 30 high TB/HIV burden countries; thus, the high TB yield observed across the country could be a clear testimony to the already high prevalence of TB in Uganda as reported from previous studies [31]. It is important to note that there were variations reported by region with the highest TB yield reported in Kabale Regional Referral Hospital while there were no TB cases detected in four (Jinja, Hoima, Masaka and Mbale) Regional Referral Hospitals. Our study did not explore the reasons for the regional variability in TB yield. However, this could be due to the late adoption of the intervention by some sites compared to others after the training. Nevertheless, our finding of a TB yield of 5.29% for PBC suggests that TB-CI could be a worthwhile intervention that can be used to increase TB cases detection.

We found that it cost seven-times more to diagnose a case of TB using TB-CI compared to ICF. Our TB-CI costs were higher than those reported by Sekandi *et al*. [10] who found that it cost US$ 416.35 to diagnose one case of TB [10]. This is maybe because Sekandi *et al*. [10] used Smear microscopy which costs, on average, US$1–3, while we used MTB/RIF GeneXpert which costs, on average, US$ 21 (range US$16–58) [28]. The other probable reason is that our study was of a shorter duration (i.e. 6 months) compared to the duration of the study conducted by Sekandi *et al*. [10] which lasted 18 months. The longer study duration could have helped the study team to diagnose more TB cases which could have reduced the cost per case. Our study was also more extensive–i.e. it included data collected from 12 health facilities across the country yet the study by Sekandi *et al*. [10] only covered the capital city, Kampala. Despite the higher cost, TB-CI could be a worthwhile intervention given that patients are likely to be diagnosed early, thereby decreasing their morbidity and mortality, and the use of TB-CI might result in reduced stigma to the patient since the household has a better understanding of the disease. But it may be helpful to integrate TB-CI with other interventions (such as immunization, malnutrition, family planning or HIV testing) to reduce the cost but also provide more holistic care to families and communities.

Our retrospective observational study was not without limitations. First and foremost, some of the cost data were obtained from published studies but there could have been a publication bias since we did not collect the said data ourselves. It is also worth noting that the data were mainly collected for operational purposes and not for research. Therefore, some data were missing; we tried to circumvent this by corroborating information from a patient's clinical notes and excluding the missing data from the analysis. Secondly, since this study was conducted in an operational setting, we did not have access to sputum cultures and chest radiographs for most of the presumptive TB Cases. Only patients that were pulmonary bacteriologically confirmed using the MTB RIF GeneXpert were considered for study enrolment. The number of TB cases diagnosed using TB contact investigation might have been much higher than anticipated had other diagnostic modalities been considered.

Conclusions

The yield of TB-CI was four-times lower than that of ICF but it cost seven-times more to identify a single case of TB under TB-CI than ICF. These findings suggest that ICF can improve TB case detection at a low cost, particularly in high TB prevalent settings.

Supporting information

S1 File. The intensified case finding tool.
(PDF)

S2 File. Contact investigation tool.
(XLSX)

S3 File. Costing data.
(XLSX)

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