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EXAMINING THE EFFECT OF SERVICE DELIVERY FACTORS ON TIMELY INITIATION OF TUBERCULOSIS TREATMENT WITHIN PRIMARY CARE SETTINGS IN UGANDA

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EXAMINING THE EFFECT OF SERVICE DELIVERY FACTORS ON TIMELY
INITIATION OF TUBERCULOSIS TREATMENT WITHIN PRIMARY CARE
SETTINGS IN UGANDA

by

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2018

DEDICATION

To my late uncle Dr. Wandera Nabaho for the sacrifices made to give me an all-round education

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PREFACE

This dissertation explores missed opportunities in identifying and managing patients presenting with Tuberculosis symptoms. Quite often emphasis is placed on increasing demand for services. But how often do patients present to a qualified health professional and are missed or frustrated and forced to leave before being attended to? Whether right or wrong it, I have always argued that the supply side of healthcare needs more attention especially in developing countries. After all, word about an excellent service will get out quickly! Equally poor service will force patients to seek care elsewhere even if the health facility in question is nearer to them than alternatives. Unlike other diseases, diagnosis and treatment of TB early in the illness is critical to stopping transmission. I am particularly interested in streamlining TB care pathways as part of the innovative ways to eliminate it. Investigating why having efficacious protocols may not necessarily translate into efficient TB care has added another dimension to my understanding of process improvement. Hopefully I can make a humble contribution to the end TB agenda with the skills acquired during this research.

ACKNOWLEDGEMENTS

In a special way I would like to appreciate my dear wife Dr. Dorothy Adong Olet and sons Jeremiah and Jesse for their patience and support that has enabled me come this far.

I am eternally grateful to all dissertation committee members: Dr. Gretchen Gemeinhardt who has always prioritized my academic needs and has supported me throughout my studies at the University of Texas Science Center, Houston; Drs Sheryl MCurdy and Paul Rowan for mentoring me in various aspects of research right from conception of the topic. May God bless you all!

Without the financial and social support from my mentor for decades, Dr. Adeodata Kekitiinwa, and the entire team at BIPAI, I would not have realized my academic dreams. May God reward you abundantly!

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Background: Timeliness of Tuberculosis (TB) treatment is critical to stopping its transmission and preventing disease complications and death. Efficiency in identifying and treating presumptive TB cases is critical to reducing delays.

Aims: We determined the association between health service-related factors and delays in initiating TB treatment within primary care settings in Uganda. Perspectives of healthcare workers on practices underlying healthcare facility level delays were also described.

Methods: A mixed methods study was conducted based on facility-register records of 1199 treated TB cases and key informant interviews with 27 outpatient staffs. Health service-related factors (size, ownership, number of laboratory personnel, diagnostic technology used for diagnosis, sequencing of TB tests and timing with the week of the lab test) were fitted into a linear regression model to identify predictors of TB care process durations and to identify predictors of treatment delay. Qualitative data was analyzed for themes related to healthcare workers' observations and experiences regarding facility level delays.

Results: Median total time for treatment initiation was two days with median time for laboratory results turnaround and for initiating treatment each being one day. Independent predictors of prolonged TB care processes were a weekend laboratory visit ($\beta=0.36$, 95%CI 0.11, 0.60) and retesting after an index negative result ($\beta=1.17$, 95%CI 0.64, 1.69) for laboratory turnaround time; and diagnosis by Gene Xpert test ($\beta=0.39$, 95%CI 0.07 0.71) and having a repeat test irrespective of index result (($\beta=0.51$, 95%CI 0.08, 0.93) if index result was negative, and ($\beta=0.26$, 95%CI 0.06, 0.45) if positive). Factors that increased likelihood of prolonged TAT and or TxIT were weekend lab visit 2.06(1.49, 2.84), diagnosis by Xpert test (aOR 1.79, 95% CI 1.04, 3.10) and repeat testing [aOR 3.49, 95%CI 1.81, 6.75] if index result is negative and [aOR 1.81, 95%CI 1.27, 2.60] if positive). Healthcare workers observed that presumptive TB cases were kept in queues alongside other patients, and staff had a negative attitude to TB patients despite knowing recommended timesaving TB care procedures.

Conclusion: Factors increasing risk of healthcare facility level delay were related care procedures more than a healthcare facility's structure. Despite knowing recommended procedures that minimize delays, healthcare workers report several challenges hampering implementation of protocols.

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BACKGROUND

In 2015 the End TB Agenda was launched with an ambitious goal of reducing global annual Tuberculosis (TB) incidence to less than 10 cases per 100,000 population and TB related deaths to zero by 2035 (WHO, 2015). To achieve this, there must be a precipitous decline in TB levels in the high TB burden countries (HBCs) in Africa and South East Asia. In 2015, Uganda's TB burden was 202 new TB cases per 100,000 population (WHO, 2016); which is 20 times the 2035 target. The case for strengthening healthcare systems in TB control is twofold. First, strong healthcare systems will result into optimal use of current TB control interventions (Chiang et al, 2013). Further, a strong healthcare system is needed to maximize incremental effects of the much-needed new TB-related medical technologies (Lin, Dowdy, Dye, Murray, & Cohen, 2012). Assessing how current TB control interventions are being delivered is therefore a crucial step in transforming the epidemic.

Treatment of symptomatic cases is central to TB control as this stops transmission and prevents adverse disease outcomes simultaneously, unlike other interventions. Because most new TB cases arise from recent transmission, as opposed to reactivation of dormant infection, scaling up treatment alone can substantially reduce TB incidence (Dye & Williams, 2010). This involves patients initiating treatment and adhering to a multiple drug protocol for at least six months. Bottlenecks in diagnosis and initiation of effective medication continue to undermine the population level impact of this TB control strategy. In 2016, Uganda reported a case detection rate of 55% but a treatment completion rate of 73% (WHO, 2016).

Therefore besides its being an entry point, urgent attention to problems surrounding initiation of treatment is dictated by a poor case detection.

National programs do not routinely track proportions of TB cases starting treatment late during the illness (Marais and Raviglione, 2010). Significant transmission and mortality can still occur if most TB cases are treated late in the illness. Improving the count of TB cases initiated on treatment must therefore go along with efforts to minimize delays in care seeking and also within healthcare facilities (HFs). However, there are differences in definitional criteria for TB treatment delay, making it difficult to reliably estimate its extent (Finnie et al, 2011). Also it is not clear how much healthcare system factors contribute to delays, compared to patient-related ones. This lack of crucial information may hamper consideration of TB care related delays among quality improvement priorities. But access to definitive TB care has substantially expanded in most of the HBCs (MoH, 2012; WHO, 2013), which calls for increased attention to quality of TB care being provided within HFs with TB services.

Problem statement

Most TB programs in HBCs, including Uganda, depend on TB patients' self – reporting for consultation before they are identified and treated (Yuen et al, 2015). Considerable time is therefore lost before disease symptoms are serious enough to warrant seeking health care (Ho, Fox & Marais, 2016). When there are HF-level delays in identifying and treating patients with TB symptoms, additional time is lost before effective treatment is eventually initiated. In addition, experience(s) of delay while receiving care also shape

subsequent decisions about seeking care at a particular HF or related ones. Long wait and process turnaround times are major underlying factors for patients shunning publicly owned HFs and yet these are the majority TB services outlets. Even after a patient has an initial consultation, prior experience of delay increases risk of non-adherence to follow up appointments and eventually loss to follow up (MacPherson et al, 2014). Thus, HF level delays not only increase the time of the HF phase of TB care but may also negatively affect care-seeking behavior.

Within a HF, delay may be in identifying and referring presumptive TB cases for testing, completing the required tests, receiving results, or initiating treatment for those with disease. Several service delivery factors causing delays at any one of these steps have been described in TB care literature. These relate to adherence to treatment protocols (Davis et al, 2011); use of antibiotics and other symptom suppressants (Rabin et al 2013); behavior of healthcare workers (Chimbatata, Zhou, Chimbatata, & Xu, 2017); and diagnostic technologies (Yuen et al, 2015). Also, quality of care literature has consistently raised weekend effect to highlight problems faced by patients after hours (Bray et al, 2016). In Uganda there are efficacious TB treatment protocols that are mandated nationally (MoH, 2017a; MoH, 2017b). A key question is whether they are being adhered to. Another aspect is whether delays differ among the types of HFs. Besides type of ownership, Uganda's HFs are organized in a hierarchy depending on daily patient load and number and type of staff skills and available technologies. Publicly-owned HFs may differ significantly from non-profit private ones. Knowing the differences among HF types helps to decide whether the problem of delays requires tailored solutions.

Justification of the study

From a health systems angle, it is important to understand the relationship of service delivery factors with delay in initiating treatment within HFs accredited for TB services. Existing literature on HF level delays has many limitations, which diminishes its value to quality improvement initiatives. Most studies are based on patient interviews limiting detail of care procedures since patients have limited comprehension of technical processes. Also by design, most studies do not distinguish between HFs providing TB care from those that are not. This makes it difficult to tailor interventions to HFs that are providing TB care as a one-stop service. A study design that addresses the above two major weaknesses within existing literature is necessary to understand the problem of delays in the context of expanding access to TB services.

A study undertaken from the perspective of healthcare workers allows for a more comprehensive list of service delivery factors to be studied. Existing records provide a data source from which verifiable details of care processes can be obtained at minimal cost. In-depth interviews with healthcare workers provide an opportunity for personnel to describe the real-life context of the TB care initiation process and suggest ways to improve it. Also through interviews, one can understand various work-arounds in response to existing challenges in TB care.

Specific aims and hypotheses

This study's goal was to examine the association between service delivery factors and timeliness of Tuberculosis treatment initiation within accredited primary care facilities in

Uganda. Service delivery factors are characteristics relating to HF structure (ownership, geographical location, level within health system hierarchy, number of laboratory personnel), and care delivery (number of prescreening visits, diagnostic technology used, two specimen testing, use of antibiotics, and weekend specimen submission).

The specific aims and hypotheses were:

Aim-1: To explore the association between service-delivery factors (structural and care delivery characteristics) and TB care process times (laboratory turnaround time and treatment initiation time)

Aim 1 part 1: Measure the association between service delivery factors and laboratory turnaround time (time from submission of specimens to reporting of results)

Hypothesis 1: Service delivery factors increase laboratory turnaround time

Aim 1 part 2: Measure the association between service delivery factors and treatment initiation time (time from reporting of results to initiation of treatment)

Hypothesis 2: Service delivery factors increase treatment initiation time

Aim 2: Measure the association between service delivery factors and Tuberculosis treatment initiation delay

Hypothesis: Service delivery factors have delay Tuberculosis treatment initiation

Aim 3: Describe perspectives of healthcare workers (heads of OPD, clinical teams and laboratory services) on delays within selected health facilities providing Tuberculosis services.

Review of relevant literature

A major concern about current TB control efforts is that expansion in service coverage has not translated into a substantial decline in TB levels. By 2013, there were reports of substantial expansion in access to free TB care across most of the high TB burden countries (WHO, 2013). But decline in TB incidence has stagnated at 1.5% annually compared to a projection of 5-10% necessary to significantly impact the epidemic by 2020 (WHO, 2015). TB is now the number one cause of infectious disease mortality ahead of HIV; and is among the top 10 contributors to all-cause mortality (GBD 2015 Mortality and Causes of Death Collaborators, 2016).

There are calls for superior technologies but some counter that a lot more can be achieved with existing ones, especially in developing countries where economic constraints disfavor diffusion of technology (Chiang, Van Weezenbeek, Mori, & Enarson, 2013). Across south Asia, for example, there were substantial differences in TB burden despite using comparable technologies for diagnosis and treatment (Onozaki et al., 2015). A strong health system environment free of delays is important to optimizing use of existing tools and maximizing the incremental effect of new ones (Lin, Dowdy, Dye, Murray, & Cohen, 2012). Thus, it is important to understand how health systems in an environment of expanded access is affecting progress towards TB elimination.

Literature review will be limited to high burden countries for relevance to the study setting. This is in four sections. First is the relevance of treatment to TB control. We then discuss the effect of health systems on timely initiation of TB treatment. We then review

literature on the association of service delivery factors with health system -level delays. Finally, we review factors related to the observed practices among healthcare workers involved in TB care.

Contribution of treatment to Tuberculosis control

Global control efforts aim to stop TB transmission while simultaneously improving outcomes of those with disease (Onozaki & Raviglione, 2010). Each year there are close to 10 million new symptomatic TB cases worldwide (WHO, 2016). In addition, it is estimated that one-fifth of the world's population has latent TB infection, which under conditions of immune compromise may be reactivated, progressing into symptomatic disease (Dye, Scheele, Dolin, Pathania, & Raviglione, 1999). Therefore, eradication requires tackling these two facets of TB (Rangaka et al., 2015). However, the global focus currently is on elimination, which creates room for decisions on which facets to tackle to quickly reduce TB levels to a set benchmark.

Prioritization of Tuberculosis control interventions

The current TB control goal is to reduce annual disease incidence to below 10 incident case per 100,000 population globally by 2035 (WHO, 2015). Over 90% of prevalent TB cases are new as opposed to chronic ones (Chiang et al., 2013). Further, these new cases are mostly from recent infection arising from symptomatic cases as distinct from reactivation of latent TB (Dye & Williams, 2010). So most of the TB burden is due to incident cases arising from recent transmission. Accordingly, an intervention that significantly reduces

transmission can turnaround the TB epidemic since this accounts for most of the prevalent cases.

The options for TB control have for decades remained limited to treatment of symptomatic cases to affect cure, prevention therapy to eradicate latent infection, and use of the BCG vaccine (Marais et al., 2010). The biological action of the BCG vaccine currently in use is limited to only preventing progression into severe disease, but it does not stop development of symptomatic disease following exposure to TB bacilli (Marais et al., 2010). Between the other two options, treatment is rated higher than prevention therapy because of the much higher contribution to disease incidence by symptomatic cases relative to latent infection. A patient with pulmonary TB becomes non-infectious within two weeks of initiating treatment (Brooks, Lassiter, & Young, 1973; Rouillon, Perdrizet, & Parrot, 1976). Further, only treatment regimens have adequate drug doses to eradicate bacilli in a symptomatic TB case and thus improve clinical outcomes. Hence treatment is the best TB control strategy as it has the simultaneous action of stopping transmission and TB levels and preventing adverse outcomes.

Significance of treatment initiation in Tuberculosis control

TB treatment currently involves at least six months of an intensive drug regimen. A key question is how is initiation of treatment temporally related to stopping transmission and prevention of adverse disease outcomes? Without treatment, a single TB case will result in 10 to 15 additional cases per year and up to 16-23 new infections over the three-year natural history of the disease (Dye & Williams, 2010). Following initiation of treatment, majority of

TB patients become noninfectious within two weeks (Rouillon et al., 1976). This brings to the fore the importance of treatment early to minimize transmission. Also associated with early treatment is a potential cost saving on care seeking that accounts for most of the high TB related costs currently reported in HBCs (Abimbola et al., 2015; Tanimura, Jaramillo, Weil, Raviglione, & Lonnroth, 2014). Hence the milestone of treatment initiation is a turning point in transmission and economic costs of the disease especially if initiated early in the illness.

Beyond initiation of treatment, however, a longer period of effective treatment is needed to prevent disease complications and death. Mortality, sequelae and disease recurrence is higher among patients who discontinue treatment than those who complete TB treatment (Kolappan, Subramani, Karunakaran, & Narayanan, 2006). Furthermore, discontinuation of treatment increases the risk of developing resistance. Most of the cases of multi-drug resistant TB occur among patients treated that never completed their course of treatment. Therefore, in terms of relevance of treatment initiation, a lot can be gained if treatment is early in the disease, but these gains can be reversed if patients do not complete the treatment course. In this case the milestone is critical as an entry point since the population level impact of treatment ultimately depends on what proportion of prevalent TB cases are on effective medications.

It is important that most prevalent TB cases are initiated on treatment to improve TB incidence and related mortality. Unfortunately, the regular case reporting process cannot be used as an accurate measure of performance because most countries exclude diagnosed TB patients who are not initiated on treatment (Harries, Rusen, Chiang, Hinderaker, & Enarson,

2009). This includes Uganda's national TB control program (MoH, 2017c). Reporting only treated TB cases serves to emphasize linking diagnosis to effective treatment. In 2015, Uganda reported a TB case detection rate (CDR) of 55% (WHO, 2016). This represents the proportion of prevalent TB cases that were treated and therefore effectively removed from the infectious pool. Exclusion of untreated cases underestimates true case detection and case fatality, and also over estimates treatment success. Addressing delays and LTFU therefore helps narrow the gap between treatment initiation and true CDR leading to a more accurate measurement of TB program performance.

Health systems and timeliness of Tuberculosis treatment

The main approach to providing TB services is by integrating TB diagnosis and treatment into primary care in HBCs, in contrast to setting up stand-alone TB clinics. This means effective delivery of TB services is dependent upon a strong health system functioning well in all locations and all primary care services (Cazabon et al., 2017). However, what constitutes a start point for the health system remains unclear especially regarding the setting where care is provided (MacKian, 2003). Here we describe care destinations to which patients with symptoms suggestive of TB may present for consultation.

Conceptual issues on health systems and TB control

Studies on TB care seeking differ in how they identify the start point of a health system. In a systematic review, Finnie et al (2011) noted that what constituted a health system varied among different authors. Some defined this as any facility with a professional

with training in modern medicine while others restricted themselves to settings with both diagnosis and treatment onsite.

The WHO's six building blocks describe desirable attributes of a health system for it to achieve a desired health outcome (WHO, 2007). These are: numbers and skills of healthcare workers, medical logistics and technologies, leadership and governance, health management information systems (HMIS), financing, and service delivery. With regard to TB services, health systems strengthening (HSS) mainly aims to increase access to services, improve quality and reduce financial burden (WHO, 2016). In integrating TB services into primary care in Uganda, the minimum requirements are use of standardized treatment and HMIS protocols, trained personnel, steady stock-levels of medicines and laboratory supplies, and providing services at no charge (MoH, 2012). At a minimum, HSS efforts aim to improve referrals to HFs with definitive diagnostic TB diagnostic services. Developing countries have mushrooming private clinics and other small medical outlets where consultation for most illnesses is first sought and yet their capacity to provide TB services is questionable (Cazabon et al., 2017). Therefore, these present a gap as far as HSS for TB services is concerned.

Effect of health systems on timeliness of Tuberculosis treatment initiation

The period from the onset of symptoms up to the point of initiation of TB treatment in most literature is divided into patient and health system phases (Cai et al., 2015; Finnie et al., 2011; Li et al., 2013; Sreeramareddy, Qin, Satyanarayana, Subbaraman, & Pai, 2014; Storla, Yimer, & Bjune, 2008). The former is when a patient with TB symptoms is seeking care, and

the latter after he or she has presented for consultation. There is heterogeneity in defining the start point for the health system phase and accordingly it is difficult to compare durations of the two phases (Finnie et al., 2011). Even studies which compared the same start point, different cut off thresholds were used to decide whether a patient experienced delay or not differ. The resulting difficulty in comparing the two phases to each other, and the individual phases among studies makes it impossible to decide which phase to prioritize to minimize time to initiation of TB treatment. Studies that define the health system phase as starting when a patient consults with an accredited TB care provider generally report a shorter health system phase (Takarinda et al., 2015). Those that disregard presence of TB services at the start point generally report a longer health system phase because they take referral between providers into consideration (Makwakwa, Sheu, Chiang, Lin, & Chang, 2014). In Angola a much shorter health system phase was observed because of efficient referral of presumptive cases by non-accredited providers. Nevertheless, it is important to consider any time lost after a patient has presented for consultation as a missed opportunity that should be prevented.

Besides its relative contribution to the time before treatment initiation, health systems also influence health-seeking behavior. Characteristics of the health system shape acceptability and subsequent decisions on utilization of services (MacKian, 2003). Convenience of working hours, poor experience with professionals, perceived poor quality of services and requirement for multiple visits have often been cited in explaining delays in consulting with TB service providers (Cai et al., 2015; Finnie et al., 2011; Li et al., 2013; Storla et al., 2008). In Angola, delay in care seeking care at a HF with TB services or

returning for follow up was higher among patients who rated services poorly based on opening hours, waiting time and attitude of health workers (Segagni Lusignani et al., 2013). Similar reasons related to the health system partly explained why patients were lost to follow up (LTFU) even after a diagnosis of TB had been established (MacPherson et al., 2014). A national service survey in Uganda found that only 46% of the population rated services in public facilities as good (UBOS, 2016). But majority of TB cases are currently being treated in government facilities (Cazabon et al., 2017); demonstrating need to engage the private sector to increase odds of a presumptive case engaging with a source of definitive care early in the illness.

The above two contributions of the health system to timeliness of TB treatment are amplified by the fact that resource constraints in HBCs hamper efforts to screen at risk groups before they seek care (Yuen et al., 2015). In waiting for TB patients to self-report for consultation before they are identified and managed, a lot of time is already lost when the patient reaches a HF with TB services. Under such circumstances minimizing delays not only cuts the total time to treatment but also shapes a patient's perception of quality and subsequent utilization of services.

Service delivery factors and health system level delays

The basis for TB treatment protocols is to minimize delays in identifying patients for TB testing, completion of tests and initiation of treatment (TBCARE 1, 2014). Emphasis is on same day physician turnaround of laboratory results and initiation of treatment (Davis et al., 2012). Among the plethora of studies on delays within the health system, a number of issues stand out regarding measurement of delays and the multilevel factors affecting delays.

Measurement of health system level delays

Most studies measure delays as a binary outcome but in a few, this was reported as a time to event outcome. The former report a proportion of patients whose time to event exceeds a cutoff threshold. Some of the recent studies in Africa highlight several issues in describing the magnitude of health system delays as shown in Table 1.

Table 1: Summary of recent studies on health system level delays in Africa

Table 1: Summary of recent studies on health system level delays in Africa

Author/ year	Country	Data source	Study subjects	TB care provider as a start point	Diagnosis time (days)			Treatment initiation time(days)			Total health system time (days)		
					Median time (IQR)	Cut off threshold	% delay	Median time (IQR)	Cut off threshold	% delay	Median time (IQR)	Cut off threshold	% delay
Bogale et al, 2017	Ethiopia	Patient interviews	PTB+EP TB	No	NR	NR	NR	NR	NR	NR	5 (4-7)	NR	NR
Gebreegziabher et al 2016	Ethiopia	Patient interviews	PTB+EP TB	No	NR	NR	NR	NR	NR	NR	22 (4-88)	15	55.8
Mukwakwa et al 2015	Malawi	Patient interviews	PTB+EP TB	No	NR	NR	NR	NR	NR	NR	59 (26-108)	14	47.8
Yimer et al 2013	Ethiopia	Patient interviews	PTB+EP TB	No	NR	NR	NR	NR	NR	NR	27 (8-60)	14	68.7
Buregeya et al 2013	Uganda	Patient interviews	PTB	No	NR	NR	NR	NR	NR	NR	77 (35-168)	7	88
Segagni Lusignani L et al 2013	Angola	Patient interviews	PTB	No	NR	NR	NR	NR	NR	NR	7 (5-15)	14	27.5
Saifodine et al 2013	Mozambique	Patient interviews	PTB	No	NR	NR	NR	1(0-3)	NR	NR	62 (37-120)		
Ukwaja et al 2013	Nigeria	Patient interviews	PTB	No	NR	NR	NR	NR	NR	NR	21 (7-28)	21	25.3
Takarinda et al 2013	Zimbabwe	Patient interviews	PTB	No	NR	NR	NR	NR	NR	NR	2 (1-5)	4	31%
Belay et al, 2012	Ethiopia	Patient interviews	PTB+EP TB	No	NR	NR	NR	1 (1-4)	5	98%	33.5 (17-87)	NR	NR

NR-Not Reported; PTB- Pulmonary Tuberculosis & EPTB- Extra Pulmonary Tuberculosis

Most studies on health system level delays were based on patient interviews. Each study measured both care seeking (patient phase) and the health system phase. Reporting on the health system phase was limited to the total duration of time; none of the studies attempted to compare door to diagnosis and diagnosis to treatment initiation times. The duration of the health system phase varied considerably from 7 to 62 days and respective interquartile ranges that varied from 4 days in Ethiopia (Bogale, Diro, Shiferaw, & Yenit, 2017) to 120 days in Mozambique (Saifodine et al., 2013) . Most of the studies used a 14-day cut off threshold in defining health system level delays. The proportion of patients experiencing delays more than 2 weeks ranged from 47.8 to 68.7% in those studies that included all forms of TB and less than 26% where patients with a microbiological diagnosis were studied.

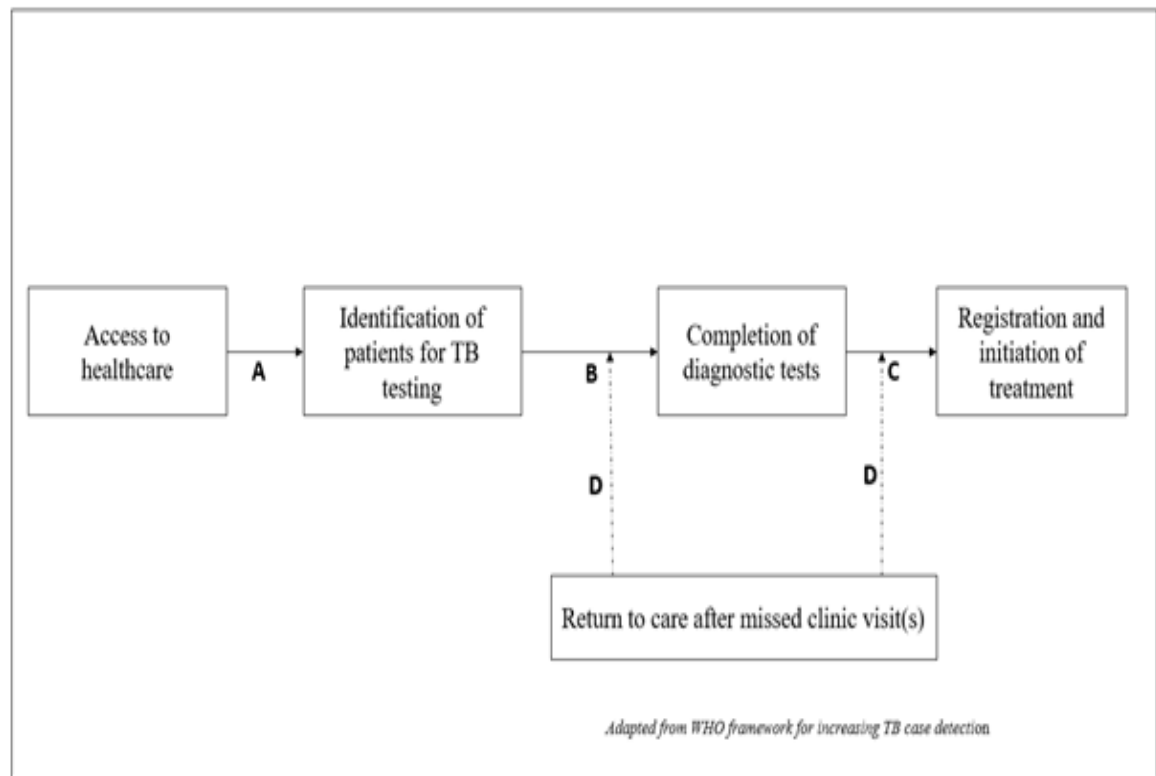
Measurement criteria may make it impossible to compare health system level delays across studies and geographical settings. Finnie et al (2011) observed that the start point for the health system varied among different studies. In Zimbabwe and Angola, only contact with a TB service provider was considered part of the health system phase, and as such fewer patients experienced health systems delays compared to those non-accredited providers who were considered part of the health system phase (Saifodine et al., 2013; Takarinda et al., 2015). Furthermore, although most of these studies defined health system level delay as exceeding 14 days, variability in cut off thresholds has also been previously reported (Finnie et al., 2011). Finnie et al (2011) observed that most studies take into consideration whether the provider offered TB services when defining the health system phase of TB care. There is

limited literature excluding provider-provider referrals and thus measuring delay within health facilities accredited to provide both diagnosis and treatment in a single stop. Even in Angola where a very short duration of the health system phase was reported, this was attributed to efficiency of the referral network rather than most patients having consulted first at a HF providing TB services (Segagni Lusignani et al., 2013).

Association of service delivery factors with health facility delays

Care cascade models provide a framework to visualize and systematically analyze the different care steps leading to a desired care endpoint, in our case initiation of TB treatment. The WHO developed a model to help improve TB case detection by analyzing steps along the TB care cascade up to the point of treatment initiation (WHO, 2011). The figure below is adapted from the section corresponding to care steps between arrival for consultation and initiation of TB treatment.

Figure 1: Care pathway between arrival for consultation and TB treatment initiation



From the above framework, service delivery factors associated with delays primarily relate to identification of patients for TB testing, completing required tests and initiating those with disease on treatment. In addition, a mechanism that traces and returns patients missing follow up could also substantially reduce treatment delays.

The WHO recommends systematic screening of all patients in HFs for TB in settings with HIV prevalence of 5% or more (WHO, 2015b). At the level of screening, ideally all patients presenting with TB symptoms should be identified and referred for testing on their index visit. But studies in HBCs in Africa show that patients make multiple visits to the same provider before they are eventually diagnosed (Bogale et al., 2017; Takarinda et al., 2015). In Tanzania, 50% of TB patients were diagnosed after more than three times seeking care from

the same provider even though they had clear TB defining symptoms (Said et al., 2017). In a study among primary care facilities providing TB services in Uganda, only 20% of patients with cough lasting more than two weeks were referred for TB testing (Davis et al., 2011). Apart from the direct effect of LTFU and prolonging time to eventual diagnosis and treatment, inefficiencies in the screening process also increase costs of care to the patient.

At the level of diagnosis, the current standard is to confirm disease diagnosis and immediately initiate treatment basing on a single positive sputum test (TBCARE 1, 2014). But some HFs require a second test before an individual is eventually diagnosed. Five to eight percent of TB patients are diagnosed on a repeat test the following day after the initial test. Further, microscopy will diagnose only 50% of TB cases that are positive when Gene Xpert is used. In Peru, 42% of TB patients required repeat clinical encounters having previously tested negative on microscopy (Bailey et al., 2011). Additional literature from Africa has also reported patients who initially test negative thus taking longer before a definitive diagnosis was made (Belay, Bjune, Ameni, & Abebe, 2012; Gebreegziabher et al., 2016; Makwakwa et al., 2014). Therefore, at the level of establishing the diagnosis of TB, the type of technology contributes to delay through required repeat visits for testing or return after initially testing negative.

Violation of good clinical and laboratory practices by personnel can also lead to prolonged delays. Fast tracking of services for patients with TB symptoms through shorter wait times and laboratory TAT are essential for TB control (WHO, 2009). Chaisson et al (2015) attributes unnecessary repeat testing, late reporting of laboratory results and poor patient hand offs to non-adherence to standard operating procedures (Chaisson et al., 2015).

In Angola, long waiting times were associated with health facility level delays (Segagni Lusignani et al., 2013). Violations of operating procedures are common under conditions of heavy workload and late or weekend presentation for consultation (Bray et al., 2016). Besides throughput time, a large part of laboratory TAT is contributed to by adherence to standard operating practices (Chauhan, Trivedi, Patel, Gami, & Haridas, 2014). Therefore, even with use of faster and more accurate technologies such as Gene Xpert, treatment delays may still occur due to poor practices by healthcare workers.

A system to trace missing patients and return them to care is a mechanism through which delays and LTFU could be reduced. In looking at HIV care, Hallet et al (2013) proposed a side door into the care cascade to account for patients who are lost temporarily but return at later steps of the care pathway. Absence of pre-appointment and default reminder systems have been reported to have a positive correlation with prolonged delays in returning for follow up and LTFU. Some HF interventions, for example giving antibiotics, may undermine adherence to appointment time and expectations by providing temporary relief of symptoms (Wang et al., 2011; Yimer, Holm-Hansen, Storla, & Bjune, 2014). In settings with inadequate mechanisms to enforce prescription drug regulations, use of antibiotics may provide temporary relief of symptoms (Wang et al., 2011). Thus, at the structural level, lack of a system to track missed visits may exacerbate delays in confirming a diagnosis or initiating those with disease on treatment. But during the process of providing care, relief of symptoms through antibiotics may cause treatment delay.

Besides factors that relate to the care cascade, there are structural factors that may impact health facility level delays. Characteristics of the health facility where the patient first

consults for TB related symptoms have been reported to increase delays in diagnosis. For example, unaccredited HFs fail to identify and refer patients with TB symptoms for definitive diagnosis and treatment (Makwakwa et al., 2014; Segagni Lusignani et al., 2013). At the level of HFs with TB services, ownership of the health facility and its ranking within the health system have been reported to have a causal association with delays. Delays have been reported to occur more among TB patients diagnosed in privately-owned facilities compared to publicly-owned ones (Belay et al., 2012). Regarding ranking in the health system hierarchy, some studies report more delays are at smaller health centers, like health clinics, (Bogale et al., 2017; Gebreegziabher, Bjune, & Yimer, 2016a) while others find this occurs more at district and tertiary hospitals (Saifodine et al., 2013).

Existing studies examining health system level delays focused on facility structural characteristics (Storla et al, 2008; Finnie et al, 2011). This is probably because they are based on patient interviews, which limits details about care processes. An analysis of the care cascade offers an opportunity to identify and analyze process factors. Subsequently a wide array of health service delivery factors that include structural and process ones should be studied and their importance in TB care understood.

Personnel characteristics and health facility level delays

Personnel are a building block for health systems and are thus critical to delivery of TB services (WHO, 2007). Integration of TB diagnosis and treatment into primary care means that personnel should be able to integrate identification and management of presumptive TB cases into their work routines.

Human resources and TB treatment in primary care settings

Developing countries have often faced deficiencies in numbers and skills of healthcare workers due to brain drain amidst increased need to meet demands for decentralized health services (Dovlo, 2004). Task-shifting has accordingly taken center stage in plugging these human resource gaps with outcomes comparable to those with internationally recognized counterparts (Dovlo, 2004). In most primary care settings, most services are provided by medical assistants and enrolled nurses who have taken on responsibilities of medical doctors and registered nurses. It therefore follows that TB services are mostly provided by mid-level healthcare workers.

In addition to pre-service education, mid-level healthcare workers often are trained to be task-oriented with standard operating procedures (SOPs) for providing services. In Uganda, for example, SOPs are simplified and standardized, which is essential to overcoming skill limitations amongst mid-level healthcare workers (MoH, 2017a; MoH, 2017b). In such seemingly good work environments one needs to understand how personnel link to timeliness of TB care.

Personnel characteristics and TB treatment delay

Practices among healthcare workers are the major link between personnel and TB treatment delay. This is in form of communication between service points and activities in identifying presumptive TB cases, ordering and conducting diagnostic tests, providing results to patients, and linking those with disease to treatment (Storla et al, 2008). Significant gaps between knowledge levels and practices in managing patients have cast doubt on adequacy of

training in improving practices of healthcare workers (Grimshaw et al., 2001). Therefore, it is important to develop theory-based interventions to address knowledge and other determinants of behavior concurrently. A critical task however is to identify practices among healthcare workers that these theory-based interventions may address.

Practices that need to be addressed to prevent delays come from observation and intervention studies along the TB care cascade. In an observational study in Uganda, Davis et al (2011) attributed low rates of referral for TB testing, completion of TB testing and initiation of treatment to poor adherence to standard operating procedures [SOPs]. Chaisson et al (2015) and Manabe et al (2015) attributed didactic training and on-site mentorship to better adherence to SOPs and feedback among healthcare workers to improvements in TB case detection and treatment. Feedback enabled healthcare workers to analyze performance and identify areas for improvement (Chaisson et al., 2015). Further, a study in Malawi found that treatment delays often stemmed from efforts by healthcare workers to handle heavy workloads (Chimbatata, Zhou, Chimbatata, & Xu, 2017). Often healthcare workers gave priority to more urgent cases leading to delays in attending to patients with presumptive TB cases. In summary therefore, personnel practices leading to treatment delay relate to adherence to SOPs, dealing with a heavy workload and limited performance feedback.

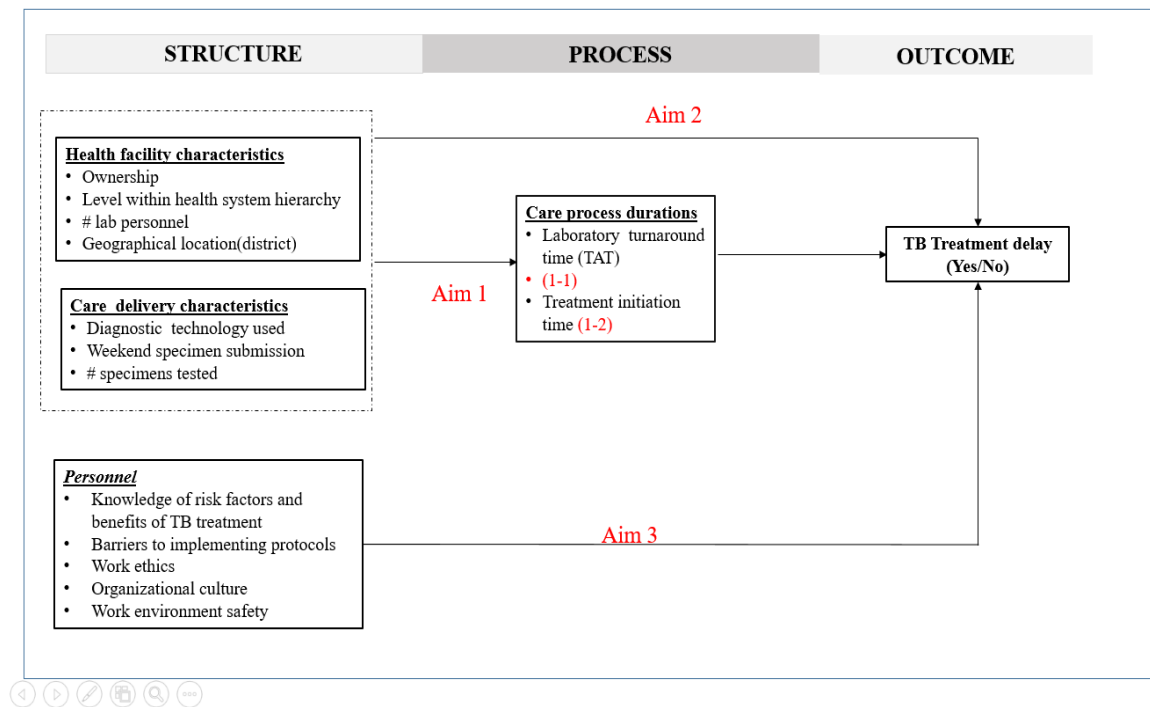
Conceptual framework

The conceptual framework for this study was based on the WHO framework for increasing TB case detection (Onozaki & Raviglione, 2010) and the Donabedian model (Donabedian, 1988). These two frameworks provided us with a frame to visualize the

associations between system and process factors and the outcome of treatment initiation. The Donabedian model links structure, process and outcome to show how health system factors relate to timing of TB treatment initiation. The WHO framework is a pathway to care model describing two ways to realize early TB case detection. The first is a patient-initiated pathway in which a patient with TB symptoms self-reports to a health facility for consultation. Being diagnosed early during the illness depends on a patient's ability to recognize TB symptoms and knowing where to seek care; access to high quality health care services; sufficient capacity of the health facility to identify those who should be tested for TB; providing quality-assured diagnostic testing; and a well-functioning referral system. The second is a screening pathway in which the TB care provider traces and screens close contacts of TB cases and other at-risk individuals who have not yet sought care or have initiated the patient pathway but are not adherent. The patient-initiated pathway is most relevant to this study since the recommended approach to identifying TB is by screening patients within HFs. This encompasses the section of the screening pathway concerning patients initiating the patient pathway but are not adherent.

For the purposes of this study, applicable steps were identification of patients for TB testing, the process of testing for TB onsite by microscopy or Xpert test, referral for treatment initiation within the health facility. From the literature review, several factors related to characteristics of the health facility, care delivery and personnel were identified as contributing to timing of TB treatment as indicated in Figure 2 below:

Figure 2: Conceptual model of service delivery factors related to treatment delay



Public health significance

The goal of this study was to deepen understanding of delays in identifying and managing presumptive TB cases within Ugandan healthcare facilities accredited to provide TB services. These are missed opportunities to prevent transmission, improve individual outcomes and cut TB related costs. This is particularly important in the current context of the current global agenda of eliminating TB by 2035 requiring multi-pronged efforts to accelerate TB control. Delay being a measure of the quality dimension of timeliness makes study findings even more important in identifying areas for improvement in TB care, and by extension the primary care setting within which TB services are integrated. Understanding

service delivery factors from the perspective of the provider especially, through qualitative interviews, is important in prioritizing areas for intervention.

In contributing to the literature needed to minimize missed opportunities in initiating TB treatment, this study's findings contribute to reducing controversies in reporting of untreated TB cases. Diagnosed patients that remain untreated at the time of reporting are excluded from case notification, which underestimates case detection and overestimates positive treatment outcomes. Getting all diagnosed TB cases treated on time avoids such scenarios and gives an accurate and complete picture of TB program performance.

MATERIALS AND METHODS

Study design

The goal of this study was to examine the association between service delivery factors and timeliness of Tuberculosis treatment initiation within primary care facilities. Service delivery factors were characteristics relating to the HF's structure (ownership, geographic location, level within health system hierarchy, number of laboratory personnel), and its care delivery processes (number of prescreening visits, diagnostic technology used, two specimen testing, use of antibiotics, and weekend specimen submission).

The specific aims were:

Aim-1: Explore the association between service-delivery factors (structural and care delivery characteristics) and TB care process times (laboratory turnaround time [TAT] and treatment initiation time)

Aim 1a: Measure the association between service delivery factors and laboratory turnaround time (time between submission of specimen for testing and reporting of test results)

Hypothesis 1: service delivery factors increase laboratory turnaround time

Aim 1b: Measure the association between service delivery factors and treatment initiation time (time between results reporting and initiation of treatment)

Hypothesis 2: service delivery factors increase treatment initiation time

Aim 2: Measure the association between service delivery factors and Tuberculosis treatment initiation delay

Hypothesis: service delivery factors delay Tuberculosis treatment initiation

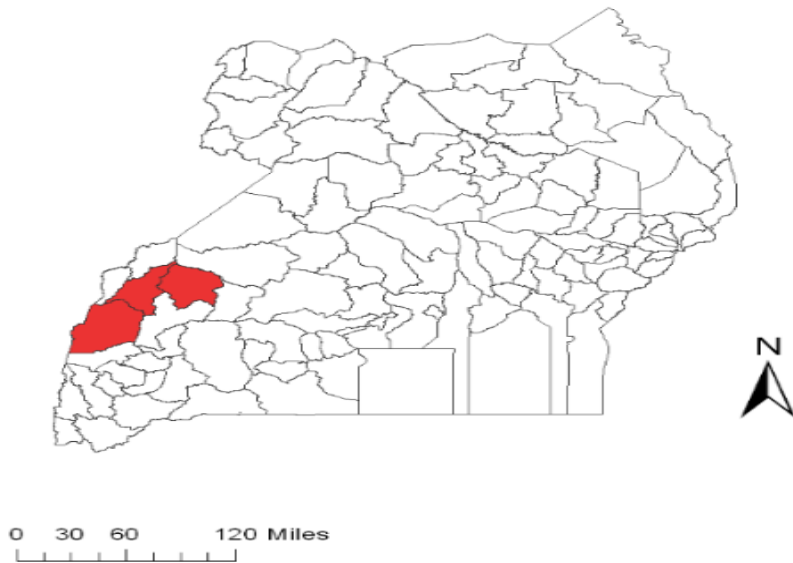
Aim 3: Describe perspectives of healthcare workers (in-charges of OPD, heads of clinical teams and heads of laboratories) on delays within selected health facilities providing Tuberculosis services.

A mixed methods design comprising of a retrospective cohort study using existing TB care records and a case study involving in-depth interviews with healthcare workers was used. Mixed methods is important in understanding complex interactions among a health system's components (Ozawa & Pongpirul, 2014). In this case the qualitative component was necessary to understand practices of personnel providing TB care. A case study design is suitable as the phenomenon (actions of personnel) needs to be studied in the real-life context (Carolan, Forbat, & Smith, 2016).

Study setting

The study was conducted in the districts of Kabarole, Kasese and Kyenjojo in mid-western Uganda shown in the map (*Figure 3*).

Figure 3: Location of study districts in Uganda



Source: Uganda Bureau of statistics, 2016

Here HFs are organized in a hierarchy by size of the catchment population and available scope of services. Primary care HFs comprise of hospitals and, below this, different levels of health centers while tertiary care comprises of regional and national referral hospitals. Unlike tertiary hospitals that under direct control of the central government , the work of primary care facilities are under district local governments that oversee planning and provision of services in line with policies and care standards set by the central government.. All HFs with a functional laboratory (district hospitals, and levels IV and III health centers [HCs]) are eligible for accreditation to provide TB diagnosis and treatment. Catchment populations for the different HF levels are 30,000 people for a level three Health Center (HCIII); 100,000 people for a level four Health Center (HCIV); and 300,000-500,000 people

for a district hospital. Each HF level has a defined staffing standard with technical teams headed by medical officers at HCIVs and district hospitals, and medical clinical officers at HCIIIs.

TB care is provided free of charge as an outpatient service across all publicly owned and non-profit HFs. Each of these HFs provide diagnostic testing through microscopy or Gene Xpert (Xpert). A mechanism also exists for certain categories of presumptive TB patients to have their specimens referred for a more advanced Xpert test if microscopy is negative or drug resistance is suspected. Laboratory services are supported by an external and internal quality assurance system run by the national TB reference laboratory. Decisions on treatment are based on nationally mandated protocols. A decision to start TB treatment is based on either laboratory confirmation of the diagnosis or clinical grounds. The protocol recommends treatment be initiated at the HF where diagnosis is made before a request to transfer to another HF is considered.

In the period January 2016 to June 2017, the three districts accounted for 59.9% of the diagnosed TB cases in the region; 60% in 2016 and 57.9% in 2017 respectively.

Table 2: Tuberculosis case load from January 2016 to June 2017

DISTRICT	Number of Health Facilities	2016	2017 (up to June)	Total
Kabarole*	34	565	239	804
Kasese	33	338	168	506
Kyenjojo	18	303	135	438
TOTAL	85	1206	542	1748

** Approximately 45-50% of TB cases are diagnosed at the regional referral hospital*

(Source: Mid-Western Zonal TB and Leprosy program office)

QUANTITATIVE COMPONENT (AIMS 1&2)

Study design

The association between service delivery factors (structural and care delivery characteristics) and process time (aim 1) and that between service delivery factors time and TB treatment (aim 2) were assessed using existing care records for patients with laboratory confirmed TB from January 1st, 2016 to December 31st, 2017. This start point was chosen because this is the time when most of the current TB care data capture tools were introduced.

Study population

The study population was TB cases within the districts of Kabarole, Kasese and Kyenjojo in Western Uganda diagnosed using either microscopy or Xpert test, which are the recommended laboratory tests for diagnosis of TB in primary care settings (MoH, 2017a). The study excluded TB patients diagnosed using radio imaging or on clinical grounds since these are not the gold standard for diagnosis.

Sampling frame, sample selection and sampling strategy

The sample frame comprised of all laboratory confirmed TB cases diagnosed at accredited HFs within the three districts during the period January 1st, 2016 to December 31st, 2017. Data for all TB patients with a positive microscopy or Xpert test were screened for eligibility. Patients who were not diagnosed and initiated on TB treatment at the same study site were excluded. This included patients diagnosed after referral of specimens for Gene Xpert and other advanced diagnostic tests; patients transferred in or out of the HF before starting. These are patients among whom exogenous causes of delay that are associated with referral could not be excluded.

A purposive multi-stage sampling approach was used in which the top three high TB burden districts in the region (Kabarole, Kyenjojo and Kasese) were selected for data collection. In each district, all laboratory confirmed TB cases in any HFs providing single stop TB diagnosis and treatment were included.

Data sources

Existing data on TB care was obtained from the district health office registry and TB care registers. Each district health office registry has a paper-based register that contains information about all HFs operating in the district in terms of ownership, geographic location, level within the health system hierarchy, and staffing levels. This registry was updated by the district health officer whenever licensure for new services, changes in personnel and opening of new HFs occurred.

TB care registers are nationally standardized, paper-based records. There are two main registers: laboratory sputum register and unit's TB register. Patient information is entered into these registers at all TB care service points within a HF. Each register has an illustrated set of instructions to guide healthcare workers' entering records. Only the Ministry of Health (MoH) reviews and revises the registers. Full or obsolete registers are securely archived within the records department stores in each HF. The table below describes information entered about each TB patient in each of the two HF registers and facility information in the district register. This information entered in the registers had not significantly changed among the different versions of the registers in use since 2016.

Table 3: Data Elements in Each Tuberculosis Care Register

Register	Place of deployment	Purpose/description	TB care related information**
Laboratory register	Laboratory	<ul style="list-style-type: none"> Registry of patients submitting sputum for TB testing including samples referred to a central laboratory 	<ul style="list-style-type: none"> Sputum specimen submission date Diagnostic test used (Microscopy/Xpert) Number of specimens tested Test results for each specimen HIV status Patient sociodemographic characteristics- name, age, sex
Unit TB register	Pharmacy/ HF dispensary	<ul style="list-style-type: none"> Registry of patients treated for TB at HF including transfers-in 	<ul style="list-style-type: none"> Results reporting date Treatment initiation date Previous TB treatment history Patient sociodemographic characteristics- name, age, sex
District health office registry	District health office	<ul style="list-style-type: none"> Record of HFs and staff deployment in the district 	<ul style="list-style-type: none"> HF name and ownership Level within health system hierarchy District name Number of personnel by cadre

**** Up to the point of treatment initiation**

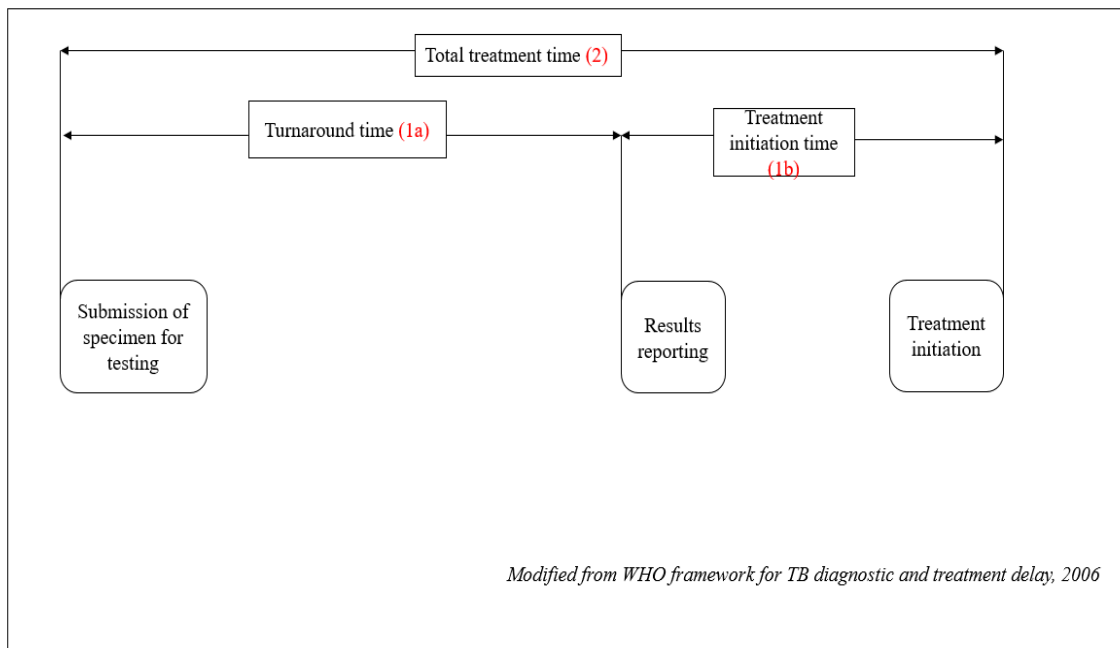
Quarterly unit TB register data is reported by the district TB supervisor who transfers this information from all HFs into the district TB master register. The district register was used to check for missing information in the laboratory and treatment registers on sociodemographic variables and care dates.

Measurements and instruments

Individual patient data start and end points were sputum submission date and initiation of TB treatment respectively. The sputum submission date was when a patient visited the lab for testing and his/her personal details were entered in the laboratory sputum register. Initiation of treatment date was when the TB patient was issued a treatment card and dispensed his/her first dose of anti-Tuberculosis medicines, which was entered in the unit TB register..

Study variables were derived or computed from TB care related information in the clinical registers or district health office registry. Three key TB care milestone dates -- specimen submission, results reporting and treatment initiation -- were used to compute the following time related variables as shown in Figure 4 below:

Figure 4: Timeline diagram for Tuberculosis treatment initiation



From the above timeline diagram, three time related variables were computed:

- Total treatment time – interval in calendar days between specimen submission and initiation of treatment ([initiation of treatment date minus specimen submission date] +1)
- Laboratory turnaround time- interval in calendar days between submission of sputum specimen to the laboratory and reporting of the diagnosis ([resulting reporting date minus first sputum sample submission date]+1)

- Treatment initiation time interval in calendar days between reporting of the diagnosis and initiation of treatment ($[\text{treatment initiation minus resulting reporting date}] + 1$)

The primary outcome was treatment delay. This was measured by dichotomizing treatment delay as more than two calendar days, and no delay if less. This cut off threshold was based on ISTC guideline, which recommends same-day physician TAT of laboratory TB results and initiation of treatment (TBCARE1). A two-day threshold allowed for patients who needed a repeat test having initially tested negative on the first specimen. All study measures were categorized as outcome process or structure measures depending on the component of the Donabedian model they best describe as shown in the table below:

Table 4: Categorization of study variables

Variable category	Measured variable
Outcome	
<i>Timeliness of TB treatment initiation</i>	Treatment delay
Process	
<i>Process time</i>	Laboratory TAT
	Treatment initiation time
Structure	
<i>Health facility characteristics</i>	Ownership, geographic(district) location, level within health system hierarchy, and number of laboratory personnel
<i>Care delivery characteristics</i>	Technology used for diagnosis, Use of antibiotics prior to diagnosis, Number of pre-diagnosis visits, Use of two specimens for diagnosis, and Submission of a TB specimen on a weekend
<i>Patient characteristics</i>	Name, age, sex, previous history of TB and HIV status

The above variables are dependent or independent variables, or co-variates depending on the aim being assessed as shown in the measurement matrices below:

Table 5: Measurement matrix (aims 1a & 1b)

Measured variable	Data source(s)	Definition	Variable type
<i>Dependent variables</i>			
Laboratory Turnaround time (1a)	Laboratory register, Unit TB register	Time interval in days between specimen submission and results reporting dates	Continuous
Treatment initiation time (1b)	Unit TB register	Time interval in days between results reporting and treatment initiation dates	Continuous
<i>Independent variables</i>			
<i>Health facility characteristics</i>			
Health facility Ownership	District registry	Health facility affiliation	Categorical (Public/Private)
HF Level	District registry	Ranking of HF within health system hierarchy	Categorical (HCIII/ HCIV/district hospital)
Number of laboratory personnel	Laboratory reports	Sub-grouping of unduplicated number of laboratory personnel on duty register during study period	Categorical
Geographic location	Laboratory register	District location of HF	Categorical
<i>Service delivery characteristics</i>			
Weekend specimen submission	Laboratory register	Specimen submission date on a Friday, Saturday or Sunday	Categorical (Yes/No)
# specimens tested	Laboratory register	Number of specimens tested during diagnostic episode	Categorical (1,2 or 3)
Lab test sequence	Laboratory register	Order of tests conducted	Categorical (single or repeat)
<i>Covariates</i>			
<i>Patient characteristics</i>			
Age	Laboratory register	Years	Continuous
Sex	Laboratory register	Male/Female	Categorical (Male/Female)
HIV status	laboratory register	Documented HIV status	Categorical (positive/ negative)
Previous history of TB treatment	Treatment register	TB treatment prior to current diagnosis episode	Categorical (yes/No)

Table 6: Measurement matrix (aim 2)

Measured variable	Data source(s)	Definition	Variable type
Dependent variable			
Treatment delay	Lab & Unit TB registers	≥ 3 days between sputum submission and treatment dates	Categorical (Yes/No)
Independent variables			
<i>Health facility characteristics</i>			
Health facility Ownership	District registry	Health facility affiliation	Categorical (Public/Private)
HF Level	District registry	Ranking of HF within health system hierarchy	Categorical (HCIII/ HCIV/district hospital)
Number of laboratory personnel	Laboratory reports	Sub-grouping of unduplicated number of laboratory personnel on duty register during study period	Categorical (1-2,3-4 & 5+)
Geographic location	Laboratory register	District location of HF	Categorical (Kasese/Kabarole/Kyenjojo)
<i>Service delivery characteristics</i>			
Weekend specimen submission	Laboratory register	Specimen submitted on a Friday, Saturday or Sunday	Categorical (Yes/No)
# specimens tested	Laboratory register	Number of specimens tested during diagnostic episode	Categorical (1,2 or 3)
Lab test sequence	Laboratory register	Order of tests conducted	Categorical(single/repeat)
Covariates			
<i>Patient characteristics</i>			
Age	Laboratory register	Years	Continuous
Sex	Laboratory register	Male/Female	Categorical (Male/Female)
HIV status	laboratory register	Documented HIV status	Categorical(positive/negative)
Previous history of TB treatment	Treatment register	TB treatment prior to current diagnosis episode	Categorical (yes/No)

Sample size and power calculation

We used known estimates of TB cases over the study period to compute power to detect significant difference among hospitals, level four Health centers (HCIVs) and level three Health centers (HCIIIs). These are the three different levels within the health system hierarchy that provide TB services. We estimated a two year total TB case load of 240 patients among hospitals, 150 among HCIVs and 720 among HCIIIs as summarized in Table 7 below:

Table 7: Estimated sample size by health facility level

Health facility level	Number of Health Facilities	Average # TB cases	Total
Hospital	6	40	240
HCIV	5	30	150
HCIII	72	10	720
TOTAL	85		1,110

Based on the above estimated totals for each HF, we determined the power to detect significant difference in treatment delay between district hospitals and HCIVs. A study in Zimbabwe found 20.5% delay at district hospitals compared to 37.6% at health centers (Takarinda et al, 2015).

Power estimation was computed using OpenEpi version 3, version three based on a formula for cohort studies.

Using the above estimates of delays as a guide and with TB cases at HCIV as exposed group (150) and those among hospitals as non-exposed (240), risk ratio of delays between the two groups was used to compute power of the study as shown in table 8 below:

Table 8: Power estimation for the study

Parameter	Input data
Confidence interval (%)	95
Number of exposed (TB cases at HCIV level)	150
Risk of delay among exposed	37.6
Number of non-exposed (TB cases at Hospital level)	240
Risk of disease among non-exposed	20.5
Risk ratio	1.8
Power (based on normal approximation)	96.15

Therefore, a sample size involving 150 TB cases at HCIV and 240 at hospital level had power of 96.15% to detect significant differences in delay at the two levels as shown in table 8.

Data collection and management

Data abstraction: Data was abstracted from TB care registers for the period between January 1st 2016 and December 31st, 2017 by trained research assistants using paper abstraction forms (*appendix ii*). At each HF, all registers were collected at a central point before data abstraction commenced. Assisted by HF record assistants, research assistants identified each patient in the laboratory register that had a positive microscopy or Gene Xpert result and followed him or her into the treatment register. With exception of a HCIII that lacked a

laboratory register for the period January 1st to July 25th, 2016, each HF had both registers. For six confirmed TB patients in another HCIII however, corresponding records in the treatment register were missing. These six patients were assumed not to have started TB treatment and thus were excluded since there was no evidence of them ever being started on treatment.

Starting with the laboratory register all patients with one or more positive Xpert or microscopy test results were identified and screened for study eligibility. After abstraction of relevant study information each patient was then traced through the unit treatment register. Each study subject had an individual abstraction form for recording all relevant information across the two TB care points. Four patients whose laboratory records lacked a specimen submission date were excluded because they lacked a critical study start point. Sociodemographic characteristics were concordant between the two registers except for a few instances where last names were used to determine a patient's missing gender.

Data on HF's structure (ownership, geographical location, level within health system hierarchy and number of laboratory personnel) was collected from the district health office registry using a health facility data extraction form (appendix ii). Abstracted data from the district health office registry was then confirmed with the health facility in-charge officer at the time of obtaining consent to conduct research. Periods of drug stock outs were recorded at each facility from stock cards and contrasted with each patient's results reporting date to establish whether diagnosis was made during outage of drugs or not.

Data storage: The principal investigator checked filled abstraction forms for accuracy and completeness daily. Repeat facility visits were conducted to make necessary corrections and

collect missing data. All collected data was stored in a filing cabinet in a room only accessible by the principal investigator. Electronic data was stored in folders on a password-protected computer and encrypted mobile devices.

Reliability and validity of measurements: The following activities were conducted to improve accuracy and inter-rater reliability of study findings:

- Training of research assistants by the principal investigator that also included practice sessions
- Pilot testing of data collection tools for content, flow and clarity as well as acceptability
- Daily review of collected data for accuracy and completeness
- Repeat site visits to correct data
- Quality assurance check conducted by principal investigator by randomly selecting 5% of the study subjects, re-abstracting their TB care information and comparing it to information already collected by research assistants.

Data analysis

The unit of analysis was a patient with laboratory confirmed TB basing on a Gene Xpert or microscopy test. Data for each study subject was entered in epi-Data version 7 and exported into STATA version 15 (College Station, TX USA) for analysis.

Descriptive statistics were summarized using frequencies and counts for categorical data; and means (SD) and medians (IQR) for continuous variables as appropriate. Findings were displayed in frequency tables. A complete case analysis approach in which patients with missing records are excluded was used. Multiple regression models were used to test hypotheses in both aims 1 and 2.

Independent variables with p-value >0.25 at univariate analysis were excluded during multivariable regression. Selection of factors for the final model was done using a backward –forward stepwise approach for both aims 1 and 2. Predictors with p-value<0.15 and those with known scientific relation to the outcome were then retained in the final model. A level of 5% was used to assess statistical significance of predictor variables.

To test the association between service-delivery factors and process time, structural and care delivery factors were fitted in a multiple linear regression model while controlling for patient characteristics. In this case the primary outcomes were continuous variables (Turnaround time (TAT) for aim 1a and treatment initiation time (TIT) for aim 1b).

The baseline statistical model for aim 1 was:

$$Y = \beta_0 + \beta_1 HF_1 + \dots + \beta_4 HF_4 + \beta_5 CD_1 + \dots + \beta_8 CD_4 + \beta_9 PC_1 + \dots + \beta_{12} PC_4 + \epsilon$$

Where:

Y = process time (Turnaround time [TAT] for aim 1a or Treatment initiation time [TIT] for aim 1b)

β_0 - β_{13} = coefficients for model variables

HF1-HF4 = Health facility characteristics (Ownership, Geographical location, level within health system hierarchy, and number of laboratory personnel)

CD1-CD4= Care delivery characteristics (diagnostic technology used, number of specimens tested, sequence of tests and weekend lab visit)

PC1-PC4= Patient characteristics (age, sex, HIV status, previous history of TB treatment)

The analysis matrices for aims 1a and 1b are summarized below:

Table 9: Analysis matrix for study aim 1

	#Aim 1a	#Aim 1b
Hypothesis	Service delivery factors increase laboratory turnaround time	Service delivery factors increase treatment initiation time
Dependent variable(s)	Turnaround time (TAT)	Treatment initiation time (TXIT)
Independent variables	Service delivery factors <ul style="list-style-type: none"> - Health facility characteristics [HF] - Care delivery characteristics 	Service delivery factors <ul style="list-style-type: none"> - Health facility characteristics [HF] - Care delivery characteristics CD]
Covariates	<ul style="list-style-type: none"> • Patient characteristics [PC] (age, gender, HIV status, previous TB treatment) 	<ul style="list-style-type: none"> • Patient characteristics [PC] (age, gender, HIV status, previous TB treatment)
Statistical approach	Linear regression	Linear regression
Estimate	Coefficient	Coefficient
Level of significance, α	5%	5%

For aim 2, we used multiple logistic regression model since the primary outcome (treatment delay) was a binary categorical outcome defined as 1= treatment delay and 0= no treatment delay. The final logistic regression model controlled for patient characteristics. All the service delivery factors were tested using a single model shown below:

$$\text{Logit (TD)} = \beta_0 + \beta_1 \text{HF}_1 + \dots + \beta_4 \text{HF}_4 + \beta_5 \text{CD}_1 + \dots + \beta_8 \text{CD}_4 + \beta_9 \text{PC}_1 + \dots + \beta_{12} \text{PC}_4$$

Where:

TD = treatment delay (treatment delay = 1 & no treatment delay =0)

β_0 - β_{13} = coefficients for model variables

HF₁-HF₄ = Health facility characteristics (Ownership, Geographical location, level within health system hierarchy, and number of laboratory personnel)

CD₁-CD₄= Care delivery characteristics (Diagnostic technology used, number of specimens tested, sequence of tests and weekend lab visit)

PC₁-PC₄= Patient characteristics (age, sex, HIV status, previous history of TB treatment)

Parameters were estimated using odds ratios (OR) as shown in the analysis matrix below:

Table 10: Analysis matrix for aim 2

#Aim 2	
Hypothesis	Service delivery factors will delay initiation of Tuberculosis treatment
Dependent variable(s)	Treatment delay [TD](delay =1 & no delay =0)
Independent variables	<ul style="list-style-type: none"> Service delivery factors (Health facility characteristics [HF] & Care delivery characteristics [CD])
Covariates	<ul style="list-style-type: none"> Patient characteristics [PC] (age, gender, HIV status, previous TB treatment)
Statistical approach	Logistic regression
Estimate	Odds Ratio (OR); and 95%CI OR
Level of significance, α	5%

QUALITATIVE COMPONENT (AIM 3)

Study design

In-depth interviews with three representatives from a sample of HF in one district (in-charge of OPD, head of clinical team and head of laboratory services) were conducted.

Specifically, the respondents were interviewed by the principal investigator on the causes of TB treatment delay and how this should be addressed based on what they routinely did or had

observed. Field and interview notes including descriptions of care process flow maps were also collected to supplement data collected during interviews.

Study population

The study population comprised of all in-charges of OPD, heads of clinical teams and heads of laboratories in the region. These were key positions in the provision of out-patient services including TB diagnosis and treatment. Appointments to these positions of responsibility is by the HF in charge, usually based on seniority within the department or unit. In-charges of OPD are usually registered nurses while heads of clinical teams are either medical officers or medical clinical officers. Heads of labs vary from technologists in HCIVs and hospitals to technicians in HCIIIs.

Sampling, sample size and recruitment

Interviews were conducted from health facilities in Kabarole district; the district with the highest number of TB cases in the region and therefore likely to have more healthcare workers with experience managing TB. Respondents were from the top nine HFs serving populations at very high risk of TB -- populations from tea plantations, fishing villages and slum areas. If the selected respondent was unable to participate, a replacement was selected from the same health facility according to the hierarchy since these individuals would stand in for absent team leaders.

Measurements and instruments

The study aimed at eliciting perspectives of healthcare workers on delays based on their experience and observations within HFs that were continuously providing TB services. Respondents described and explained practices in identifying presumptive TB cases and

completing subsequent care steps that led to delays. Available qualitative literature discusses TB treatment delay within the context of implementing recommended infection control procedures (Buregeya et al, 2013; Chimatata et al, 2017). The proposed themes and codes from this angle relate to institutional and personnel factors such as knowledge of TB care best practices and benefits of using protocols, attitude towards TB patients and even healthcare workers caring for them (Chimatata et al, 2017) . Other factors were professional attitude to work and concerns and fears in caring for TB patients and available measures to address those (Buregeya et al, 2013). In other literature staff expressed concern about perceptions of others' support to TB patients (courtesy stigma) especially TB patients whose care falls outside work routines and for which health workers are not rewarded (Link and Phelan, 2006; Philips et al , 2011). Table 11 shows the pre-selected themes and codes were:

Table 11: Measurement matrix for aim 3

family	Themes/code groups	Explanation
Knowledge of risks & benefits	Infection control	Measures necessary to prevent transmission of TB within HFs
	Stigma among staff about attending to TB patients (courtesy stigma)	Dishonor or disgrace associated with being responsible for treating TB patients
	Protection for healthcare workers	Measures to prevent healthcare workers from getting infected with TB
Barriers to implementing protocols	Volume of workload	Number of patients attended to by a healthcare worker on a working day
	Acceptability	Attitude towards use of TB treatment protocols
	Knowledge of protocols	Ability to describe treatment protocol and explain why it is established
	Quality of support by external technical teams	Rating of support supervisory visits by district and national TB teams
Organizational culture	Ranking of TB care on task priority list as per described specimen handling schedules	Stigma / discrimination
	Shared care decision making	Involvement of patients in making care decisions
	TB task specialization	TB care tasks allocated to specific individuals in HF
	Reward and punishment system of the organization	Feedback system on task performance
	Management of missed visits	Mechanisms to trace patients who miss appointments
Work environment safety	Availability of safety equipment	Masks, sputum testing cabinets
	TB in healthcare workers	Incidents of TB among healthcare workers
	Safety concerns	Poor infrastructure set up-space and ventilation
Work ethics	Attendance to duty	Absenteeism, neglect of duty
	Adherence to good clinical/lab practice	Violations of standard practices

Data collection

At each selected facility in-charge of OPD, head of clinical teams and head of laboratories were interviewed. In- depth face to face interviews that lasted 17 to 50 minutes were conducted using a semi-structured interview guide (*appendix III*). The interview guide was based on knowledge of the TB care cascade and probes for respondent's own experiences or observations at the HF where he or she worked. The guide related to the potential problems described in the WHO framework for improving TB case detection and treatment (Marais and Raviglione, 2011).

Interviews were conducted by the principal investigator and a research assistant with experience in qualitative research. Respondents were contacted by phone to make an appointment for the interview. Before each interview, informed written consent was obtained, and no financial or any other form of incentive was provided. Interviews were audio-recorded and handwritten field notes were made by interviewer. All audio recordings were transcribed by the interviewer and each transcript cross checked with the audio-recording by the principal investigator for concordance.

To ensure validity and reliability of study findings, we hired a research assistant who had prior experience conducting qualitative interviews. Pilot interviews were conducted at two HFs in a neighboring non-study district to assess content, flow and clarity as well as acceptability of the study tool. All transcripts were compared with audio-recordings and corrections made as appropriate.

Data analysis

This part of the study aimed to understand workers' perceptions of the relationship between service delivery factors and TB treatment delay. Data was entered in ATLAS.ti software for coding and analysis by the principal investigator. Data in the ATLAS.ti software and interview notes were organized into folders by category of respondent. Data was analyzed using the thematic content analysis in which text data was aggregated and assigned a code; similar codes were aggregated into themes. Additional codes and themes emerging from the transcripts were added to those already mentioned in table 11. Before coding, each respondent's interview and field notes were reviewed two to three times while highlighting major organizing ideas. Code names were mostly based on health sciences and behavioral literature. A mix of pre-selected and emergent codes and themes was used. The coding was done independently by two people (the principal investigator and someone with experience in coding qualitative data) and their findings compared.

HUMAN SUBJECTS AND SAFETY CONSIDERATIONS

Approval for the study protocol was obtained from the Joint Clinical Research Center (JC0718) (*Appendix 5*), Uganda National Council for Science and technology [HS205ES] (*Appendix 5*), and the committee for protection of human subjects at the University of Texas Health Science center, Houston (HSC-SPH-18-0264) (*Appendix 3*). Written administrative consent was obtained from the ministry of health prior to data collection.

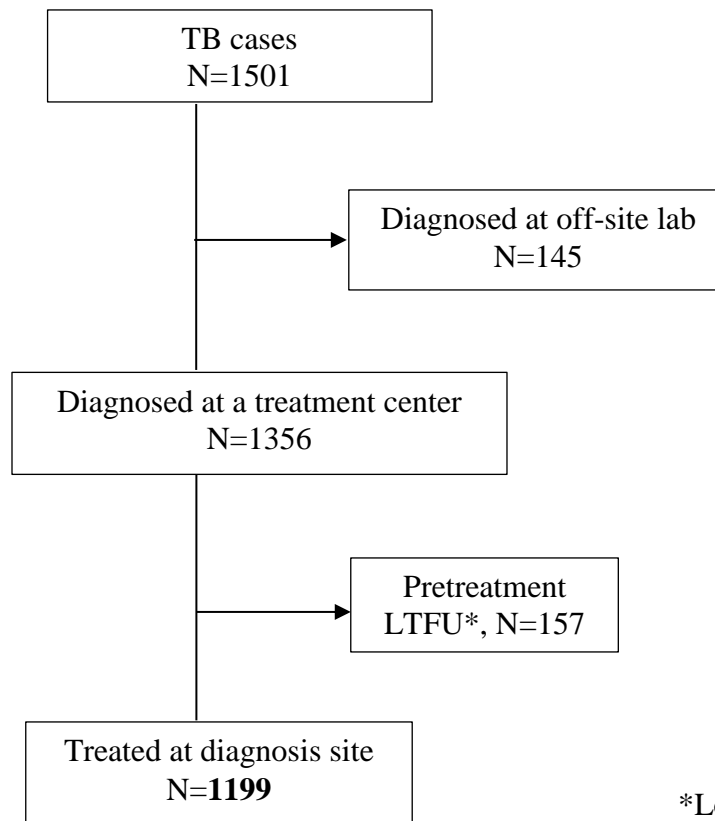
RESULTS

QUANTITATIVE COMPONENT (AIMS 1 & 2)

Descriptive characteristics

A total of 1501 adults were tested for TB between January 1st, 2016 and December 31st, 2017 across the three study districts. Among these were 145 (9.7%) who were diagnosed upon referral of their specimens for Gene Xpert testing. As indicated in Figure 5 below only the 1199(79.9%) patients who were diagnosed and treated at the same site were included in the study since only these reached the study end point of treatment initiation.

Figure 5: Study profile



*Loss To Follow Up

Structural characteristics associated with treated TB patients

Sixty-four HFs provide both TB diagnosis and treatment onsite. Kabarole district had more HFs (35) providing TB services (three hospitals, two HCIVs and 29 HCIIIs) compared to 19 HFs in Kasese (three hospitals, two HCIVs and 14 HCIIIs) and 10 HFs in Kyenjojo (one hospital, one HCIVs and eight HCIIIs). Three quarters of HFs with TB services were publicly owned HFs compared to the remaining ones that were exclusively nonprofit, religious affiliated facilities. In 60 (93.3%) of HFs, the primary TB diagnostic technology was microscopy. More than two thirds of HFs small labs had one to two laboratory personnel; 50% of the HCIIIs that had only one laboratory worker.

Table 12: Characteristics of healthcare facilities providing TB services

Characteristic (N=64)	Frequency	Percentage
Number of facilities in district		
<i>Kabarole</i>	35	54.69
<i>Kasese</i>	19	29.69
<i>Kyenjojo</i>	10	15.63
Types of health facilities		
<i>HCIII</i>	50	78.13
<i>HCIV</i>	7	10.94
<i>Hospital</i>	7	10.94
Health facility ownership		
<i>Public</i>	48	75.00
<i>Private not for profit</i>	16	25.00
Primary TB Diagnostic technology		
<i>Microscopy</i>	60	93.75
<i>Gene Xpert</i>	4	6.25
Number of laboratory personnel		
1-2	46	71.87
3-4	9	14.06
5+	9	14.06

Table 13 shows HF characteristics associated with treated TB patients. Two fifths (41.9%) of the TB cases were from Kabarole district with the rest equally distributed between Kasese and Kyenjojo districts.

Table 13: Structural characteristics associated with treated TB patients

Characteristic		Frequency (N=1119)	Percentage (%)
District	Kabarole	502	41.9
	Kasese	348	29.0
	Kyenjojo	349	29.1
Health facility level	Hospital	398	33.2
	HCIII	622	51.9
	HCIV	179	14.9
Health facility ownership			
	Public	846	70.6
	Private not for profit	353	29.4
Health facility laboratory personnel			
	1-2	469	39.1
	3-4	271	22.6
	5+	459	38.3

Over two thirds (70.6%) of the patients received TB services in publicly owned HFs. All the remaining patients that were treated in in non-profit religious affiliated healthcare facilities. TB cases at level three health centers (HCIII) were more than those at hospitals and level four health centers (HCIV) combined. The total TB case load at HCIIIs was 1.6 times those at hospitals and 3.5 times those at HCIVs. However, hospitals had a median of 64 TB cases (IQR, 49-71) compared to 17 (IQR, 12-65) at HCIVs and 8.5 (IQR, 5-22) at HCIIIs reflecting a relatively low number of cases in hospitals and HCIVs compared to HCIIIs. Close to two fifths of TB cases were diagnosed at HFs with one to two laboratory personnel including 207(17.3%) patients diagnosed among HFs (HCIIIs and HCIVs) with only one

laboratory staff. Nearly two fifths of the patients were diagnosed at a HF with five or more laboratory personnel.

Personal characteristics of TB patients treated at diagnosis sites

There were 111(16.9%) less TB patients in 2017 compared to the 655 that were treated in 2016. The mean patient age was 36.9 (SD, 14.3) years with three in four patients (75%) aged less than 45 years. Males represent 2.4 times (70.2%) as many cases of TB compared to females (29.8%). Less than 5% of TB patients had previously been treated for the disease. Close to one third (31.2 %) of the patients were HIV positive 469 (39.1%). Characteristics of the treated TB patients are summarized in table 14.

Table 14: Demographic characteristics of treated TB patients

Characteristic		Frequency (N=1119)	Percentage (%)
Age in years (mean, SD)*		36.9	14.3
Gender	Male	843	70.2
	Female	357	29.8
HIV status	Negative	792	66.1
	Positive	374	31.2
	Unknown	33	2.7
Previously treated for TB	No	1166	97.3
	Yes	33	2.7
Year of diagnosis	2016	655	54.6
	2017	544	45.4

*Described in terms of median with corresponding standard deviation

Care delivery characteristics of treated TB patients

Disease diagnosis was based on a single test per specimen submitted. Approximately six in ten patients (59.3%) were tested for TB two or three times during the care episode. Of these 711 patients that had a repeat test, 655 (92.1%) had a positive index test, demonstrating

a high rate of retesting even when the first specimen is positive. Disease diagnosis centered on microscopy technology. Eighty-one percent of patients were diagnosis based solely on microscopy while 168(14%) were diagnosed using the Xpert test only. Compared to use of the Xpert test, two thirds (65.6%) of single-test based diagnoses and 92.5% of retests were solely microscopy based. Microscopy was the preliminary test for in all patients who had an Xpert test as their repeat test.

As shown in table 15 below, only 20 percent of patients visited the laboratory for testing on a weekend; most patients were tested during the week.

Table 15: Care delivery characteristics of treated TB patients

Characteristic	Number	Percentage
Technology used for diagnosis		
Microscopy	978	81.6
Gene Xpert	168	14.0
Both tests	53	4.4
Samples tested		
1	488	40.7
2	684	57.0
3	27	2.3
Laboratory test sequence		
Single test	488	40.7
Repeat after negative result	56	4.8
Repeat after positive result	655	54.6
Weekend lab test		
Yes	242	20.2
No	957	79.8

Duration of Tuberculosis care processes

The median TB treatment time was one day (IQR 1, 3). Slightly over half (52.3%) of the patients received TB test results and started treatment on the same day they first visited a facility for testing. Further, 75% of patients started treatment with three days of their initial visit for a TB test.

The time intervals of laboratory turnaround time (TAT) and treatment initiation time (TxIT) are summarized in table 16.

Table 16: Tuberculosis care process durations in days

Process duration (days)	Median* (Q₁,Q₃)	Minimum	Maximum
Laboratory TAT	1(1,2)	1	108
Treatment initiation time	1 (1,1)	1	88
Total treatment time	1 (1,3)	1	108

**1 day =same day event*

The median laboratory TAT was 1 day (IQR 1, 2), which was like the treatment initiation time. Two thirds of the patients received TB test results on the same day they submitted a specimen for testing.

The proportion of TB patients starting treating treatment rapidly rose to approximately 90% within the first six days and tapered off. By day fifteen, 95.8% of the TB patients had started treatment, up from 71.4% by day three. There was no statistically significant difference in the patient, health facility and care delivery characteristics between these patients starting treatment within 14 days and those whose treatment was extremely

delayed. The rest of the study findings are based on these 1142 (95.2%) TB patients that were initiated on treatment within 14 days of first visiting the laboratory for a test. Because this small number of outliers would greatly affect regression analysis of typical treatment-initiation times, they have been excluded from outcomes analyses. To understand the small portion with anomalous, egregious delays, a separate examination of those should be conducted.

Association of service delivery factors with duration of TB care processes

We considered the relationship of service-related factors with laboratory TAT and then with treatment initiation time (TxIT). Process times (TAT and TxIT) were minimally correlated ($r = 0.06$, $p = 0.029$) but each had a strongly positive correlation with total time ($r = 0.85$, $p < 0.001$ for TAT, and $r = 0.58$, $p < 0.001$ for TxIT). Among care delivery characteristics, number of TB specimens tested had a strong positive correlation with sequencing of tests ($r = 0.87$, $p < 0.001$) indicating that each extra specimen collected meant a repeat test had been ordered.

Association of service delivery factors with laboratory turnaround time

Table 14 describes multivariable analysis for TAT. The following patient and structural factors with p-value > 0.25 at univariate analysis were not selected for multivariable regression: age of the patient ($p = 0.661$), gender ($p = 0.957$), previous history of TB treatment ($p = 0.873$), year of diagnosis ($p = 0.627$) and HIV status ($p = 0.61$).

Factors that independently predicted laboratory TAT were submitting a TB specimen to the laboratory during a weekend and having a repeat TB test (table 14). Submitting a

specimen over the weekend increased laboratory TAT by 0.37 days compared to specimens submitted during the week, ($\beta=0.37$, 95%CI 0.11, 0.60). Patients who had a repeat TB test after initially testing negative had 1.17 day longer TAT than those who had a single test ($\beta=1.17$, 95%CI 0.64, 1.69). However, a repeat test after an initial positive test did not change laboratory TAT ($\beta=0.22$, 95%CI -0.02, 0.46) pointing to urgency in reporting each individual positive result. Laboratory turnaround did not differ by type of TB test conducted ($\beta=0.29$, 95%CI -0.08, 0.65 for Xpert test compared microscopy) and whether a patient was tested at a health center compared to a hospital ($\beta=0.10$, 95%CI -0.16, 0.35 for HCIII and $\beta=0.26$, 95%CI -0.08, 0.59 for HCIV).

Table 17: Association of service delivery factors with durations of TB care process

Characteristic	TAT (N=1336)		Treatment initiation time (N=1336)		
	Univariate analysis	Multivariable analysis	Univariate analysis	Multivariable analysis	
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	
Health facility level					
	HCIII	0.04(-0.18,0.26)	-0.06(-0.62,0.49)	0.04(-0.14 ,0.22)	0.26(-0.19,0.70)
	HCIV	0.81(-0.13,0.49)	0.13(-0.30,0.56)	-0.11(-0.36,0.14)	-0.01(-0.35,0.34)
Health facility ownership					
	Private	-0.12(-0.34,0.10)	-0.22(-0.49,0.05)	-0.07(-0.25,0.11)	-0.17(-0.39,0.05)
Laboratory personnel					
	3-4	0.19(-0.08,0.46)	0.10(-0.23,0.44)	-0.29(-0.50,-0.08)	-0.07(-0.34,0.21)
	5+	0.02(-0.21,0.24)	-0.09(-0.66,0.48)	-0.07(-0.25,0.11)	0.26(-0.20,0.73)
Weekend lab visit					
	Yes	0.35(0.10,0.59)	0.37(0.11,0.62)*		-0.02(-0.23,0.18)
Technology used					
	Gene Xpert	0.05(-0.24, 0.34)	0.30(-0.10,0.69)		0.39(0.07 0.71)*
	Microscopy and Xpert	-0.04(-0.54,0.49)	-0.36(-0.89,0.17)		0.01(-0.42,0.43)
Lab test sequence					
	Repeat after negative result	1.09(0.59,1.59)	1.23(0.70,1.75)*	0.48(0.08,0.89)	0.51(0.08,0.93)*
	Repeat after positive result	0.12(-0.09,0.32)	0.21(-0.04,0.45)	0.14(-0.02,0.31)	0.26(0.06,0.45)*
District					
	Kasese		0.26(-0.03,0.54)	-0.14(-0.34,0.05)	-0.16(-0.39,0.07)
	Kyenjojo		-0.08(-0.38,0.21)	-0.28(-0.48,-0.09)	-0.42(-0.66,-0.18)*

*P-value<0.05

Association of service delivery factors with treatment initiation time

Table 14 also describes results of multivariable analysis for treatment initiation time. The TxIT for patients in Kyenjojo district was 0.42 days less compared to those in Kabarole district ($\beta = -0.42$, 95%CI -0.66,-0.18). Receiving treatment at a HCIV was associated with 0.3 day shorter initiation time than at a hospital ($\beta = -0.29$, 95%CI -0.56,-0.02) but there was no difference when HCIIIs were compared to hospitals ($\beta = -0.12$, 95%CI -0.32, 0.08). Having had a repeat TB test significantly increased TxIT irrespective of the initial test result

($\beta = 0.51$, 95%CI 0.08, 0.93) for an initial negative result and ($\beta = 0.26$, 95%CI 0.06, 0.45) for an initial positive result).

Association of service delivery factors with treatment delay

The rate of TB treatment delay was 25.0% (95% CI 22.6%, 27.7%). For the multivariate analysis, the following patient and HF structural characteristics with p-value >0.25 at univariate analysis were excluded: year of diagnosis ($p=0.975$), previous history of TB treatment ($p=0.585$) and HF ownership ($p=0.725$).

As summarized in table 15 below, the odds of delay were 1.79 times when Xpert test was used for diagnosis compared to microscopy (adjusted OR [aOR] 1.79, 95%CI 1.04, 3.10). Compared to having a single test, having a repeat TB test significantly increased odds of delay; 3.5 times if index test was negative (aOR 3.49, 95%CI 1.81, 6.75) and 1.8 times if index test is positive (aOR 1.81 95%CI 1.27, 2.60). The odds of treatment delay were two times more (aOR 2.06, 95%CI 1.49, 2.84) when a patient presented on a weekend compared to a week day.

Receiving TB services at a health center (aOR 1.58, 95%CI 0.73, 3.42 for HCIII; aOR 1.28, 95%CI 0.73, 2.24 for HCIV) compared to a hospital was not associated with TB treatment delay. No patient characteristics had a statistically significant association with TB treatment delay.

Table 18: Association of service delivery factors with TB treatment delay

Characteristic		Delayed, n (%)	Crude OR (95% CI)	Adjusted OR (95%CI)
District				
	Kabarole	120(25.1)	1.00	1.00
	Kasese	100(30.3)	1.32(0.95,1.78)	1.34(0.91,1.97)
	Kyenjojo	66(19.8)	0.74(0.53,1.04)	0.72(0.48,1.08)
Health facility level				
	Hospital	105(27.1)	1.00	1.00
	HCIII	140(24.0)	0.85(0.63,1.14)	1.58(0.73,3.42)
	HCIV	41(24.0)	0.85(0.56,1.29)	1.28(0.73,2.24)
Lab Personnel				
	1-2	105(23.8)	1.00	1.00
	3-4	56(22.1)	0.91(0.63,1.31)	0.98(0.62,1.56)
	5+	165(28.0)	1.24(0.92,1.68)	1.75(0.79,3.89)
Weekend lab visit				
	No	201(22.1)	1.00	1.00
	Yes	85(36.4)	2.02(1.48,2.76)	2.06(1.49,2.84)*
Technology used				
	Microscopy	228(24.4)	1.00	1.00
	Gene Xpert	26(28.2)	1.22(0.84,1.77)	1.79(1.04,3.10)*
	Both	12(26.7)	1.13(0.57,2.22)	0.71(0.35, 1.47)
Test sequence				
	Single test	103(22.0)	1.00	1.00
	Repeat after negative result	22(44.0)	2.79(1.53,5.09)	3.49(1.81, 6.75)*
	Repeat after positive result	161(25.8)	1.24(0.93,1.64)	1.81(1.27, 2.60)*
Age				
	years	286(25.0)	1.00(0.99,1.01)	1.00(0.99, 1.01)
Gender				
	Male	194(24.3)	1.00	1.00
	Female	92(26.7)	1.14(0.85,1.52)	1.08(0.78,1.46)
HIV status				
	Negative	176(23.3)	1.00	1.00
	Positive	98(27.8)	1.27(0.95,1.69)	1.35(0.99,1.84)
	Unknown	12(36.4)	1.88(0.91,3.90)	1.75(0.82,3.78)

*P-value<0.05

QUALITATIVE COMPONENT (AIM 3)

Sample and field work description

A total of 27 face-to-face interviews were conducted with three representatives from each of 9 (three hospitals, three HCIVs and three HCIIIs). The mean age of respondents was 32.4 years (SD 6.9). There were 8 female and 19 male respondents; all six females serve as heads of OPD services and three females were clinical team leaders; all heads of laboratory services were males. Respondents for head of OPD services comprised of five nursing officers (Hospital =2 and HCIV = 3), two clinical officers (one at a hospital and another at a HCIII) and two enrolled nurses (both at HCIIIs). Among heads of laboratory teams were three laboratory assistants (Hospital =1, HCIV = 1 and HCIII=1), five technicians (Hospital =2, HCIV = 1 and HCIII=2) and one technologist (at a HCIV). All heads of clinical teams were clinical officers.

All interviews were conducted at the health facilities during working hours. With exception of one laboratory assistant representing the laboratory services head, and two enrolled nurses representing the head of OPD services, all respondents were appointed heads of services. Except for two respondents (both heads of lab at HCIVs) who had to be re-interviewed due to interruptions, all the interviews were completed in one sitting. The interviews lasted on average 30 minutes. During the interview it was observed that most respondents answered each question individually instead of broadly discussing the subject. In this case, interviews were conducted in a question and answer fashion often with prompting to encourage them to continue talking. Because of patient confidentiality issues it was not

possible to observe respondents in the TB care process. Respondents generally were unwilling to describe what they did as individuals. Even where a respondent identified a problem in his/her unit, this was attributed to workmates. However, each respondent was able to confidently describe patient flow even at service points where she/he did not work.

Coding and themes development

Initial reading of transcripts was done within two days of conducting each interview, but coding was done after all interviews were completed. Because each respondent discussed the whole TB patient care flow map, there were little differences among the respondent categories.

Focus at theme development was on descriptions and explanation of practices that a respondent felt resulted into delays in the TB care process. Most of the preselected codes groups were identified during the coding process but were interrelated in a much different way from groups and themes from existing literature. Workplace safety was the only theme that emerged as having a direct relationship with TB treatment delays. The remaining themes, though widely cited in literature on implementation of infection control measures, were not directly related to patient care delays. All respondents reported good comprehension of recommended practices so lack of knowledge was not a cause for delays.

Besides work environment safety (renamed as concerns about spread of TB amongst healthcare workers), there were five emergent themes. These were perception of delays among healthcare workers, attitude towards attending to TB patients, care decision making approach, schedule of TB care tasks and their completion, stock out of TB drugs and supplies. Each theme is addressed in detail below:

Perception of delays among healthcare workers

Across the three respondent categories, quickly attending to presumptive TB cases was primarily to prevent disease transmission. Regarding transmission, workers explained that quickly initiating anti-TB drugs reduced chances of workers or other patients contracting TB. A laboratory technologist viewed this as an infection control measure with benefits to healthcare workers and the wider community observing that “we will have put there (sic) control measures for the staff not to be infected with TB. And also we will have safeguarded the community...we will have really improved [health] in the community that we are serving and it will also help us to be healthy” (R5-02). One respondent also observed that timely response improved patient satisfaction with services, noting thus: “You know when you delay a patient, the patient also loses morale, and next time the person gets sick, [he or she] may fail to come to the facility [where he has previously experienced delays]”(R4-01).

At all facilities, respondents felt patients with TB ought to be diagnosed and treated within 20 minutes to a few hours of presenting for consultation. Most respondents agreed they could attend to TB patients in a much shorter time than they were currently. Interviewees suggested that a threshold of within a day but felt that it was not generally achievable, especially when there was a heavy workload or a patient presented towards the end of business hours. One respondent who proposed more than a day as a cut off threshold for defining delay observed that “A day or two [is a good cut off]....becausesometimes you find the lab very busy [with] many TB sputum tests [and] delays to give them the results that daysometimes they are promised (sic) to come the next day” (R5-01). Another one argued that:

At least if it is very long [it shouldn't last more than] one day. But it depends. If a patient came like around evening hours, he may be told to come back tomorrow. Now let's say like here we work up to 5. If a patient is screened like at 4 and is sent to the lab and by the time the lab person does the whole process, to stain and get the results, it might be 5. And this patient is told to bring another sputum in the container the next day. So this one may be call for coming back tomorrow (R7-01)

Comparing TB care points, all three categories of respondents agreed that the most time was spent in the laboratory and therefore that is where most delays occurred. A clinical care team head who felt that longer periods spent in the lab had to be considered while defining upper limits of duration of a TB care episode observed that:

“... Maximum time [to get tested and started on TB treatment] should be five to six hours. Yeah because I know..... But because I know the only delay is in the lab. The rest are okay. What I know in the lab they wait for two, three hoursbut then there is some information am not well acquainted with how much time it takes to diagnose and to come out with clear results in the lab” (R1-01)

A laboratory technician concurred but argued that specimens are not brought on time. He argued that “... when the [samples] come in the lab as soon as possible, of course the treatment is also done very early. But when the [samples] delay, the treatment also does delay....delay in treatment depends on the release of the results.we don't just tell them that go to the clinicians, we just escort that patient direct to the clinician” (R6-01). A clinical officer heading a clinical team at a busy hospital even suggested that with the prevailing workload it was better to have a standalone TB laboratory to reduce delays in testing and reporting TB tests.

What I think, I can now look at the lab side first, if there could be a separate lab that is to handle that [big number of TB tests] so as to avoid the overload. The OPD patients, ANC, may be samples from the ward, so that overwhelming number, if there could be a separate

lab, then it could be of function. ...the greatest time is actually taken in the lab while processing sputum sample. (R6-03)

Asked what caused treatment delays, most respondents first mentioned external factors, like low stock levels of TB drugs and diagnostic supplies. One respondent was emphatic saying that only stock outs of drugs and supplies caused delays stating that “I don’t think there is [any other cause of delays] apart from drug stock outs ...apart from those items like lack of may be sputum mugs. You find that they are out of stock, ahh slides and stains. Those are the only things that can cause delay at this healthcare facility” (R8-03). A laboratory technologist at a HCIV also noted stock out of supplies as a top cause of delays saying “The first issue [causing delays in treating TB] will be the supplies. We don’t have supplies like sputum mugs. Like for children you have to do gastric lavage” (R5-02).

The understanding was that health facilities could aim for shorter time windows within which presumptive TB cases could be identified and treated. Improving laboratory turnaround times and having sufficient levels of supplies were key to reducing time windows.

Concern about contracting TB

Presumptive TB cases were seen by staff as different from other patients solely on account of having an infectious disease, which might impact staff and other patients’ health. A clinical officer observed that “They are like any other patient [in all other aspects] but because they have the infectious disease, they can transmit the bacteria to another person. So you cannot keep them with other patients” (R9-01). A comprehensive nurse heading OPD services at a HCIII explained that:

They are like the same patients but them, I handle them in a special way because they, they’re infectious patients. I don’t see them like malaria patients because they are infectious. The

way in which we handle them? First of all, these patients are contagious, we triage them. So when they come and we know that these are our clients, we give them a special place, a special place where to sit. They don't sit with other clients (R8-01)

Another explained the great length they went to ensure that presumptive TB patients understood why they were being isolated from the rest of the patients saying “Yes we treat them differently from other patients.... but after getting them, after screening them and confirming them. Of course [as we isolate them] we health educate and we try to explain, how infectious TB is and how it is spread” (R1-01).

Respondents expressed their fear of contracting TB from patients in different ways. A clinical officer heading OPD services narrated that “But I do fear, to get TB each time, I have this thing in me each time I look at a TB client, I also start coughing” (R6-02). A laboratory technician appeared to worry more about his workmates saying “Actually we are worried that our staff might contract TB anytime because of those infection control measures not being in place” (R4-02). A female clinical team head was more worried about acquiring TB and transmitting it to children in her household saying “Some [of us] fear ... like I have a child at home so if you give it to me I will take it to my baby at home” (R9-01). Having measures to protect staff at the health facility helped to lessen fears. One respondent who felt they had adequate measures and this had lessened his fears, “I don't have fears because in most cases we are given face masks. We are also taught about other preventions, like opening windows and doors; the coughers to always cough in their hands or handkerchiefs to stop the spread of the bacteria. So I don't see how I can fear because the simple methods to use are there” (R4-03)

Even those who strongly felt they were at risk of acquiring TB, it did not affect their personal attitude towards attending to TB patients. A head of OPD services who felt frustrated that personnel did not see themselves as being at most risk reported he had embarked on in-house sensitization about risk of TB. She observed that by appreciating their own risk, less staff shunned attending to TB patients:

And some staff, after knowing that they are at risk and we have a higher risk, people, some people appreciated to work on them so fast so that they can go....To take the care, to take that caution to make sure that we are not infected especially when I wanted to show them the register that even wanted to capture the number of health workers being affected by TB.....So people started fearing TB and so, one would manage in order to protect himself or herself and even protect the patient.....Yes. But at first it was like hmm may be she is being paid for it. You can go and see her, she is down, you go with the register.....those days they were not assisting (R5-01)

Healthcare workers working with TB patients never felt discriminated by the rest of HF staff suggesting risk of contracting disease from them was perceived to be low. Further, it was perceived that all staff had some level of exposure to TB during their duty and therefore no one individual could be singled out as being more likely to spread disease than others. One outpatient clinician team lead observed that because everybody in her unit attended to TB patients, they shared risk and therefore nobody could be seen as being any different. She reasoned that “[here] Hhmm there is no that discrimination because for example, you may find that everybody in OPD has worked on the patient not only me. Because somebody registered another one did vitals, then me I touched, the patient continues, so you may not pinpoint [who is responsible for TB services]” (R9-01). Even when called a nickname with a suffix of TB, this in anyway did not make one TB service provider feel she was being

discriminated by other staffs. In stating that this did not affect her commitment to work, she observed that:

We even have nicknames, they even call you [her first name] TB.....they say it in good faith, they give you a nick name.... I don't have any problem with it. They don't have any problem they don't even say anything [bad about your work], they just know you as Rosette who works on TB clients or Florence who works on TB clients that's all or Violet who makes reports for TB drugs just (R9-01).

In expressing fear of getting infected, respondents were worried about themselves as well as family members. Fear was heightened by lack of personal protection measures. However, this did not affect their attitudes towards attending to TB patients; nor did it translate to their being stigmatized by others for providing TB services. It was believed that understanding one's risk could potentially change attitudes towards attending to TB patients.

Determinants of attitude and willingness to participate in providing TB care

Even as they attended to TB related tasks, most respondents expressed preference for tasks that did not involve TB patients. A laboratory services head shared his experience working in a well-staffed hospital noting that "The experience is that as in lab (eeh) people, most of the people don't like (eeh) working on TB clients. Though it is in most cases...though it is in most cases a requirement but people don't do it with a 'good heart'" (R9-02). Attitude to TB related tasks within anyone HF varied with some staffs giving excuses to avoid attending to presumptive TB patients while others willingly participated in TB care. TB care was often left or referred to the latter group and patients had to wait if they were busy with other tasks or were absent. It was felt that staff were simply giving excuses when they claimed to lack knowledge and skills necessary to participate in TB care. A

nursing officer at a HCIV who attended to TB patients despite not having had training remarked that “I think they may think we are the only health workers who are experienced .But I think they have no interest, because here the health workers who ever gone for TB workshops, they are two. I personally am not there, but I think I am going an extra mile to ask them how we are to handle these patients” (R8-01). Another respondent was more concerned about individuals who are trained but still had a negative attitude reasoning that:

[Negative attitude] has caused delays and actually not only delays but even we have lost clients, because not every staff... is actually a well-wisher for diagnosing or assessing one with TB. So, even if you give this person knowledge ...you will never induce this person to do something that his mind or her mind has not actually welcomed. So there is a knowledge gap, but which is attitudinal coated also.(R4-02)

Negative attitude to TB care was attributed to several factors. A nursing officer observed while some had fear of contracting TB, others were reluctant to take on the time consuming tasks in dispensing TB medicines. She observed that “That negative attitude....we have different levels of training. One thinks if I interface with this patient, he is going to give me TB. Another one may say now, I have to go to the registers, now I have to fill the cards, now I have to fill the drugs ah...and even [I don’t have] the confidence” (R4-01). One respondent reasoned that dispensing was shunned because of the paperwork one was required to fill before issuing drugs noting that “Most people think (sic) this thing of recording... they are not interested” (R5-01). In other instances questions about selective facilitation often contributed to negative attitude. One respondent had noticed other staff thought she was being facilitated saying “Hmm yeah partly because someone will feel like you are given airtime, you are given an allowance so this is your job not mine” (R9-01).

But because attitude among HF staffs varied, there was always at least one individual willing to see TB patients if designated personnel were absent and could not easily be reached. A clinical team head reasoned that “You see we have different attitudes yeah, some others may even say no for me...those clients are for so and so, he is the one who treats those clientsSome others say no, let’s treat this patient because we may acquire diseases, so we have different attitudes” (R8-03).

It was also observed that several circumstances resulted into personnel changing their attitude and attending to TB patients. A nursing officer had noticed often staff changed attitude after observing others attending to patients noting that “But the moment they see us working on the patients, they also they improve but gradually. The improvement would be gradual slowly by slowly, even for the other people who had very negative attitude, after the training they can work with me” (R5-01). A laboratory assistant noted that improving perception of one’s risk also changed attitude emphasizing that:

[Awareness] should be created on the burden of TB. So they [healthcare workers] should appreciate how tough or how bad TB is. And they should know the route despite you dodge it from the facility but the person you dodged at the facility but you meet him in the vehicle or along the bar or whatever you might think T B is just coming to the facility but at any later time you will get it anywhere from the person you actually distanced yourself from (R4-02).

In summary, most healthcare workers preferred to attend to non-TB related tasks but were compelled by the duty assignments. A number of factors that included fear of acquiring TB, lack of experience, complexity of tasks involved in TB care and suspicions of selective financial motivation shaped attitudes towards attending to TB patients. Lack of knowledge

and skills to attend to TB patients was a commonly used excuse to avoid attending to TB patients.

Scheduling and completion of TB care related tasks

There were standardized protocols for attending to presumptive TB cases that emphasized prioritization of their care at all service points within a health facility. This was done alongside attending to general patients. Some respondents said they suspended ongoing tasks whenever they received a presumptive or confirmed TB case to give them priority. A female clinical officer heading OPD services observed that to her TB care was a priority ranking next to life threatening illnesses. Community volunteers and some other staff at triage reminded responsible personnel to attend to these patients in isolation corners so they could quickly leave HF premises. At work stations, presumptive TB cases were checked for among waiting patients and attended to first. The following expressions exemplify prioritization of TB care over other tasks at work stations. A clinical officer who doubled as head of clinical team stressed that “Well, the first thing as I told you, when youyou can get a person with TB [symptoms], we give them a chance andsend them to the lab. Then in the lab, at least they are given a chance faster to make sure they work upon them” (R5-03). Even in the laboratory a respondent who routinely checked for TB patients among waiting patients reported that “if somebody is sent in the lab for TB, actually I give them the first priority to work on them. If I leave them there, they might spread to other clientsonce they sit there, as I am passing through I ask them, I check in their books” (R7-02). There was more urgency once a patient was confirmed to have TB than while still undergoing tests. A

laboratory assistant at a HCIV emphasized that, “When we produce resultssupposing the result on the spot came to be having or containing mycobacterium bacilli, we start that person, rather there and then on anti-TB drugs” (R4-02). A clinical officer described how they often escorted newly diagnosed TB patients saying that:

.... remember on the dispensing window, there are many other patients who may not have TB so we normally prefer after prescribing, we give it [prescription form] to the VHT..... Who takes the patient to the dispensing nurse andthe dispensing nursewill call the patient and give treatment immediately before others. (R7-03)

But checking for presumptive TB cases among patients in the waiting area was not done all the time. One laboratory technician stated that in his HF, triage was done only in the morning hours; and on some days not done at all. Patients with TB symptoms who presented when checking was not being done were attended to like any other patient on a first come, first served basis. A laboratory technician expressing frustration with failure to segregate between patients being sent for TB tests and others observed that, “triage is done first thing in the morning. Normally, when they do the triaging in the morning, the results normally takes 20 to 30 minutes. Those who come after the triage process, because triaging is done first thing in the morning we [see them]... on first come first serve [basis]” (R1-02). Another laboratory technician who was concerned that TB patients mixed with other patients in the waiting area reported that:

Yeah, actually, the biggest huddle in contribution to the delays of these patients is lack of a clear triage system in the facility. So when they [all patients] come here, it is just a mixture and there is no one to sort them out like this one has this problem, this one has this problem, the can be categorized and worked on according to their needs

because you know that someone who is presumed to have TB is dangerous to the community. (R5-02)

Even if presumptive TB cases were identified early enough, there were often competing tasks, in which case one either both the TB patient and other task simultaneously or first completed an ongoing task before attending to a TB patient, which caused delays. A head of OPD services at a hospital who often had competing priorities remarked that “you see, there are some cases that you can’t just escape for one patient someone is dying there and your like let me first work on this one[presumptive TB case]” (R6-01). Another one urged patience with the laboratory where they had one laboratory personnel observing that “..... Sometimes we send some clients to be screened in the lab and we find the lab also having some test it’s carrying out or as we continue also with the programs of the health center. So, we also give some time to do those things” (R8-01). One respondent observed that on HIV clinic or immunization outreach days, personnel took on extra responsibility, which conflicted with attending to TB patients in the OPD. This prolonged wait times for TB patients at triage, testing and even starting treatment:

.....on ART [Anti-Retroviral Therapy] clinic day, there are many clients. Somebody may be screened for TB and is being sent in the lab, we work on that client but taking back the results ,you find [prescriber] is not there he has gone down to attend [to] the ART clinic patients. So I have to go down and call for [him or her] in case if the patient is having TB. (R7-02)

One respondent reported that TB patients were attended on a first come first serve basis in the interest of being fair to patients who had waited for long. In such a case presumptive TB cases would sent to the isolation corner and attended to after the queue had been substantially reduced. This respondent who felt he had a moral obligation not to discourage patients with non-TB related illness noted thus:

... You tell them [non TB patients] that your tests are going to be out in 30 minutes, and a TB client comes, if you are to first go and work on the TB client, then it means you are going to delay the other one you told that the tests will be out in 30 minutes. It is always challenging in that way but now if these people come later and find us in the middle of digging, they are the ones who are going to wait. They will be affected, somehow, somewhere. (R4-02)

Furthermore, some healthcare facilities had set specific times during the off-peak hours when TB tests were conducted. In this case patients had to wait until it was time to run TB tests and report results or were given an appointment to return for the results. Tests were often done in late afternoons or evenings when the clinic was less busy. A clinical officer who expressed frustration with turnaround times of TB results observed a much shorter time was spent deciding whether to treat on clinical grounds or not than was spent conducting a lab test. A laboratory technician admitted that unless urgency of the test was expressed, both samples were collected over two successive days and tested at once. He reported that:

It [getting results on the same day a test is requested] always happens may be if this client is coming from OPD and is an out-patient and is going back... That's when you find that a test is requested and it is done there and then.... [When] a doctor wishes to see the results of the spot sample. But for these other ones who are on ward, may be ART, clients hurry to collect the samples but we haven't been in a hurry to examine the samples....Because we give out results after examining two sputum samples. (R9-02)

Several reasons were given for running tests in batches collecting all the patient's TB specimens first and/ or having each day's tests done at once. A head of OPD services sympathized with the laboratory staff noting the heavy workload involved in TB testing compared to other tests:

In case if you are busy with the facility work. Now you may find the lab man is having a lot of people of TB, he is having people of HCT, he having and other tests like H-pylori, there are what.

Then you find he has to first stain, and then leave them to dry, and then he first works on these patients then after he will carry out the testing in the afternoon when he is off duty. (R4-02)

Respondents involved in laboratory services felt testing samples in batches reduced the period when staff were exposed to possible infection as well as reducing cleanup time needed to transition between TB and other tests.

That's how I found it hear but ideally I think we are trying to minimize exposure [to infection]. Exposure...working on one sample and after 30 minutes another client brings in another sample. Trying to minimize exposure so they decided to work to collect and to gather them and to process them at once (R9-02).

...we collect all the sputum and work on them at once..... it doesn't matter whether you are the first or the second or what....because this procedure for ZN [TB testing], its nature if you separate these patients so much, you waste reagents, then two, you may not ...ah you may make mistakes here and there.....we give them at least ten minutes apart .We first clean off the other stuff (sic), then you begin again. So you would rather prepare the samples at once...it saves you time. If we had someone responsible for doing that procedure [TB testing] alone ... just waiting for TB specimens. (R5-02).

Therefore, just as much as attempts were made to check for presumptive TB cases and give them priority, this was not done regularly or at well in some HFs. In HFs that were understaffed, there were often competing priorities, which resulted into patients waiting for long hours before they were attended to. To compound the above problems with scheduling of TB tasks, laboratories had institutionalized work routines that involved attending to TB patients at specific hours in batches.

Care decision making

Treatment protocols are used routinely to identify presumptive TB cases, conduct test and prescribe treatment. Even after presumptive TB cases had been identified using a screening protocol, a second opinion was often sought from a clinician before ordering the

TB test. A 29 year male clinical officer leading a clinical team at a HCIII reported what was routinely done at his HF noting that “So we screen them and if we think others they don’t qualify hmm other it can be minor RTI, hmm, we send them to the lab”(R7-03). An enrolled nurse acting as head of OPD services at a hospital was more explicit:

We receive these patients at OPD, with mostly complaints related to cough and we normally ask questions [as] per WHO card [screening guide], to find out the real case of TB, in case it is there. After finding out those signs and symptoms of fevers and uncontrolled weight loss; after all that, we take these patients mostly to the clinician, and the clinician does further examination. And then after that if the patient requires x-ray we do chest x-rays. If the patient requires sputum analysis or requires doing any other investigations, we send them to the lab. (R2-01)

Besides seeking a second opinion, some facilities have HFs designated personnel to conduct specific TB care procedures. Such procedures were left until the designated person was available or deferred if she/he was absent. One laboratory technician reported often the staff had to discard patient samples because the clinician meant to refer a case was not available, stating that:

You find a client [who] has been sent to the lab.... needs a gene expert this specimen is supposed to be referred but you need a filled referral form [issued] by a clinician or a doctor. So the delay happens when this client...when the clinician, the time to fill this referral form the time he is communicated to, you find this clinician has delayed to fill this form and eventually even in the specimen ends up misplaced from the lab because of lack of this referral form... it would be better if these referral forms were designed to be filled from the lab (R9-01)

At the level of starting treatment, patients had to wait for a designated staff (TB focal person) to dispense the medicine. A TB focal person at a HF boasted that, “A few people are dealing on these anti-T.Bs, because people who initiate people on anti-TBs... I think it could be me, the in-charge and even maybe the lab man. I think no one [else] can do this” (R8-01).

Another one however observed that often the focal person was busy attending to other tasks and patients had to wait for long hours

Then when the results are got, and we realize that this patient is a case of TB.....we call in the TB focal person to come and witness (sic) the case. So this case is always sent to the TB focal person for treatment and other advice that is related to TB treatment and other procedures.....she might be busy and you need to take this patient to the focal person for treatment and management. So it might take some time. (R2-01)

Regarding care decision making, patients delayed either waiting for designated personnel to whom TB care tasks had been left or waiting for a second opinion before sanctioning stipulated TB care procedures.

Availability of necessary drugs and other supplies

Respondents expressed frustration when they diagnosed TB patients only to find out there were no drugs for their treatment. Available quantities were small and often got used up with a single TB patient. It was noted there were weaknesses in the supply chain with supplies being inadequate or lacking completely. One respondent observed that the available supplies are usually adequate for one to two patients, beyond which the HF immediately reports a drug stock out. He observed thus: “these [anti-TB] drugsof course they don’t supply us with [anti-TB drugs] ... they supply but in small quantities” (R8-02). Another one was more emphatic saying “We have the knowledge, we have identified the patient, we have done everything but the drugs are not there” (R4-01). Although stock outs were attributed to failure to deliver adequate quantities, some respondents admitted that they sometimes did not request adequate quantities.

Besides anti-TB drugs, stock outs were also observed for laboratory reagents leading to suspension of testing until reagent supplies were restored. Often this involved borrowing from other facilities, in which case patients would wait for hours to days. Alternatively, patients would be referred to other HFs, which equally prolonged the process of establishing disease diagnosis. A clinician team leader noted that:

Hmm sometimes you can request for a sample, you find may be you have no slides. That patient is likely to wait, may be you give him or her the next appointment until when the slides are back. Sometimes the stains ah you find that the stain are not there ah sometimes we run out-stocks on drugs. So that patient may spend an hour or even two hours because you might not be having the drugs right now but you go to requisition from another facility. So it may take an hour or two hours like that. (R8-03)

Often patients were told to wait as they searched elsewhere within the HF or at neighboring health facilities. One such respondent who had had the experience of searching around the health facility without success remarked that:

Drugs, stock supplies because these days there are issues when the patient is in front of you and you have no drugs you check all other places there are no drugs and it is so demoralized...the patient gets so much demoralized and says now am dying if [hospital] doesn't have the drug then am finished (R9-03)

In some cases, they borrow from neighboring facilities. A respondent from a health facility which often borrowed reagents noted that “To make sure that the reagents are provided. Now when it comes to the point of [testing] if the reagents are not enough this person [lab assistant] will have to walk around look for which facility that can help to have the reagents where ever they are” R2-03. Sometimes patients were either given a return appointment when drugs and other supplies are expected to have been delivered or were referred to HFs where supplies are known to be adequate. One respondent noted that “Early January, we

were referring them to our sister hospitals because we can't keep them here when they need treatment. So we could refer to them to nearby hospitals".

So just as much as there were mitigation measures against lack of TB drugs and basic testing supplies they often involved patients waiting for long times or rescheduling procedures, which exacerbated delays

DISCUSSION

QUANTITATIVE COMPONENT (AIMS 1&2)

This study assessed how health service-related factors affected time taken to establish a diagnosis of TB and start treatment after a patient presented for consultation. Our findings show that there are opportunities to prevent delays in the TB care process. This study shows that 75% of patients' treatment was initiated within three days. Though this compares favorably with five days in Zimbabwe (Takarinda et al, 2015) and six days in Ethiopia (Dimissie et al, 2002), a three-day window in our study points to missed opportunities to diagnose and treat TB on a patient's first HF visit. The World Health Organization recommends same day laboratory TAT and treatment initiation if a positive result is reported (Davies et al, 2011). We found that HF level delays resulted from factors surrounding the TB testing processes and was independent of a HF's structural characteristics. Therefore, care processes, and by extension quality of existing TB services, must be streamlined to eliminate HF level delays that may frustrate patients who seek care with TB symptoms.

Association of service delivery factors with laboratory turnaround time

Only two-fifths of TB test results were reported on the day a patient submitted a specimen suggesting most patients made at least two HF visits before receiving TB test results. Patients receiving TB test results two or more days after submitting a specimen has previously been found by other researchers where delay was attributed to use of a centralized laboratory system prolonging turnaround time (Claassens et al, 2013). Our study excluded patients diagnosed at an external laboratory and still showed delays suggesting that there are

inefficiencies in the onsite TB testing process. Knowing that most patients had two or more TB tests, it is possible specimens were being tested in batches after all required specimens have been submitted. Only 6.2% of our study patients required a repeat test after an index negative result. Therefore, unnecessary repeat laboratory visits and hence TAT can be reduced substantially if TB test results are reported the day the patient first visits a laboratory for testing.

We found that length of laboratory TAT was independent of HF structural characteristics. There were no differences by ranking of a HF within the health system hierarchy and nor were there differences by HF ownership or number of laboratory personnel. Previous studies have focused mainly on how these structural factors were associated with TB testing in terms of whether a TB test is available onsite or not, and bottlenecks in ordering tests (Belay et al, 2012; Buregeya et al, 2013; &Yimer et al, 2003). In Uganda, higher level HFs by design have more and better trained laboratory personnel than those at lower level ones. This numerical and skills advantage should translate into a shorter TAT. But these HFs also have a higher patient load and hence the personnel to work volume ratio result in similar wait times across all HF levels. In addition, it appears in-service training on TB testing has narrowed the skills gap between personnel between smaller and larger HFs.

Our findings demonstrate a weekend effect on TAT of TB tests. Patients tested for TB on a weekend had a longer TAT than those tested during weekdays. A weekend effect in TB care has not been studied before. Evidence that quality of health care declines outside of business hours has previously been reported in studies involving in-patient treatment and

reported in terms of adverse disease outcomes (Bray et al, 2016; Aldridge et al, 2016). In Uganda, it is mandatory that all services, including outpatient ones, are available even on weekends. However, it is possible that on weekends, TB testing is not a priority since patients are unlikely to present as emergencies requiring urgent attention. TB testing being an outpatient procedure, our study finding suggests that a weekend effect applies to both in-patient and outpatient care. Further research involving interviews with weekend staffs or patient simulations could help us understand factors underlying the weekend effect.

Interestingly, retesting for TB prolonged TAT following an index test was negative but had no effect when it was positive. Uganda's national TB care protocol recommends collection and testing of a second sample a day after the index test (MoH, 2017b). The procedure for retesting, including timing of specimen collection, does not depend on the index TB test result. It is possible there is more urgency to repeat a TB test if the index result is positive than when it is negative. But also our study had a major limitation of not having a provision for recording results date in the laboratory register, and instead relied solely on the treatment register to compute TAT. The date in a treatment register is likely to correspond to a specific positive result based upon which treatment is started, and not for each test done for a patient as part of evaluation for the disease. This makes TAT for patients initially testing negative to appear longer since intervening periods when from negative results were not recorded. On the one hand, those retesting following a positive result may have the date of this result recorded even as they await a repeat result. Relative to the lab visit date, TAT is essentially timing of a positive result, not a true duration of each TB test. Provision for a

results date in the laboratory register is necessary to improve accuracy of lab TAT since this will capture information by each individual test.

Association of service delivery factors with treatment initiation time

We found that 75% of the TB patients started treatment within one day of results reporting showing most patients had prompt initiation of treatment. This contrasts with findings in Ethiopia (Belay et al, 2012), Ghana (Lawn et al, 1998) and China (Xu et al, 2013) where 75% treatment initiation was reached after 4, 14 and 73 days respectively. Only in Mozambique was treatment initiated in three days (Saifodine et al, 2013). In our study, it is apparent that once a positive TB result was reported, most patients start treatment, having waited until results were reported or the system was being efficient at tracking patients with positive results and initiating them on treatment.

We observed that health facilities structural characteristics had no statistically significant effect on TxIT suggesting that actions taken to trace newly diagnosed patients and start them on treatment were similar regardless of HF size, location, ownership or even laboratory staffing. Prolonged TxIT has previously been described in the context of lacking extra personnel to trace patients upon receipt of TB test results from an external laboratory (Claassens et al, 2013); unlike in our study where both diagnosis and treatment were onsite. In another study involving structural factors, a longer TxIT in private HFs compared to public ones was attributed to patients in the former having to wait until guidance on drug regimens, dosage and other treatment decisions were obtained from the latter (Belay et al, 2012). In our study setting, opportunities for training and ongoing technical support have penetrated all HFs equally. Having a nationally mandated treatment protocol has ensured

standardized approaches to treatment initiation. There was a significantly lower TxIT in Kyenjojo compared to other districts pointing to a better coverage of these capacity building interventions.

Patients diagnosed by Gene Xpert test had a longer TxIT than those tested by microscopy suggesting operational challenges in using the Gene Xpert technology. A similar finding with use of Xpert technology has previously been reported in a centralized laboratory setting (Cohen et al, 2015; Page et al, 2016). Here a return visit to receive TB results was mandatory and therefore TxIT depended on a patient returning as scheduled and the HF having adequate default reminder systems. When results were not returned as scheduled, patients may give up after repeated HFs visits to get results (Claassens et al, 2012). Since all our study patients were diagnosed and treated at the same facility, we expected identical treatment initiation procedures between the two diagnostic approaches. Notable in this study is that Xpert sites serve as referral laboratories services for surrounding facilities and as such have a higher work load than those only providing microscopy. The resulting increase in wait time and hence prolonged TAT means these patients are more likely to require multiple visits before they receive results and start treatment. Therefore, it is important to put in place a system to absorb the additional samples brought from surrounding HFs.

Association of service delivery factors with treatment delay

In this study, 25% of the patients experienced treatment delay of more than two days having had a prolonged TAT and /or TxIT. This compares favorably with a rate of 31% that was reported in Zimbabwe even after a longer cut off threshold of four days was used (Takarinda et al, 2015). However, it is also possible that a higher rate in the reference study

was due to some patients being tested at external laboratories. Nonetheless, our finding still suggests the need to reduce delays. The current recommendation is for each presumptive TB patients to be tested and, if positive, commence treatment on the same day the patient presents for consultation (Davies et al, 2011). We selected a two day cutoff to accommodate patients who had an index negative result and needed an additional test to establish a positive TB diagnosis. Thus, much effort is needed to reduce delays knowing that with 75% of patients beginning treatment in three days, we are still far from achieving what is currently recommended.

Notably, health facility size (level within health system hierarchy), ownership and laboratory staffing did not affect treatment delay. Previous studies have reported that public and higher-level HFs had less delays compared to private and lower-level HFs (Getnet et al, 2017). Underlying reasons for these differences were relatively poor TB care knowledge and skills among health care professionals at lower level HFs and private ones (Takarinda et al, 2013; Buregeya et al 2013). Uganda has a standardized TB treatment protocol suggesting that knowledge and skills should not differ by healthcare facility structural characteristics. Also it is possible that small size HFs that typically have low staffing also had low patient volumes allowing for an appropriate patient to staff ratio regardless of HF size. None of the facilities in our study were private for profit HF, which limits our ability to compare private and public HFs. Thus, a better conclusion about structural characteristics could be drawn if the inclusion of a better representation of private for-profit HFs that are often small clinics and dispensaries.

Use of Gene Xpert technology still faces operational challenges since patients diagnosed by Gene Xpert testing had higher odds of delays than those tested by microscopy. Concerns with use of Gene Xpert have mainly been from centralized laboratory settings where delays were attributed to long TAT for results from the referral laboratory coupled with inefficient systems for tracing patients to start treatment (Takarinda et al, 2015; Cohen et al, 2015; Page et al, 2016). Though we excluded patients that received an Xpert test from an external laboratory, it is important to note that HFs with Xpert machines in Uganda also serve as referral laboratory services to surrounding facilities on top of processing specimens collected on site. As such TB test work volume was relatively higher at HF with Gene Xpert than those with microscopy, which may prolong TAT. Under such circumstances delays were due to failure to absorb extra workload associated with an Xpert site serving external patients.

We also found that retesting for TB increased delays irrespective of the initial test result. It appears there are no studies evaluating the effect of retesting on TB treatment delay. It is not surprising patients with a negative index TB test result has a treatment delay since they must make additional visits before being eventually diagnosed. Among those whose index test was positive, it appears initiation of treatment was done mostly after they have received a second TB test result. The national TB treatment protocol recommends commencing treatment for any one positive test result (MoH, 2017a). Given only 6% of the patients had an index negative result, most patients should have commenced TB treatment after the index test. Therefore, preventing unnecessary repeat TB testing could go a long way in reducing treatment delays.

We found being tested on a weekend increased odds of treatment delay suggesting inefficiencies in TB care processes at this time of the week. Studies reporting weekend effect are mainly from inpatient and emergency room settings, and report differences in outcomes (Bray et al, 2016; Aldridge et al, 2016). Here outcomes being worse on weekends was attributed to delays in responding to needs of inpatients.. An observation of a weekend effect in our study is evidence that while TB services were available throughout the week, there were missed opportunities to identify and manage presumptive TB cases. However, there appears to be less dedication to caring for presumptive TB cases compared to other tasks on weekends. Qualitative interviews comparing patients presenting on a weekday to those seen on weekends would clarify how timing of the lab visit translates into treatment delay.

In summary, our study shows there are delays even after a presumptive TB patient presented to a one stop center for diagnosis and treatment. There were opportunities for patients to receive TB test results and have appropriate care decisions taken promptly. Independent predictors of delay were being tested on a weekend, being diagnosed at a site where primary diagnostic technology was Gene Xpert, and non-adherence to the TB testing protocol. Health service factors related to structural characteristics of the health care facility did not affect the extent of TB treatment delay. However, a lot more on how these factors are associated with treatment delay can be learned from observation and time motion studies to examine TB care processes.

QUALITATIVE COMPONENT (AIM 3)

The study sought to understand practices among healthcare workers that lead to delays in initiating TB patients on treatment. We found a big knowledge - action gap about recommended practices in the diagnosis and /or initiation of TB treatment. Healthcare workers understood that presumptive TB cases had to be identified and given priority over other patients, but this was not implemented consistently. Care decisions were often deferred awaiting designated personnel to sanction them. In addition, TB testing had a separate time schedule, often off-peak hours, which prolonged TAT for TB results compared to other laboratory services. Accordingly, trained healthcare workers must be supported to put acquired knowledge into practice.

We found that individuals with TB symptoms often waited in queues alongside other patients showing that triage and fast tracking of presumptive TB cases was not being done consistently. Under these circumstances, TB patients must wait a long time before they are assisted or be forced to defer care, thereby hindering timely diagnosis of TB. This is consistent with findings of presumptive TB patients waiting in long queues at OPD, laboratory and even at dispensing windows in Uganda (Buregeya et al, 2013) and Malawi (Chimbatata et al, 2017). Here lack of consistent triaging was attributed to lack of staff dedicated to attending to TB patients, inadequate space for isolating presumptive TB patients and healthcare workers not understanding how this ultimately prevented disease transmission. In our study, we found that community volunteers reminded HF staff to attend to presumptive TB cases, which highlights the need for staff dedicated to TB patients. Without a dedicated team, HF staff will always be faced with competing priorities and hence

inefficiencies in the triage process. On the other hand, it is possible that triage protocols were simply ignored due to a perceived need to be fair to all waiting patients.

We found that TB testing was done at a specific time, usually during off peak hours, which suggests lack of integration of TB testing into routine laboratory services. It appears existence within a HF of a TB test schedule parallel to that of other laboratory services has previously not been reported. Uganda's TB treatment protocol does not explicitly recommend turnaround of a TB test result. But such institutionalized schedules mean that TB specimens were tested in batches and therefore patients must wait until late in the day or make a return visit to receive TB test results. Laboratory personnel felt this minimized the number of times they were exposed to infectious specimens and eliminated time loss that comes with elaborate clean up required after each TB test. It is also possible that a separate time schedule is a strategy to deal with heavy specimen volumes knowing that TB treatment guidelines do not emphasize urgency of TB over other laboratory tests. Therefore, fully integrating TB testing into routine laboratory services requires addressing the above concerns as well as recommending TB test TAT.

Our findings suggest that care decision making also delayed TB treatment. Patients identified at triage had to be reviewed by a clinician before they were sent to the lab, which prolonged wait times. Furthermore, in some HF only designated personnel could initiate TB treatment. We did not come across literature highlighting bottlenecks associated with waiting for second opinion or designated personnel before sanctioning a TB care procedure. In Uganda, all TB care procedures have accompanying decision support tools that are simplified

for use by all cadres of healthcare workers. Accordingly, there was a need to train and support more staff to participate in providing TB care.

Interestingly fear of contracting TB motivated healthcare workers to get involved in TB care as much as it shaped a negative attitude towards TB among others. The more healthcare workers fully appreciated they were at higher risk than the general population, the more they got involved in providing TB services. Existing literature largely associates fear of contracting TB among healthcare workers with discrimination of presumptive cases (Chimbatata et al, 2017; Buregeya et al, 2013). A study in Russia reported that fear of passing infection to loved ones did motivate healthcare workers to attend to TB patients (Woith et al, 2012). In our study, linking TB treatment to reduction of transmission to themselves and their families as well as other patients motivated healthcare workers to attend to TB patients. Healthcare workers are inevitably exposed to TB, due to frequent interaction with patients with undiagnosed and potentially contagious TB. Given HFs do not have dedicated staff to handle TB care tasks, getting more healthcare workers to take on the additional task of TB care will need to be centered on improving risk perception.

This study suggests there was no discrimination against TB patients. Further, healthcare workers attending to TB patients did not experience courtesy stigma. Though reports of courtesy stigma are limited, discrimination amongst TB patients has been reported. A study in Malawi reported discrimination of TB patients was mainly because of fear of acquiring infection while attending to them (Chimbatata et al, 2017). It appears fear of contracting TB did not influence attitude towards TB patients and to those attending to them. We found that fear of being infected was heightened by perceived lack of personal protective

measures. Therefore, it is possible that discrimination against TB patients and health workers attending to them was lessened by availability of protective measures. But it is also possible that this positive finding was because our respondents being involved in TB care and already had a positive attitude to TB patients. There could also have been social desirability bias since our findings were not corroborated by observation of TB care processes at study sites. A better approach to confirm this finding would be to conduct observations along with interviews.

This study demonstrates that lack of appropriate knowledge and skills was both a genuine explanation as well as an excuse for health workers not promptly attending to TB patients. We learnt that some trained staff avoided TB care tasks and yet some that were not trained did not. This contrasts with studies on failure to implement TB infection control measures that make no reference to use of excuses by healthcare workers to avoid attending to TB patients (Woith et al, 2012; Buregeya et al, 2014). In Uganda, HFs hold continuing medical education sessions during which staff(s) returning from trainings share acquired knowledge and skills with the rest. Accordingly, non-participating staffs were seen more as giving excuses than expressing genuine lack of knowledge.

In summary, expressed knowledge of measures to prevent delays were not accompanied by appropriate practices. TB care processes were characterized by patients waiting in queues alongside general patients and a parallel test schedule, which prolonged turnaround times. Identified presumptive TB cases had to wait for a second opinion before ordering a TB test and there was lack of contingency measures to deal with staff absences.

Key barriers to timely diagnosis of TB were negative attitude among healthcare workers and understaffing.

Despite the above findings the study has several limitations. All respondents reported were actively participating in providing TB care, which could have overrepresented a positive rating of existing services given there was no comparison group. The study did not verify by observation or other objective tests some of the findings especially positive ones. Using key informant interviews, it is possible that respondents reported socially desirable practices.

STUDY SUMMARY AND IMPLICATIONS

This study shows how critical efficiency of laboratory services is to initiating TB treatment. Health service-related factors that were associated with increased risk of TB treatment delay, which were use of Gene Xpert test technology, being retested during the course of diagnosis, and undergoing a TB test on a weekend, were all laboratory related. A qualitative component helped highlight healthcare workers' perspective about the adoption and implementation of efficacious TB care protocols. Existing records present a cheaper option of data collection compared to other methods given records abstraction is cheaper and less time consuming than other data collection approaches. This study examined patient records from many HF across different levels and therefore findings can be generalized to most primary care settings. Restricting the study to only HFs continuously providing TB services offers a window into quality gaps that may undermine the translation of expanding access to TB services into improved disease control. Such gaps resulting in delays are

essentially missed opportunities to treat TB early and prevent transmission. These study findings therefore contribute to finding ways to reduce the TB burden.

The study however has a few limitations. Time is measured in days instead of hours or minutes which would have given a better resolution and hence detect more variation than we observed. In measuring total treatment time, we assumed every patient was identified and tested for TB on the same date he/she first sought consultation at the HF. Using initial consultation as a start point and therefore including the screening stage in computing total time and helps determine if upstream processes before visiting the laboratory have an effect on delays. Existing TB care records used for this study contained few sociodemographic variables, which limited the number of patient characteristics and hence confounding variables that could be controlled for during analysis. There were no records of such variables as a distance to the health facility, income and occupation that have been reported to increase delays (Storla et al, 2008; Gettnet et al, 20017). A study that supplements existing records with interviews of TB patients and clinical notes can help narrow this gap.

By only enrolling TB patients that were eventually started on treatment, study findings may not be generalizable to all presumptive TB cases. Knowing that only 8-10% of presumptive TB cases test positive for TB (Chang et al, 2012), any difference between these and those that were negative results will surely undermine validity and hence external validity of study findings. Finally, findings from the interviews were not verified by observation and other objective measures, which introduces social desirability bias. Random selection of respondents would have minimized this but that staff interviewed typically had been on the frontline before moving to supervisory role. Since interviewees were in

leadership positions, they could have been motivated to portray a positive picture of TB care processes. Addressing the above limitations requires complementary data sources, which calls into consideration discussion of which one approach cross cuts across most of the limitations.

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APPENDICES

Appendix 1: Data abstraction form

Study site code _____	<div style="border: 1px solid black; width: 100px; height: 30px;"></div>
Study participant _____	

Study subject's name _____ study ID _____

Health facility name _____

Date of data collection ____/____/____

Research assistant's name _____

Part 1: Patient data abstraction form

Laboratory register

1. Age: _____ years
2. Gender
☐ Male
☐ Female
3. HIV status
☐ Positive
☐ Negative
☐ Unknown
4. Date of sputum specimen submission (dd/mm/yyyy): ____/____/____
5. Does the specimen submission date fall on a weekend (Friday, Saturday or Sunday)?
☐ Yes
☐ No
☐ Unknown

6. Number of specimens tested: _____ specimens

Tick that applies

Scenario	Smear results		NAAT e.g. Gene Xpert	Number of specimens tested
1	+			1
2	-	+		2
3	+	+		2
4			+	1
5	-	-	+	3
6	+	+	+	2
7	-	+	+	2

7. Sputum test results (write 999 to indicate no results)

Specimen 1 _____

Specimen 2 _____

Specimen 3 _____

Specimen 4 _____

8. Number of specimens tested to establish diagnosis

☐

1 specimen (*scenarios 1&4*)

☐

2 or more specimens following an initial negative result (*scenarios 2,5&7*)

☐

2 or more specimens following an initial positive result (*scenarios 3&6*)

9. Type of test(s) conducted (*circle all that apply*)

☐

Microscopy

☐

Gene Xpert test

☐

Other(specify) _____

Comments: _____

Unit TB register

10. District TB number

11. TB treatment start date: ____/____/____ (write 999 if information is missing)

12. Results reporting date: ____/____/____ (write 999 if information is missing)

13. Was patient diagnosed at a time the health facility had a stock out of anti-TB drugs?

- ☐ Yes
☐ No
☐ Unknown

14. Write TB type (disease class) indicated in the register _____

15. Has patient been treated for TB before this current episode? *Check for type of TB*

- ☐ Yes
☐ No

Out-patient department register

16. What was the date of the first visit the patient made in the 14 days prior to diagnosis?

____/____/____ (write 999 if information is missing)

17. How many visits including that of the specimen submission date, were made prior to testing of first sample? _____ (write 999 if information is missing)

18. Please indicate treatments received on all visits including the dates when patient visited health facility and when a TB specimen was submitted for testing. *Write 999 if information is missing*

Date of facility visit	Diagnosis	Treatment given (drugs)
____/____/____		
____/____/____		
____/____/____		
____/____/____		

19. Did the patient receive antibiotics on any of the above visits?

- ☐ Yes
☐ No
☐ Unknown

Part 2: Health facility data

20. Location of Health facility (name of the district) _____

21. Health facility ownership

- ☐ Publicly owned
☐ Private not for profit
☐ Private for profit

22. Level of facility within health system hierarchy

- ☐ Health center III
☐ Health center IV
☐ Hospital

Laboratory services

23. Count the unduplicated number of trained laboratory personnel (assistants, technicians and technologists) from the laboratory duty roster? _____

24. What equipment is available for TB testing at this Health facility? *tick all that apply*

- ☐ Microscope
☐ Gene Xpert machine
☐ Others (specify)_____

25. What laboratory TB tests are available to patients at this healthcare facility upon sample referral?

- ☐ Fluorescent microscope
☐ Gene Xpert machine
☐ Culture
☐ Others (specify)_____

26. Are all registers covering the study period January 1st, 2016 to December 31st, 2017 available?

Please indicate in the comments section the dates for which registers are missing

Register	Are all registers available?	Comments (indicate dates for which registers are missing)
Lab register		
TB unit register		
OPD register		

27. In the lab register, count the number of patients that were tested for TB in the following time periods. *Exclude those indicated as follow up*

Period	Total tested	Total sputum positive
Jan 1 st – Mar 31 st , 2016		
Apr 1 st – Jun 30 th , 2016		
Jul 1 st – Sep 30 th , 2016		
Oct 1 st – Dec 31 st , 2016		
Jan 1 st – Mar 31 st , 2017		
Apr 1 st – Jun 30 th , 2017		
Jul 1 st – Sep 30 th , 2017		
Oct 1 st – Dec 31 st , 2017		
Total		

Average quarterly number of cases diagnosed _____

28. Ask health facility TB focal person: How many times did the healthcare facility experience a stock out of anti-TB drugs in the period *January 1st, 2016 to December 31st, 2017*?

29. Document periods of stock outs of TB drug (*record dates when levels of any of the TB drugs (RH or EH or RHZE) were recorded as zero on the stock card*)

<u>From</u>	<u>To</u>	<u>Drug name(s)</u>
____/____/____	____/____/____	_____
____/____/____	____/____/____	_____
____/____/____	____/____/____	_____
____/____/____	____/____/____	_____
____/____/____	____/____/____	_____
____/____/____	____/____/____	_____

Appendix 2: interview guide

Interviewee data collection sheet

Level of health facility: _____

Age: _____ years

Gender of respondent: Male/Female

Job designation: Laboratory in charge/ clinical team leader/ in-charge outpatient department

Semi-Structured Interview guide

1. Tell me how you came to be treating TB patients?
2. What specific roles do you currently have in the diagnosis and treatment of TB?
3. Can you please describe the detection and treatment process for TB patients in your facility?

Probe:

How is it done in the unit where you currently work?

What happens in other units within this health facility that you collaborate with?

What specific practices might contribute to delays after a patient has presented for consultation?

What about your fellow staffs? What is it that they do that contributes to the time it takes to get diagnosed and treated for TB?

4. What about the TB patients? How different are they from other patients that you see?

Probe:

Do these differences from other patients affect the way they are attended to?

Do you have any concerns about treating TB patients? Do any of your colleagues have concerns about treating TB patients?

How do other staff feel about those of you who treat TB patients?

5. What needs to be done to get all TB patients tested for TB and treated on time?

Probe:

How much maximum time it should take to identify and treat a TB patient.

What needs to be done to fast track TB services?

Of what benefit is fast tracking TB services?

6. Is there anything else that you would like to tell me about delays in treating TB patients that we have not discussed?

Thank you for participating in this study

Appendix 3: Informed consent form

University of Texas Health science center at Houston

**INFORMED CONSENT FORM TO TAKE PART IN RESEARCH
HSC- -SPH-18-0264**

INVITATION TO TAKE PART

You are invited to take part in a research project called **Examining the effect of service delivery factors on timely initiation of tuberculosis treatment within primary care settings in Uganda (TB treatment delay study)** conducted by Dr. Juma Michael of the University of Texas Health science center at Houston (UThealth). For this project he will be called the principal investigator.

Your decision to take part is voluntary. You may refuse to take part, or choose to stop taking part, at any time. A decision to not take part or stop being part of the research project will not affect your work evaluation or any other aspect of your job.

You may refuse to answer any question asked. This research project has been reviewed by the committee for protection of human subjects of University of Texas Health science center at Houston as HSC- -SPH-18-0264.

PURPOSE

The purpose of the research study is to understand your perspective if there are delays in diagnosing and treating TB in terms of causes and ways to prevent delays if they occur. This research study looks at the time it takes to diagnose and treat TB after the patient has presented to a health facility providing the services. The interest is in understanding delays in identifying patients for TB testing, completing required tests and starting those with the disease on treatment. We would like to know what can be done to minimize delays. You are being invited to join this research.

PROCEDURES

You have been selected to participate in this interview because of the critical role your unit plays in identifying and providing care to patients with TB symptoms. You play an important role in the diagnosis and treatment of TB within the health facility.

If you agree and are able to participate in this study you will first sign a consent form before undergoing the interview. During the interview I will sit with you in a comfortable place at your place of work or any other location of your choice. This will be conducted during the working hours and interviews will therefore occur at a time when you can take a break from your work to be interviewed. Please feel free to let me know if you do not wish to answer any question and I will move to the next one. The interview will be audio-recorded in effort to capture responses during the interview. The tape will be kept in a locked cabinet in my office at school. The interviews will be deleted from the recorders once transcription is completed. The information is confidential and only my research supervisors and I will have access to it. No name of the responded or health facility will be recorded.

TIME COMMITMENT

Only a single interview will be conducted. It is planned that the interview will last 30-50 minutes.

BENEFITS

There is no immediate direct benefit to you for your participation. Your participation will contribute to finding out how to treat TB early and prevent its transmission within health facilities and communities.

RISKS AND /OR DISCOMFORTS

There is no major risk associated with participating in this study. However, you may lose some work time since the interview will be conducted during business hours. The interview will be scheduled at a time when it is convenient to take a break off your work schedule to minimize lost work time. Also you may feel embarrassed or uncomfortable answering some of the questions. You may stop at any time or skip any questions. During the interview, please feel free to seek for clarifications on interview questions and not answer those you find difficult or uncomfortable about.

There is no anticipated risk that your personal information will be shared. The information that will be collected concerns how your facility is managing patients presenting with TB symptoms. The information the researcher collects will only have a number instead of your name. The health facility name will also be replaced by a number. Only the researcher will know your number and that of your health facility. This number will be kept locked up in a filing cabinet and can only be accessed by the principal investigator and research supervisors.

Nonetheless you do not have to answer a particular question or take part in the interview if talking about a particular topic makes you uncomfortable.

STUDY WITHDRAWAL

Your participation in this research study is entirely voluntary. You can choose to participate or not. Participating or not will not affect your job or work evaluation in any way. You may also stop participating in this study at any time. This will not put you at a disadvantage in anyway. In event that you withdraw from the study, all information so far collected about you will be discarded and therefore none of it will be used.

COST, REIMBURSEMENTS AND COMPENSATION

If you decide to take part in this research study, you will not incur any additional costs. You will not be provided money or any other type of incentive for participating in this study.

Sharing the Results

The results of the study will only be published in journal articles as a whole so that there will be no way of knowing your name or that of your health facility and district. The knowledge will be shared with health sector planners, academia and the public through publications in journals so that other people can learn from the research.

CONFIDENTIALITY

You will not be personally identified in any reports or publications that may result from this study.

Please understand that representatives of the, the University of Texas Health Science Center at Houston, the sponsor of this research, and/or companies engaged with UTHHealth for the commercialization of the results of the study may review your research and/or medical

records for the purposes of verifying research data, and will see personal identifiers. You will not be personally identified in any reports or publications that may result from this study. There is a separate section in this consent form that you will be asked to sign which details the use and disclosure of your protected health information.

QUESTIONS

This research study has been approved by the committees that are responsible for protecting people participating in research from harm in Uganda. It has also been approved by the University of Texas Committee for protection of human subjects (CPHS).

If you have questions at any time about this research study, please feel to contact the following as they will be glad to answer your questions:

The principal investigator, Dr. Juma Michael on +256770898832

Dr. Jesse Kagimba, M.D., M.Sc. Chairman IRB/REC, Joint Clinical Research Centre, Lubowa Hill, Plot 101Entebbe Road P. O. Box 10005, Wakiso District, Uganda. Tel: +256 417723000 Cell: +256 712 531 656/+256 706 300 300	University of Texas Committee for the Protection of Human Subjects 6410 Fannin, Suite 1100 Houston, Texas 77030 Phone +1713-500-7943 Fax +1713-500-7951 Email cphs@uth.tmc.edu
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You can also contact the study team to voice your concerns, discuss problems, obtain information, and offer in put in addition to asking questions.

SIGNATURES

Sign below only if you understand the information given to you about the research and you choose to take part. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at (713) 500-7943. You may also call the Committee if you wish to discuss problems, concerns, and questions; obtain information about the research; and offer input about current or past participation in a research study. If you decide to take part in this research study, a copy of this signed consent form will be given to you.

_____ Printed Name of Subject	_____ Signature of Subject	_____ Date
_____ Printed Name of Person Obtaining Informed Consent	_____ Signature of Person Obtaining Informed Consent	_____ Date

CPHS STATEMENT: This study (HSC-SPH-18-0264) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston. For any questions about research subject's rights, or to report a research-related injury, call the CPHS at (713) 500-7943.

Date_____/_____/_____