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Variation in tuberculosis treatment outcomes and treatment supervision practices in Uganda

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ABSTRACT

Background: Variation in healthcare delivery is increasingly recognized as an important metric of healthcare quality. Directly observed therapy (DOT) has been the standard of care for tuberculosis (TB) treatment supervision for decades based on World Health Organization (WHO) guidelines. However, variation in implementation of DOT and associated TB treatment supervision practices remains poorly defined.

Methods: We collected individual patient data from TB treatment registers at 18 TB treatment units in Uganda including District Health Centers, District Hospitals, and Regional Referral Hospitals. We also administered a survey and did observations of TB treatment supervision practices by health workers at each site. We describe variation in TB treatment outcomes and TB treatment supervision practices.

Results: Of 2767 patients treated for TB across the 18 clinical sites between January 1 and December 31, 2017, 1740 (62.9%) were men, most were of working age (median 35 years, interquartile range [IQR] 27 – 46), 2546 (92.0%) had a new TB diagnosis, and nearly half (45.9%, n = 1283) were HIV positive. The pooled treatment success proportion was 69.4% (95% confidence interval [CI] 67.8 – 71.1) but there was substantial variation across sites (range 42.6 – 87.6%, I-squared 92.7%, $p < 0.001$). The survey and observation of TB treatment practices revealed that the majority of sites practice community-based DOT (66.7%, n = 12) and request a family member, who receives no additional training or supervision, to serve as a treatment supporter (77.8%, n = 14). At TB medication refill visits, all sites screen for side effects and most assess adherence via self-report (83.3%, n = 15). Only 7 (38.9%) sites followed-up patients who missed appointments using either phone calls (22.2%, n = 4/7) or community health workers (16.7%, n = 3/7). All 18 sites counseled patients at treatment initiation, but none provided additional counseling at refill visits other than addressing poor adherence or missed appointments.

Conclusion: There was substantial variation in implementation of DOT, including observation and documentation of daily dosing, training and supervision of treatment supporters, and follow-up for missed clinic visits. Identifying best practices and reducing uncontrolled variation in the delivery of TB treatment is critical to improving treatment outcomes.

1. Introduction

Treatment success rate, a key metric for assessing the quality of tuberculosis (TB) treatment services, continues to be below the 90% target established by the World Health Organization (WHO) in most high burden countries [1]. Improving the quality of healthcare services

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requires understanding and reducing variation in the workflows and processes of care [2,3]. Renowned physicist and statistician W. Edwards Deming has noted that "uncontrolled variation is the enemy of quality." Although directly observed therapy (DOT) has been a core component of the WHO strategy for improving TB treatment outcomes since 1994 [4], there are limited data on facility-level variation in implementation of DOT and associated TB treatment supervision practices within routine care settings in high-burden countries.

Similar to most high burden countries, TB Diagnostic and Treatment Units (DTUs) affiliated with the Uganda National TB and Leprosy Program (NTLP) use a mix of facility- and community-based Directly Observed Therapy Short-course (DOTS) models for TB treatment management. Once registered, most TB patients are asked to name a treatment supporter and are provided with a 2-week supply of medicines in the intensive phase and a one-month supply of medicines in the continuation phase. Patients are expected to take medicines with observation by the treatment supporter and return to clinic bi-weekly (intensive phase) or monthly (continuation phase) to check on side effects and to obtain refills. DTU staff are expected to assess adherence via patient self-report at refill visits, and to call or visit patients who do not return for refills [4–6].

To better understand the quality of TB treatment services and inform the integration and scale-up of newer strategies such as digital adherence technologies, we collected patient- and facility-level data from health centers in rural and *peri*-urban Uganda to understand the extent of variation in TB treatment outcomes and how TB treatment is delivered.

2. Methods

2.1. Study setting and population

We conducted a cross-sectional study at 18 Uganda NTLP-affiliated TB treatment units. Study sites were chosen in consultation with the Uganda NTLP in preparation for a planned stepped-wedge cluster randomized trial of 99DOTS, a low-cost digital adherence technology [7]. The study sites were eligible for the cluster RCT if they 1) diagnosed > 10 pulmonary TB cases per month in 2016–2017, 2) were not located within Kampala District, 3) were located within 225 km of Kampala, and 4) had a treatment success rate of < 80%. A total of 23 sites met these criteria, of which 18 were chosen in consultation with the Uganda NTLP. The 18 study sites were located in 15 districts (10 in Central, 7 in Eastern and 1 in Western Uganda), with 10 situated in General hospitals, 5 in Regional Referral hospitals, and 3 in District Health Centers.

We included data on all adults (≥18 years of age) initiating TB treatment between January 1 and December 31, 2017 at the 18 treatment units. We excluded patients being treated for extrapulmonary TB or drug-resistant TB, and patients transferred to or from another TB treatment unit. In addition, we administered a survey to the "TB Focal Person" or another senior staff member within the TB treatment unit at each participating site.

The study was reviewed and approved by Institutional Review Boards (IRBs) at the University of California San Francisco (San Francisco, USA) and Makerere University School of Public Health (Kampala, Uganda), and by the Uganda National Council for Science and Technology. All survey participants were consented prior to survey administration and the IRBs granted a waiver of consent for extraction of patient-level data from TB treatment registers.

2.2. Study procedures

Trained research staff visited all study sites to photograph TB treatment registers and upload photos to a secure REDCap server. Project staff then performed single extraction of patient-level data including demographic, clinical, and TB treatment outcome data from the photos for all eligible patients initiating TB treatment using a standardized data extraction form (Supplementary Fig. 1). All data were subsequently reviewed by a data analyst for quality control and any errors or inconsistencies fixed utilizing the treatment registers or by calling health center staff for missing data.

During the site visits, project staff also conducted repeated observations of TB treatment visits and administered a survey to the TB focal person and/or a TB treatment unit staff member after obtaining informed consent. The survey was developed in consultation with local and international experts to assess the organization of clinical services including practices around facility- or community-based DOT, and support systems in place for TB patients and their families (Supplementary Fig. 2). For clinical service organization, we collected information about the use of community- vs. facility-based DOT, and any patient reminder systems. For both facility- and community-based DOT, we asked how often patients had scheduled visits during the intensive and continuation phases of treatment, work-flow, patient wait times, how doses are observed and recorded, how adherence and side effects are assessed and followed-up, and whether treatment supporters are utilized. For support systems, we inquired what type of counseling patients receive, and if any social or monetary support systems are in place. Observations of routine clinical care were done by trained medical officers with experience in TB treatment.

2.3. Definitions

Treatment outcomes were defined according to standard WHO definitions [8]. We considered treatment success to include patients who were recorded as having been cured or completed treatment.

2.4. Data analysis

The data were cleaned and analyzed using Stata version 15.0 (Stata Corporation, USA). Summary statistics such as median and interquartile range (IQR) or proportion and 95% confidence interval (CI) were used to describe characteristics of the study population. The pooled treatment success proportion and 95% CI across sites was calculated using a random effects model. Heterogeneity between health facilities was assessed using the Chi-squared test and the I-squared statistic.

3. Results

3.1. Demographic and clinical characteristics

Of 2767 eligible patients initiated on treatment for pulmonary TB during the study period, median age was 35 years (IQR 27 – 46 years), the majority (62.9%, n = 1740) were male, 1283 (45.9%) had HIV co-infection and 1587 (57.4%) were bacteriologically-confirmed. The proportion male (57.7% vs 64.3% vs 62.8%), proportion HIV-positive (42.6% vs 49.5% vs 43.8%), proportion with bacteriologically-confirmed TB (59.7% vs 57.4% vs 56.6%) and median age (33 vs 35 vs 36 years) were similar when examined across Health Centers, General Hospitals, and Regional Referral Hospitals, respectively.

3.2. TB Treatment outcomes

There was significant variation in TB treatment outcomes across health facilities, with treatment success rates ranging from 42.6% to 87.6% (I-squared 92.7%, $p < 0.001$). Most of the variation occurred at District Hospitals (I-squared 92.9%, $p < 0.001$) and Regional Referral Hospitals (I-squared 91.9%, $p < 0.001$). The pooled proportion of TB patients treated successfully was 69.4% (95% CI 67.8 – 71.1), and was lower at Regional Referral Hospitals (61.2%, 95% CI 58.4 – 64.0) compared to District General Hospitals (72.7%, 95% CI 70.4 – 75.1) and District Health Centers (78.3%, 95% CI 73.8 – 82.7) (Fig. 1).

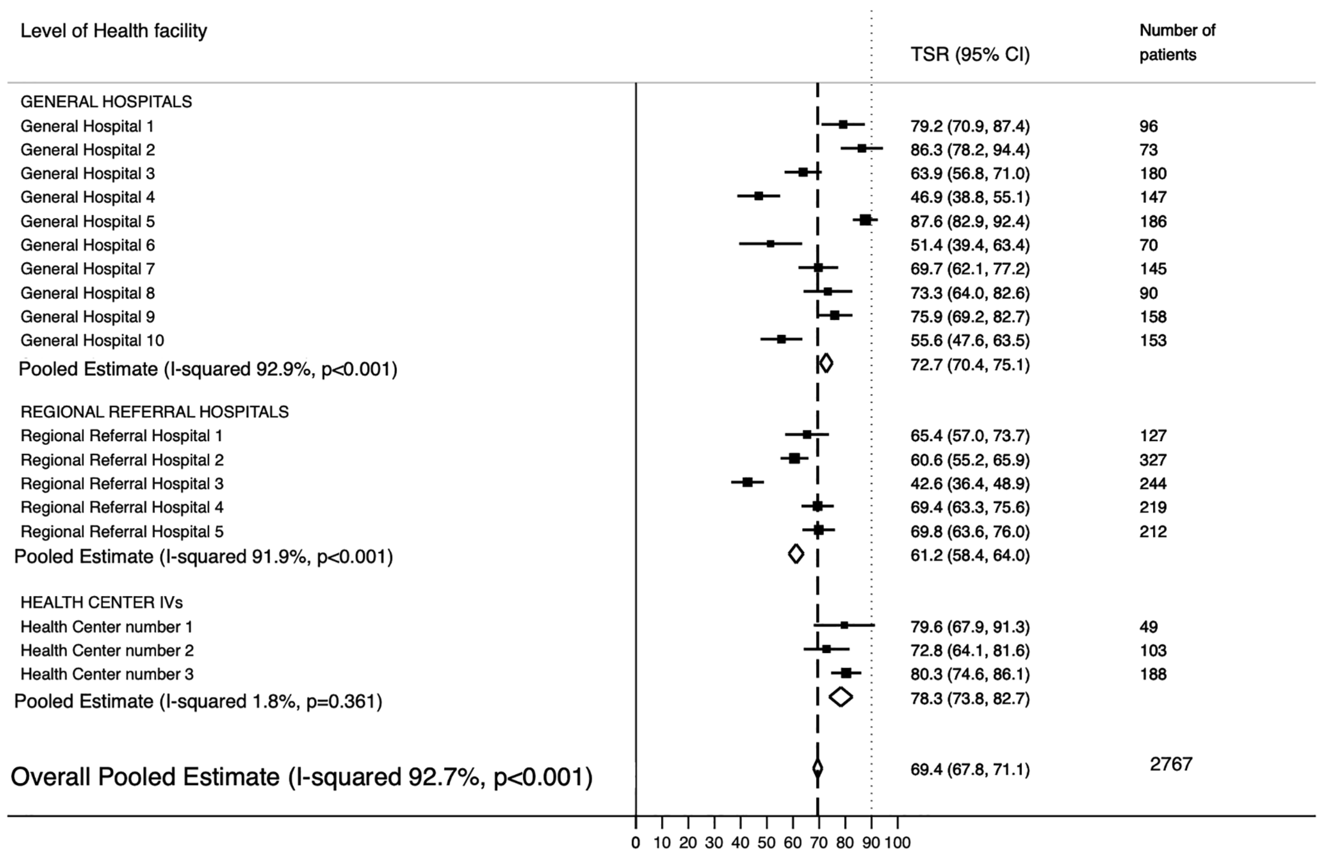

Fig. 1. Forest Plot of Treatment Success by Health Center. Forest plot showing percentage of successful tuberculosis treatment outcomes from January 1st to December 31st, 2017 and corresponding 95% confidence intervals (CI) for 18 health facilities in Uganda. The health facilities are grouped into Level IV Health Centers, District General Hospitals (Level V), and Regional Referral Hospitals. The total overall treatment success rate for the 2767 patients in the study was 69.4% (95% CI 67.8 – 71.1%). The dotted vertical line at 90 is the curative threshold recommended by the World Health Organization for achieving effective control of tuberculosis. There was statistically significant heterogeneity in treatment success across the three levels of health facility (I-squared 92.7%, $p < 0.001$). Compared to Level IV Health Centers, General and Regional Referral Hospitals had lower treatment success rates (78.3%, 95% CI 73.8 – 82.7 vs 72.7%, 95%CI 70.4 – 75.1 and 61.2%, 95% CI 58.4 – 64.0, respectively). Unlike Level IV Health Centers (I-squared 1.8%, $p = 0.381$), there were statistically significant heterogeneity in treatment success rate within General (I-squared 92.9%, $p < 0.001$) and Regional Referral Hospitals (I-squared 91.9%, $p < 0.001$). Abbreviations: TSR, Treatment Success Rate; CI, Confidence Interval.

3.3. TB Treatment supervision

Our assessment of TB treatment supervision practices also revealed substantial variation across health facilities (Table 1). The majority of health facilities practiced community-based DOTS (CB-DOTS) only (66.7%, n = 12). The remaining facilities reported admitting very sick patients (N = 6) or all new TB patients (N = 2) to the inpatient facility for several weeks prior to transitioning to CB-DOTS following hospital discharge. Treatment supporters in CB-DOTS were typically a family member (77.8%, n = 14) who received no additional training beyond what was discussed at the initial visit with the patient and no direct supervision by health workers. While the majority of health facilities asked treatment supporters to observe daily swallowing of medication (88.9%, n = 16), only 5 facilities had government-issued TB treatment cards for tracking ingestion, and none confirmed that treatment supporters were observing doses after the initial visit. Community health workers (CHWs) served as treatment supporters at two (11.1%) health facilities and received incentives to do so at both facilities. Most health facilities assessed adherence at refill visits via self-report (83.3%, n = 15), but none evaluated adherence via pill count or another objective measure. For patients who do not return for refill visits only four facilities (22.2%) regularly called patients and three (16.7%) traced patients with the help of a CHW. In order to support patients, all health facilities (100%, n = 18) reported providing TB counseling at the initial visit, but any subsequent counseling was largely limited to adherence assessment and reminders to not miss refill appointments. Posted TB educational content was present at 10 facilities (55.6%). No facility provided social or monetary support to TB patients.

4. Discussion

We used survey and observational data to examine sub-optimal and varied TB treatment outcomes at health facilities in Uganda with substantial variation in the processes of TB treatment. With increasing recognition that unplanned or random variation in processes of care are a key contributor to poor quality care and outcomes, this study demonstrates there is an urgent need to identify and monitor the implementation of best practices for TB treatment supervision. Furthermore, the suboptimal implementation of DOTS highlights the need for other methods of adherence monitoring and support, such as digital adherence technologies.

A *meta*-analysis examining seven categories of adherence interventions identified that TB treatment outcomes improved with the use of CB-DOTS and trained health workers, as well as the use of patient education, incentives and enablers, psychological interventions, reminders and tracers and digital technologies [9]. With the exception of CB-DOTS, the remaining categories of adherence interventions were either not used or used inconsistently in our study. Moreover, the implementation of CB-DOTS and practices related to adherence assessment and patient counseling and follow-up at refill visits were highly

Table 1
Tuberculosis Treatment Supervision Practices.

	Overall
	N = 18 (%)
<u>Organization of Clinical Services and DOT Practices</u>	
Form of DOT during intensive phase?	
Community-based only	12 (66.7)
Community-based +/- inpatient admission	6 (33.3)
Who observes daily dosing in the community?	
Family Member	14 (77.8)
Community Health Worker	2 (11.1)
Either	2 (11.1)
Treatment supporters:	
Receive specialized treatment supporter training?	0 (0)
Routine supervision by clinic staff?	0 (0)
Receive any incentive?	2 (11.1) *
Asked to observe patients swallow meds?	16 (88.9)
Asked to record daily doses on the treatment card?	6 (33.3)
If a patient misses a refill visit, how are they contacted?	
Phone call	4 (22.2)
SMS	0 (0)
Community Health Worker	3 (16.7)
Use of daily adherence reminders?	
Yes	0 (0)
Refill Visit practices:	
Screen for side effects at each refill visit?	18 (100)
Assess adherence via self-report?	15 (83.3)
Assess adherence via pill count?	0 (0)
<u>Support Systems</u>	
Frequency of TB counseling:	
At treatment initiation only	18 (100)
At all clinic visits	0 (0)
What tools are used for TB Counseling?	
Trained TB Counselor	18 (100)
Educational Handout for Patient	0 (0)
Posted Educational Content	10 (55.6)
Does your facility provide any social or monetary support?	
Yes	0 (0)

*Only those treatment supporters who were community health workers, and not family members, received any incentive for their work at two facilities.
Abbreviations: DOT, directly observed therapy; TB, tuberculosis; CB-DOT, community-based directly observed therapy; FB-DOT, facility-based directly observed therapy; SMS, short messaging service.

varied. Increasing uptake of effective treatment practices, and measuring and reducing variation in their delivery, are critical to improving the quality of TB treatment services and TB treatment outcomes. In the context of COVID-19, extended time between clinic visits for medication refills further reduces the feasibility and potential utility of DOT and highlights the need for alternative strategies for adherence support and monitoring.

Our study has several important limitations. Due to the small number of health facilities included, we were unable to analyze associations between specific TB treatment supervision practices and improved TB treatment outcomes. Further research is needed on how best to reduce variation in the processes of TB treatment. The small sample size also potentially limits the generalizability of our findings.

With recent evidence suggesting that adherence is the strongest predictor of treatment outcomes [10], it is increasingly important to define and scale-up effective TB treatment supervision practices in high-burden countries. While guidelines have traditionally shied away from dictating "best-practices" for DOTS in order to permit flexibility, this has allowed for incredible variation in the delivery of TB treatment. Increased efforts are needed to define best practices and to measure and reduce unplanned variation in TB treatment services in order to improve the quality of care and ultimately achieve the goal of improved TB treatment outcomes.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Author contributions

ST, AC, and AKa conceived of the study. AKi, ML, LKT, JG, ASN, CN, DO, and KC collected and entered data. CB, AKi, RC, and AC analyzed data. CB, AKi RC, AC, and AKa drafted the manuscript. All authors critically reviewed and revised the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jctube.2020.100184.

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