HHS Public Access

Author manuscript

Int J Infect Dis. Author manuscript; available in PMC 2022 August 23.

Published in final edited form as:

Int J Infect Dis. 2021 August ; 109: 129–136. doi:10.1016/j.ijid.2021.06.049.

Contact tracing is associated with treatment success of index tuberculosis cases in Uganda

Joseph Baruch Baluku[1,2,†], **Rachael Alele Kabamooli**[3], **Norah Kajumba**[3], **Martin Nabwana**[4], **David Kateete**[5], **Sarah Kiguli**[6], **Irene Andia-Biraro**[7]

[1]Kiruddu National Referral Hospital, Kampala, Uganda

[2]Makerere University Lung Institute, Kampala, Uganda

[3]Kitebi Health Center, Kampala, Uganda

[4]Makerere University – Johns Hopkins University Research Collaboration, Kampala, Uganda

[5]Department of Microbiology and Immunology, Makerere University College of Health Sciences

[6]Department of Paediatrics and Child Health, Makerere University College of Health Sciences

[7]Department of Internal Medicine, Makerere University College of Health Sciences

Abstract

OBJECTIVE: To determine the effect of contact tracing on the treatment outcomes of index tuberculosis (TB) cases in Uganda.

METHODS: We evaluated TB cases registered at an urban public health facility in Uganda in 2015–2020. We extracted data from the unit's TB and contact tracing registers. Treatment outcomes were classified as cure, loss to follow-up, death and treatment failure. Treatment success was the sum of cure and treatment completion.

RESULTS: Among 778 TB cases, contact tracing was conducted for 455 (58.5%). Compared with cases without contract tracing (n=323), cases with contract tracing (n=455) had higher treatment success (92.5% vs 79.3%) and cure rates (57.1% vs 39.9%) and lower loss to follow-up (3.5% vs 9.3%), treatment failure (0.4% vs 1.6%) and death (3.5% vs 9.9%) (P<0.001). Contact tracing was associated with higher odds of treatment success (adjusted odds ratio (aOR) 3.00, 95%

[†]Corresponding author: PO Box 26343 Kampala, +256706327972. bbjoe18@gmail.com (J.B. Baluku).

Authors' contribution

JBB – Conceptualisation, methodology, data accrual, formal analysis, interpretation of results, drafting manuscript, review and editing manuscript and final approval.

RAK – Conceptualisation, data accrual, interpretation of results, drafting manuscript, review and editing of manuscript and final approval.

NK – Conceptualisation, data accrual, interpretation of results, review and editing of manuscript and final approval.

MN – Formal analysis, drafting manuscript, review and editing of manuscript and final approval.

DK – Methodology, interpretation of results, review and editing of manuscript and final approval.

SK – Methodology, funding acquisition, interpretation of results, review and editing of manuscript and final approval.

IAB – Conceptualisation, methodology, interpretation of results, drafting manuscript, review and editing manuscript and final approval.

Competing interests

The authors declare no competing interests.

CI 1.92–4.70, *P*<0.001) and cure (aOR 3.11, 95% CI 1.97–4.90, *P*<0.001), and lower odds of loss to follow-up (aOR 0.33, (0.13–0.83), *P*=0.018) and death (aOR 0.38, (0.20–0.72), *P*=0.003).

CONCLUSION: TB contact tracing should be conducted consistently not only for the benefit of identifying new TB cases but also to promote treatment success of index cases.

Keywords

contact tracing; investigation; tuberculosis; outcomes; success; Uganda

BACKGROUND

Until 2019, tuberculosis (TB) has been the leading cause of death from an infectious agent and accounted for 1.4 million global deaths in 2019 (World Health Organization 2020). Sub-Saharan Africa has the highest observed-to-expected ratio of TB incidence and is therefore unlikely to achieve the sustainable development goal of ending the TB epidemic by 2035 (Kyu et al., 2018). Globally, 3 million TB cases were not notified in 2019 (World Health Organization 2020). To identify the missing TB cases, the World Health Organization (WHO) recommends contact tracing. Tracing involves the systematic evaluation for TB among close contacts of an index TB case to identify undiagnosed TB among household and close contacts of any TB patient who is HIV positive, has pulmonary TB (PTB) or smear-positive TB, is a child <5 years old, or has drug-resistant TB (World Health Organization 2012). Approximately 3% and 50% of all contacts of TB cases in low- and middle-income countries have active and latent TB, respectively (Fox et al., 2013). Thus, contact tracing has an established role in identifying missing TB cases.

The effect of contact tracing on treatment outcomes for index TB cases is largely unclear. Contact tracing engages the family and other social networks in the care of the index TB patient, which could facilitate treatment adherence of the index patient (Vieira and Ribeiro, 2008). Lack of a contact person was associated with poor TB treatment outcomes in Ethiopia (Amante and Ahemed, 2015). Further, index TB patients who underwent contact tracing had a higher cure rate and lower loss to follow-up rate than those for whom contact tracing was not conducted in Brazil (Oliveira et al., 2017). Only a few reports conclusively support the effect of contact tracing on the TB treatment outcomes among index patients in Sub-Saharan Africa, where the TB treatment success rate (TSR) is only 76%, below the global target of 90% (Izudi et al., 2019). Strategies to increase treatment success are needed in this region where TB/HIV co-infection is prevalent in 31% of TB cases (Gao et al., 2013).

Uganda is a TB/HIV high-burden country that registered a TSR of 74% among new and relapse TB cases and 65% for previously treated (excluding relapse) TB cases in 2018 (World Health Organization 2020). In this study, we determined the association between contact tracing and TB treatment outcomes using a 5-year retrospective cohort of patients at an urban TB clinic in Uganda.

METHODS

Study population and setting

We retrospectively reviewed treatment and contact tracing records at the TB unit of Kitebi Health Center III (KHC), an urban public health facility in Kampala, the capital city of Uganda. The TB unit at KHC offers TB diagnostic and treatment services on an outpatient basis for individuals who predominantly hail from the Kampala and Wakiso districts of Uganda. Bacteriological confirmation of TB was by the MTB Xpert/RIF assay and sputum microscopy. Urine lipoarabinomannan was performed among HIV co-infected individuals with severe immune suppression (CD4 <100 cells/mm^3). Clinical diagnosis of TB was made by the attending clinician, judging by clinical signs and symptoms, imaging abnormalities and/or tissue biopsy. The National Tuberculosis and Leprosy Control Program in Uganda recommended that all patients diagnosed with drug-susceptible TB be initiated on a 6-month regimen with an intensive 2-month phase of rifampicin, isoniazid, ethambutol and pyrazinamide and a continuation phase of 4 months with rifampicin and isoniazid (Ministry of Health 2017). More extended periods of therapy were recommended for TB involving the bones or the central nervous system.

Using the WHO symptom screening tool, contact tracing of household and social contacts of a TB patient was recommended for patients with bacteriologically confirmed TB, TB/HIV co-infected cases and children <5 years old (Ministry of Health 2017, World Health Organization 2013). Contacts with a positive symptom screen were recommended to have further workup at the health facility with a chest x-ray and/or sputum examination with the MTB Xpert/RIF assay or sputum microscopy. The outcome of the contact investigation for each index TB patient was documented in the unit's contact tracing register. The treatment outcome of the index TB patient was documented in the unit's TB register. Historically, more than 15% of TB cases have had an unsuccessful treatment outcome in Kampala TB units (Management Science for Health 2018).

In this study, we included all TB cases that received TB treatment at KHC in 2015–2020 and had a documented TB treatment outcome in the unit's TB register. We excluded cases who had drug-resistant TB and those who were transferred out from KHC.

Study tools and measurements

We used a data extraction tool to collect data from the unit's TB register and contact tracing register. We extracted data on sociodemographics, type of case (new, return after loss to follow-up, relapse and failure), TB class (pulmonary bacteriologically confirmed, pulmonary clinically diagnosed and extrapulmonary), TB treatment details, HIV status and TB treatment outcomes. Sputum bacillary load grades were determined by cycle threshold (Ct) values for cases diagnosed by MTB Xpert/RIF as: very low (Ct >28), low (Ct 22–28), medium (Ct 16–22) and very high (Ct <16) (Lawn and Nicol, 2011). For cases diagnosed by smear microscopy, sputum bacillary grade was classified by number of acid-fast bacilli (Afbs) per field as: 1+ (1– 99 Afbs/100 fields), 2+ (1–10 Afbs/field) and 3+ (≥10 Afbs/field) (Lumb et al., 2013). From the contact tracing register, we extracted data on whether contact investigation was conducted for a given TB case, the number of contacts screened, and

the yield of the contact investigation (number of contacts with presumptive TB, number subsequently evaluated for active TB and number confirmed with active TB).

Study outcomes

The study outcome was the association between contact tracing and TB treatment outcomes. Treatment outcomes of TB cases were defined according to the WHO guidelines (World Health Organization 2013) and were documented in the unit TB register. Specifically, TB outcomes were: cure, treatment failure, treatment loss to follow-up and death. Treatment success was the sum of TB cure and treatment completion, while an unsuccessful outcome was a composite of treatment failure, loss to follow-up and death.

Data management and analysis

Data were entered in EpiData 4.2.1.1 and analysed in Stata 16.0 (STATA, College Station, Texas, USA). Continuous variables were summarised as medians with the corresponding interquartile range (IQR). Categorical variables were analysed as proportions. We compared categorical variables using Pearson's chi-square test and Fisher's exact test, as appropriate. We performed binary logistic regression analysis to determine the association between contact tracing and the TB treatment success of the index TB case. First, we determined the crude odds for all factors independently associated with treatment success using logistic regression. After that, all factors with $P<0.2$ were entered in a multivariable logistic regression model to determine factors associated with treatment success. Cotrimoxazole use induced collinearity with HIV status and was not included in the final model. We performed sensitivity analysis by: i) comparing treatment success between TB cases with and without contact tracing, limited to cases eligible for contact tracing by national guidelines (bacteriologically confirmed, children <5 years and HIV positive (Ministry of Health 2017)); ii) constructing multivariable logistic regression models for factors associated with individual outcomes (cure, death and loss to follow-up) following the same procedure as described for treatment success above; and iii) comparing treatment success of TB cases with and without contact tracing across all subcategories of the variables. Further, we used the Wilcoxon test to compare time to unsuccessful outcome between TB cases with and without contact tracing conducted. Kaplan Meier survival curves were constructed for the 2 groups. Statistical significance was set at $P<0.05$ at 95% CI.

Consent and ethical approval

The study was approved by the Mulago Hospital Research and Ethics Committee (MHREC #2020-8), who provided a waiver of consent because we used retrospective data. Furthermore, patient data were de-identified by using study numbers on the data extraction forms.

RESULTS

Case records were evaluated between February and March 2021; from 1027 TB cases, we included 778 in the study. Figure 1 shows the study flow diagram.

Characteristics of study participants

Among 778 TB cases, the median (IQR) age was 32 (26–40) years, and 406 (52.2%) were co-infected with HIV. With regards to the modality of diagnosis, 323 (42.2%) were diagnosed by MTB Xpert/RIF, 121 (15.6%) by smear microscopy, 6 (0.8%) by urine lipoarabinomannan and 7 (1.2%) by both MTB Xpert/RIF and smear microscopy. Among cases diagnosed by MTB Xpert/RIF, 45 (20.1%), 54 (24.7%), 50 (22.8%) and 70 (32.0%) had very low, low, medium, and very high sputum bacillary load grades, respectively. Among cases diagnosed with smear microscopy, 30 (23.4%), 45 (35.2%) and 53 (41.4%) had 1+, 2+ and 3+ sputum bacillary load grades, respectively. The site of extrapulmonary TB (EPTB) was known in only 16 (34.0%) cases, of which 6 had abdominal TB, 5 had pleural TB, and there was 1 case each of spine TB, meningeal TB, TB of the bone, TB adenitis, and disseminated TB. Other characteristics of the study cases are shown in Table 1.

TB contact tracing and yield of contact tracing among index TB cases

Contact tracing was conducted among 455 (58.5%) index TB cases, the majority (89.9%) of whom were eligible for contact tracing by the national guidelines. Contact tracing was conducted once in 336 (73.9%) cases, twice in 97 (21.3%) and more than twice in 22 (4.8%) cases. The total number of contacts elicited was 1350, and each index case had a median (IQR) of 2 (World Health Organization 2020, Kyu et al., 2018, World Health Organization 2012, Fox et al., 2013) contacts. Among the contacts, 105 (7.8%) had presumptive TB (positive symptom screen), of whom 73 (69.5%) were further evaluated for active TB. TB was confirmed in 29 contacts (39.7%), of whom 14 (48.3%) had bacteriologically confirmed TB.

Treatment outcomes of index TB cases by contact tracing status

Overall, 389 cases (50.0%) were cured, 288 (37.0%) completed treatment, 48 (6.2%) died, 46 (5.9%) were loss to follow-up and 7 (0.9%) failed treatment. The overall TSR was 87.0%. As shown in Figure 2, among index TB cases where contact tracing was conducted, treatment success (92.5% vs 79.3%) and cure (57.1% vs 39.9%) were higher and loss to follow-up (3.5% vs 9.3%), treatment failure (0.4% vs 1.6%) and death (3.5% vs 9.9%) lower, compared with cases where contact tracing was not conducted ($P<0.001$). The median (IQR) time to an unsuccessful outcome was shorter among index cases where contact tracing was conducted (n=15) compared with those without contact tracing (n=33) (2.7 (1.4–4.1) vs 2.8 (0.5–4.9) months, $P_{\text{wilcoxon test}}=0.040$). However, there was variability in survival, as shown by the Kaplan Meier curves in Figure 3.

Factors associated with treatment success among index TB cases

At multivariable analysis, contact tracing was associated with higher odds of treatment success among index TB cases (adjusted odds ratio (aOR) 3.00, 95% CI 1.92–4.70, $P<0.001$), while extrapulmonary forms of TB (aOR 0.400, 95% CI 0.19–0.85, $P=0.017$) were associated with lower odds of treatment success. The bivariable and multivariable logistic regression analysis for factors associated with treatment success is shown in Table 2.

Sensitivity analysis for the effect of contact tracing on treatment outcomes of index TB cases

Treatment success restricted to index TB cases who were eligible for contact tracing—The TSR among index cases eligible for contact tracing (n=689) was 87.4%. Among eligible cases, treatment success was higher where contact tracing was conducted (n=409) than where it was not (n=280) (92.7% vs 79.6%, $P<0.001$).

Association of contact tracing with cure, loss to follow-up and death—As shown in Table 3, contact tracing was associated with higher odds of cure (aOR 3.11, 95% CI 1.97–4.90, $P<0.001$) and lower odds of loss to follow-up (aOR 0.33, (0.13–0.83), $P=0.018$) and death (aOR 0.38, (0.20–0.72), $P=0.003$). HIV co-infection was associated with lower odds of cure (aOR 0.55, 95% CI 0.35–0.87, $P=0.010$) and higher odds of mortality (aOR 2.34, 95% CI 1.17–4.68, $P=0.017$). Being on ART was associated with higher odds of treatment loss to follow-up (aOR 9.20, 95% CI 1.08–78.32, $P=0.042$).

Comparison of subgroup treatment success rates by contact tracing status—Across all subgroups, the TSR was significantly higher among index TB cases for which contact tracing was conducted than in those where it was not. An exception was the age group of >60 years, rural residents, HIV co-infected cases that were not on cotrimoxazole prophylaxis and retreatment cases. However, the absolute numbers were very few for these subgroups and treatment success was still numerically higher in cases where contact tracing was conducted. Table 4 shows the comparison of treatment success across subgroups by contact tracing status.

DISCUSSION

In this study, we assessed the effect of contact tracing on the treatment outcomes of index TB cases at an urban TB clinic in Kampala, Uganda. We found contact tracing to be associated with a 3-fold increase in the odds of treatment success and cure and a >60% reduction in the odds of treatment loss to follow-up and death among index TB cases. Moreover, treatment failure was 4 times lower among index TB cases who had a contact investigation conducted than those who did not. These findings highlight the need to conduct contact investigations not only to identify undiagnosed TB among contacts but also to improve TB treatment outcomes in index TB cases. In addition, contact tracing contributes to increased social support for the index TB case by engaging the household and social contacts, and this is crucial in reducing loss to follow-up (TOLA et al., 2015) and promoting treatment adherence (Vieira and Ribeiro, 2008). Our findings are similar to those by Oliveira et al., who found a higher cure rate (81% vs 57%) and lower rates of death (3% vs 7%) and loss to follow-up (8% vs 11%) among cases that had a contact investigation in Brazil (Oliveira et al., 2017). The cure rate in their study is higher than ours, possibly because their study population was composed of only new TB cases, and HIV co-infection was prevalent in only 9.8% of cases.

The TSR (92%) and death rate (3.5%) among cases that had contact tracing in our study met the End TB Strategy target to end the TB epidemic by 2035 (at least >90% TSR and <6.5% TB-related mortality) (Uplekar et al., 2015). In comparison, the TSR (79%) and

death rate (10%) among cases that did not have contact tracing conducted were below the target. Therefore, contact tracing should be encouraged as one of the strategies to achieve the End TB strategy goals for TB. Unfortunately, only 59% of the index cases in our study had contact tracing conducted. Historically, contact tracing is conducted for only 50% of eligible TB patients in Kampala TB clinics (Armstrong-Hough et al., 2017). Therefore, studies are needed to identify the barriers to conducting contact investigations in this setting to inform strategies to maximise the effect of contact tracing on treatment outcomes.

In interpreting the effect of contact tracing on the treatment outcomes, one needs to be wary of survivor bias, where cases that stayed longer in care could have had more opportunities for contact tracing. In that case, contact tracing may not be the “cause” of treatment success but rather that successfully treated cases had longer engagement with the health care system and were more likely to have contact tracing conducted. However, our results show that this is not the case. First, the time to unsuccessful outcome was shorter among cases for which contact tracing was conducted than in those who did not have a contact investigation (2.7 vs 2.8 months); therefore, it appears that cases with contact tracing did not preferentially stay longer in care. Moreover, this was a difference of approximately 2 days and is not clinically relevant. Secondly, there was no evidence that cases with treatment success had more contact tracing investigations than those with an unsuccessful outcome. Lastly, the effect of contact tracing on treatment success was observed across almost all subgroups, including HIV co-infected and EPTB cases, which were more likely to have an unsuccessful outcome.

We found HIV and EPTB to be associated with unsuccessful treatment outcomes. This association is well established in the literature (Chaves Torres et al., 2019, Ohene et al., 2019, Pepper et al., 2015). HIV impairs immune responses again *Mycobacterium tuberculosis* resulting in an increased risk of TB infection and disease progression. Therefore, people living with HIV are more likely to present with severe forms of TB disease, which carry a high mortality risk (Kwan and Ernst, 2011). EPTB is characterised by an atypical clinical presentation, immune reconstitution inflammatory syndrome when therapy is initiated and requires longer TB treatment regimens and adjunct corticosteroids (Golden and Vikram, 2005). Interestingly, in our study, the odds of having contact tracing conducted were 52% lower in cases with EPTB compared to cases with pulmonary bacteriologically confirmed TB (data not shown). However, the TSR was significantly higher (91%) among EPTB cases with a contact investigation than those without (62%). Contact screening guidelines do not recommend contact tracing among EPTB cases since the risk of TB transmission is presumed to be low. However, EPTB cases can transmit TB to contacts if they have TB of the oral cavity and larynx, open abscesses and concurrent PTB (Centers for Disease Control and Prevention 2014). Therefore, it is worth considering contact tracing in EPTB cases, especially in settings where concurrent PTB cannot be ruled out. As shown by our results, this has the additional benefit of improving treatment outcomes.

We found that the odds of loss to follow-up were higher among cases on antiretroviral therapy (ART) than those who were not. The association between ART and TB treatment loss to follow-up is not very clear. A systematic review of studies from developing countries

found that concurrent ART is equivocally associated with TB treatment loss to follow-up (TOLA et al., 2015). HIV co-infected cases at this study site received ART services on different days than their TB appointments. This lack of integrated TB and HIV services may have contributed to the loss to follow-up among cases on ART.

Our study has some limitations. First, we could not evaluate the effect of other biological markers of TB disease severity such as anaemia, cavitary disease, performance status, and comorbid conditions, other than HIV, on the TB treatment outcomes because these data were not available. Secondly, the study was conducted at an outpatient TB clinic, limiting the generalisability of study findings among TB patients with severe TB disease requiring admission. However, most cases had HIV co-infection and very high bacillary load grades, which are associated with severe TB. In addition, the TSR in our study (87%) is comparable to that observed in urban public health facilities in Uganda (81%) (Musaazi et al., 2017). Lastly, we did not enumerate barriers to contact tracing due to the retrospective nature of the study. The strength of our study lies in the large sample size and elaborate sensitivity analysis that confirmed the association of contact tracing with TB treatment success.

CONCLUSION

Contact tracing is associated with treatment success of index TB cases by increasing the odds of TB cure and reducing the odds of treatment loss to follow-up, death and treatment failure. Therefore, contact tracing should be implemented for the additional benefit of improving TB treatment outcomes in index cases. Furthermore, contact tracing should be considered even in EPTB cases, especially in settings where concurrent PTB cannot be ruled out, to improve outcomes of EPTB cases.

Availability of data

Datasets used in this analysis are available from the corresponding author upon reasonable request.

Acknowledgement

Ms. Namiiro Winnie and Ms. Nalwoga Hajara at Kitebi Health Center participated in data accrual.

Funding source

Research reported in this publication was supported by the Fogarty International Centre of the National Institutes of Health, U.S. Department of State's Office of the U.S. Global AIDS Coordinator and Health Diplomacy (S/GAC), and President's Emergency Plan for AIDS Relief (PEPFAR) under award number 1R25TW011213. The content is solely the authors' responsibility and does not necessarily represent the official views of the National Institutes of Health.

REFERENCES

World Health Organization. Global tuberculosis report 2020; 2020 Global tuberculosis report 2020.

Kyu HH, Maddison ER, Henry NJ, Ledesma JR, Wiens KE, Reiner R, et al. Global, regional, and national burden of tuberculosis, 1990–2016: results from the Global Burden of Diseases, Injuries, and Risk Factors 2016 Study. Lancet Infect Dis 2018;18(12):1329–49 Dec 1. [PubMed: 30507459]

World Health Organization. Recommendations for investigating contacts of persons with infectious tuberculosis in low-and middle-income countries. World Health Organization; 2012 Report No.: 9241504498.

Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: a systematic review and meta-analysis. Eur Respir J 2013;41(1):140–56 Jan 1. [PubMed: 22936710]

Vieira AA, Ribeiro SA. Noncompliance with tuberculosis treatment involving self administration of treatment or the directly observed therapy, short-course strategy in a tuberculosis control program in the city of Carapicuiba, Brazil. J Bras Pneumol 2008;34(3):159–66. [PubMed: 18392464]

Amante TD, Ahemed TA. Risk factors for unsuccessful tuberculosis treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia. Pan Afr Med J 2015:20.

Oliveira SP de, Carvalho MD de B, Pelloso SM, Caleffi-Ferracioli KR, Siqueira VLD, Scodro RB de L, et al. , Influence of the identification of contacts on the adherence of index tuberculosis cases to treatment in a high incidence country. Int J Infect Dis 2017;65:57–62 Dec 1. [PubMed: 28928098]

Izudi J, Semakula D, Sennono R, Tamwesigire IK, Bajunirwe F. Treatment success rate among adult pulmonary tuberculosis patients in sub-Saharan Africa: a systematic review and meta-analysis. BMJ Open 2019;9(9). [Internet]Sep 1 [cited 2019 Dec 30]Available from: https://bmjopen.bmj.com/content/9/9/e029400.

Gao J, Zheng P, Fu H. Prevalence of TB/HIV Co-Infection in Countries Except China: A Systematic Review and Meta-Analysis. PLoS ONE 2013;8(5). [Internet]May 31 [cited 2020 Aug 21]Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3669088/.

Ministry of Health. Manual for Management and Control of Tuberculosis and Leprosy. 3rd Edition. Kampala: Uganda National Tuberculosis and Leprosy Control Program; 2017.

World Health Organization. Systematic screening for active tuberculosis: principles and recommendations. World Health Organization; 2013.

Management Science for Health. Track TB: End of Project report, January 1, 2013–December 31, 2017. Kampala, Uganda; 2018 Jun.

Lawn SD, Nicol MP, Xpert® MTB/RIF assay: development, evaluation and implementation of a new rapid molecular diagnostic for tuberculosis and rifampicin resistance. Future Microbiol 2011;6(9):1067–82 Sep. [PubMed: 21958145]

Lumb R, Van Deun A, Bastian I, Fitz-Gerald M. Laboratory diagnosis of tuberculosis by sputum microscopy: The Handbook. SA Pathology; 2013.

World Health Organization. Definitions and reporting framework for tuberculosis–2013 revision. World Health Organization; 2013 Report No.: 9241505346.

TOLA HH, TOL A, SHOJAEIZADEH D, GARMAROUDI G. Tuberculosis Treatment Non-Adherence and Lost to Follow Up among TB Patients with or without HIV in Developing Countries: A Systematic Review. Iran J Public Health 2015;44(1):1–11 Jan. [PubMed: 26060770]

Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. , WHO's new end TB strategy. The Lancet 2015;385(9979):1799–801.

Armstrong-Hough M, Turimumahoro P, Meyer AJ, Ochom E, Babirye D, Ayakaka I, et al. Drop-out from the tuberculosis contact investigation cascade in a routine public health setting in urban Uganda: A prospective, multi-center study. PLOS ONE 2017;12(11) Nov 6.

Chaves Torres NM, Quijano Rodríguez JJ, Porras Andrade PS, Arriaga MB, Netto EM. Factors predictive of the success of tuberculosis treatment: A systematic review with meta-analysis. PLoS ONE 2019;14(12). [Internet]Dec 27 [cited 2021 May 13]Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6934297/.

Ohene S-A, Bakker MI, Ojo J, Toonstra A, Awudi D, Klatser P. Extra-pulmonary tuberculosis: A retrospective study of patients in Accra, Ghana. PLoS ONE 2019;14(1). [Internet]Jan 9 [cited 2021 May 13]Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6326428/.

Pepper DJ, Schomaker M, Wilkinson RJ, de Azevedo V, Maartens G, Independent predictors of tuberculosis mortality in a high HIV prevalence setting: a retrospective cohort study. AIDS Res Ther 2015;12(1):35 Oct 6. [PubMed: 26448780]

Kwan CK, Ernst JD. HIV and Tuberculosis: a Deadly Human Syndemic. Clin Microbiol Rev 2011;24(2):351–76 Apr. [PubMed: 21482729]

Golden MP, Vikram HR. Extrapulmonary Tuberculosis: An Overview. Am Fam Physician 2005;72(9):1761–8 Nov 1. [PubMed: 16300038]

Centers for Disease Control and Prevention. Chapter 2: Transmission and pathogenesis of tuberculosis. Core Curric Tuberc What Clin Should Know. 2014;

Musaazi J, Kiragga AN, Castelnuovo B, Kambugu A, Bradley J, Rehman AM. Tuberculosis treatment success among rural and urban Ugandans living with HIV: a retrospective study. Public Health Action 2017;7(2):100–9 Jun 21. [PubMed: 28695082]

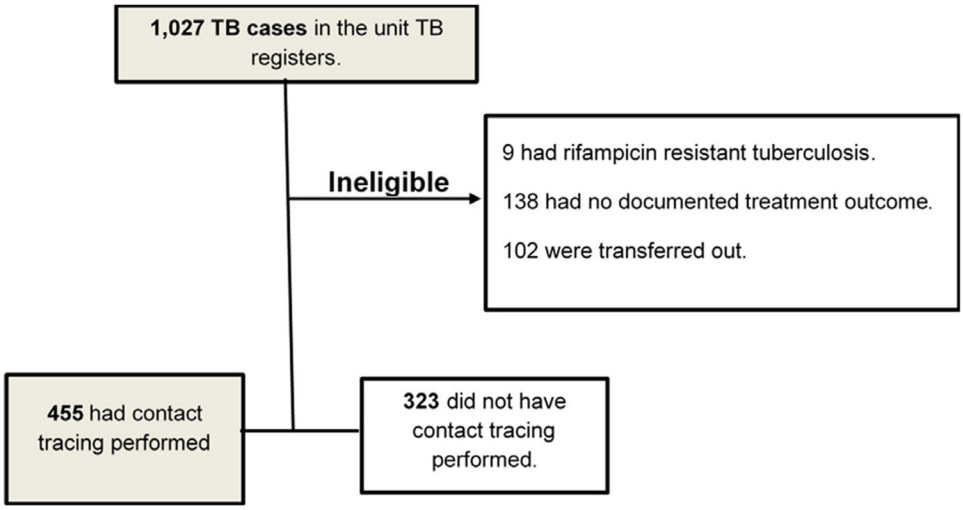

Figure 1.
Study flow diagram.

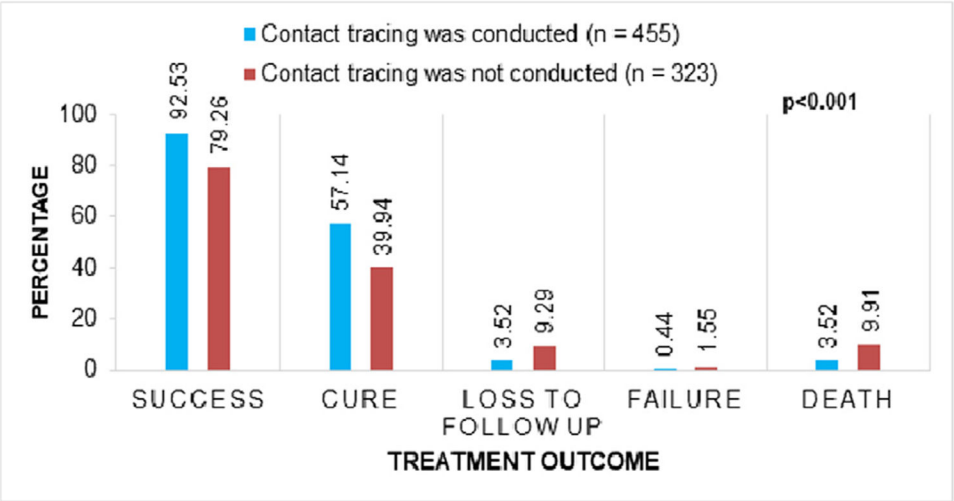

Figure 2.
Treatment outcomes of index TB cases by contact tracing status.

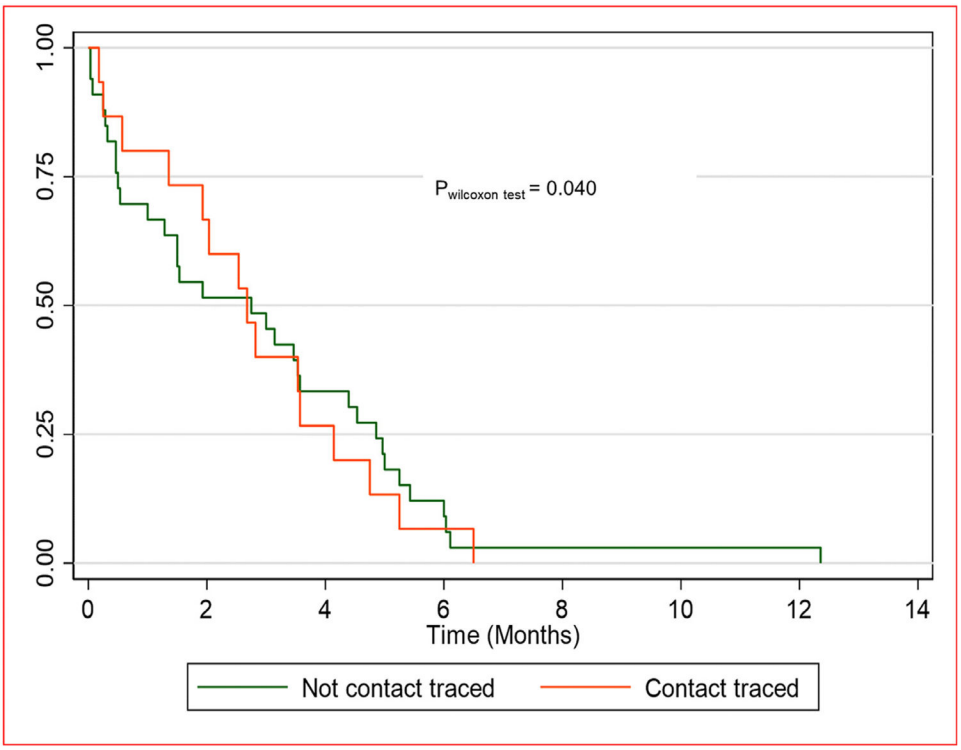

Figure 3.

Kaplan Meier curves showing time to unsuccessful outcome (compositeof loss-to-follow-up, death and treatment failure) among index TB cases by contact tracing status.

Table 1

Baseline characteristics of index TB cases

Baseline Characteristic	Total n (%) (N = 778)
Age (years) (n = 772)	
<15	42 (5.4)
15 – 34	399 (51.7)
34 – 60	317 (41.1)
>60	14 (1.8)
Sex (n = 776)	
Male	526 (67.8)
Female	250 (32.2)
Type of case (n = 763)	
New	726 (95.2)
Relapse	26 (3.4)
Treatment failure	2 (0.3)
Loss to follow up	9 (1.2)
District (n = 774)	
Kampala	568 (73.4)
Wakiso	197 (25.5)
Other	9 (1.2)
Type of residence (n = 735)	
Urban	703 (95.7)
Rural	32 (4.4)
TB disease class	
PBC	451 (58.0)
PCD	280 (36.0)
Extrapulmonary TB	47 (6.0)
HIV status	
Positive	406 (52.2)
Negative	372 (47.8)
ART use (n= 406)[†]	
Yes	325 (80.1)
No	81 (20.0)
Cotrimoxazole (n = 406)[†]	
Yes	378 (93.1)
No	28 (6.9)
Case has phone contact	
Yes	562 (72.2)
No	216 (27.8)

PBC – Pulmonary bacteriologically confirmed, **PCD –** Pulmonary clinically diagnosed, **TB** – tuberculosis, **ART –** antiretroviral therapy

[†]among HIV positive cases.

Table 2

Bivariable and multivariable logistic regression analysis for factors associated with treatment success in index TB cases.

	Bivariable analysis		Multivariable analysis	
Characteristic	**OR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**
Contact tracing done				
No	1			
Yes	3.24 (2.09 – 5.04)	<0.001	3.00 (1.92 – 4.70)	<0.001
Age (years)				
<15	1			
15 – 34	1.06 (0.43 – 2.65)	0.892		
34 – 60	1.22 (0.48 – 3.10)	0.670		
>60	1.00 (0.18 – 5.63)	1.000		
Sex				
Male	1			
Female	0.88 (0.57 – 1.37)	0.574		
Type of case				
Retreatment *	1			
New	0.81 (0.28 – 2.32)	0.688		
District				
Other	1			
Kampala	0.90 (0.11 – 7.34)	0.925		
Wakiso	0.70 (0.08 – 5.77)	0.737		
Type of residence				
Rural	1			
Urban	0.97 (0.33 – 2.84)	0.960		
TB disease class				
PBC	1		1	
PCD	0.54 (0.34 – 0.84)	0.006	0.67 (0.42 – 1.06)	0.089
Extrapulmonary TB	0.31 (0.15 – 0.64)	0.001	0.40 (0.19 – 0.85)	0.017
HIV status				
Negative	1		1	

	Bivariable analysis		Multivariable analysis	
Characteristic	**OR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**
Positive	0.59 (0.38 – 0.91)	0.017	0.68 (0.43 – 1.07)	0.099
ART use				
No	1			
Yes	0.61 (0.29 – 1.30)	0.203		
Cotrimoxazole				
No	1			
Yes	1.88 (0.76 – 4.62)	0.171		
Phone contact available				
No	1			
Yes	1.12 (0.70 – 1.77)	0.641		
No. of times contact tracing was done				
1	1.19 (0.26 – 5.38)	0.819		
2	1.52 (0.28 – 8.07)	0.625		
>2	1			
No. of contacts				
0 – 1	1			
2 – 4	0.81 (0.38 – 1.74)	0.597		
5 – 7	2.50 (0.54 – 11.48)	0.240		
>7	1.13 (0.24 – 5.31)	0.879		

PBC – Pulmonary bacteriologically confirmed, **PCD –** Pulmonary clinically diagnosed, **TB** – tuberculosis, **ART –** antiretroviral therapy, *includes relapse, treatment failure and return after loss-to-follow-up

Table 3

Three logistic regression models for factors associated with cure, loss-to-follow-up and death among index TB cases.

Characteristic	Bivariable analysis		Multivariable analysis	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
FACTORS ASSOCIATED WITH CURE				
Contact tracing done				
No	1		1	
Yes	2.01 (1.50 – 2.68)	<0.001	3.11 (1.97 – 4.90)	< 0.001
Age (years)				
<15	1		1	
15 – 34	6.94 (2.86 – 6.84)	<0.001	1.21 (0.46 – 3.14)	0.701
34 – 60	5.96 (2.44 – 4.55)	<0.001	1.33 (0.50 – 3.53)	0.573
>60	10.80 (2.68–43.52)	0.001	0.80 (0.14 – 4.73)	0.805
Type of case				
Retreatment *	1		1	
New case	0.47 (0.23 – 0.96)	0.038	0.68 (0.20 – 2.30)	0.535
HIV status				
Negative	1		1	
Positive	0.39 (0.23 – 0.96)	<0.001	0.55 (0.35 – 0.87)	0.010
Phone contact available				
No	1		1	
Yes	1.43 (1.05 – 1.97)	0.025	1.07 (0.66 – 1.73)	0.792
FACTORS ASSOCIATED WITH LOSS TO FOLLOW UP				
Contact tracing done				
No	1		1	
Yes	0.36 (0.19 – 0.66)	0.001	0.33 (0.13 – 0.83)	0.018
Age (years)				
<15	1		1	
15 – 34	0.49 (0.18 – 1.37)	0.175	0.51 (0.05 – 5.00)	0.560
34 – 60	0.32(0.11 – 0.94)	0.038	0.21 (0.02 – 2.26)	0.197
>60	1.23 (0.21 – 7.20)	0.816	4.90 (0.18 – 133.03)	0.345

Characteristic	Bivariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
TB disease class				
PBC	1		1	
PCD	1.82 (0.99 – 3.38)	0.052	1.55 (0.63 – 3.79)	0.341
Extrapulmonary TB	0.91 (0.21 – 4.01)	0.901	1.10 (0.22 – 5.57)	0.905
ART use				
No	1		1	
Yes	6.38 (0.85 – 47.87)	0.072	9.20 (1.08 – 78.32)	0.042
FACTORS ASSOCIATED WITH DEATH				
Contact tracing done				
No	1		1	
Yes	0.33 (0.18 – 0.61)	<0.001	0.38 (0. 20 – 0.72)	0.003
TB disease class				
PBC	1		1	
PCD	2.60 (1.33 – 5.08)	0.005	1.92 (0.96 – 3.83)	0.065
Extrapulmonary TB	7.86 (3.30 – 18.71)	<0.001	5.68 (2.31 – 13.92)	<0.001
HIV status				
Negative	1		1	
Positive	2.92 (1.49 – 5.70)	0.002	2.34 (1.17 – 4.68)	0.017

PBC – Pulmonary bacteriologically confirmed, **PCD –** Pulmonary clinically diagnosed, **TB** – tuberculosis, **ART –** antiretroviral therapy, *includes relapse, treatment failure and return after loss-to-follow-up.

Table 4

Comparison of sub-group treatment success rates by contact tracing status

Characteristic	Contact tracing not performed	Contact tracing performed	p-value
AGE (years) (n = 772)			
<15			
Treatment success, n (%)	15 (71.4)	21 (85.7)	0.008
15 – 34			
Treatment success, n (%)	143 (79.4)	202 (92.2)	<0.001
34 – 60			
Treatment success, n (%)	93 (79.5)	186 (95.0)	<0.001
>60			
Treatment success, n (%)	3 (100.0)	9 (81.8)	1.000
SEX (n = 776)			
Male			
Treatment success, n (%)	174 (81.3)	286 (91.7)	<0.001
Female			
Treatment success, n (%)	81 (75.0)	134 (94.4)	<0.001
TYPE OF CASE (n = 763)			
New			
Treatment success, n (%)	242 (79.3)	389(92.4)	<0.001
Retreatment			
Treatment success, n (%)	11 (84.6)	22 (91.7)	0.602
DISTRICT (n = 774)			
Kampala			
Treatment success, n (%)	194 (81.90)	305 (92.2)	<0.001
Wakiso			
Treatment success, n (%)	57 (72.2)	110 (93.2)	<0.001
Other			
Treatment success, n (%)	5 (83.3)	3 (100.0)	1.000
RESIDENCE (n = 735)			
Rural			

Characteristic	Contact tracing not performed	Contact tracing performed	p-value
Treatment success, n (%)	11 (78.6)	17 (94.4)	0.295
Urban			
Treatment success, n (%)	230 (79.9)	383 (92.3)	<0001
TB DISEASE CLASS			
PBC			
Treatment success, n (%)	136 (84.5)	272 (93.8)	<0.001
PCD			
Treatment success, n (%)	104 (76.5)	130 (90.3)	0.002
Extrapulmonary TB			
Treatment success, n (%)	16 (61.5)	19 (90.5)	0.042
HIV STATUS			
Positive			
Treatment success, n (%)	131 (74.4)	211 (91.7)	<0.001
Negative			
Treatment success, n (%)	125 (85.0)	210 (93.3)	0.009
ART USE (n= 406)[†]			
Yes			
Treatment success, n (%)	106 (74.1)	164 (90.1)	<0.001
No			
Treatment success, n (%)	25 (75.8)	47 (97.9)	0.003
COTRIMOXAZOLE (n = 406)[†]			
Yes			
Treatment success, n (%)	118 (75.2)	203 (91.9)	<0.001
No			
Treatment success, n (%)	13 (68.4)	8 (88.9)	0.371
CASE HAS PHONE CONTACT			
Yes			
Treatment success, n (%)	176 (80.4)	315 (91.8)	<0.001
No			
Treatment success, n (%)	80 (89.6)	106 (96.4)	<0.001

PBC – Pulmonary bacteriologically confirmed, **PCD –** Pulmonary clinically diagnosed, **TB –** tuberculosis, **ART –** antiretroviral therapy.