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# Facilitators and barriers to initiating and completing tuberculosis preventive treatment among children and adolescents living with HIV in Uganda: a qualitative study of adolescents, caretakers and health workers

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## Abstract

**Introduction** People living with HIV (PLHIV) have a 20-fold risk of tuberculosis (TB) disease compared to HIV-negative people. In 2021, the uptake of TB preventive treatment among the children and adolescents living with HIV at the Baylor-Uganda HIV clinic was 45%, which was below the national target of 90%. Minimal evidence documents the enablers and barriers to TB preventive treatment (TPT) initiation and completion among children and adolescents living with HIV (CALHIV). We explored the facilitators and barriers to TPT initiation and completion among CALHIV among adolescents aged 10–19 years and caretakers of children below 18 years.

**Methods** We conducted a qualitative study from February 2022 to March 2023, at three paediatric and adolescent HIV treatment centers in Uganda. In-depth interviews were conducted at TPT initiation and after completion for purposively selected health workers, adolescents aged 10–19 years living with HIV, and caretakers of children aged below 18 years.

**Results** The desire to avoid TB disease, previous TB treatment, encouragement from family members, and ministry of health policies emerged as key facilitators for the children and adolescents to initiate TPT. Barriers to TPT initiation included; TB and HIV-related stigma, busy carer and adolescent work schedules, reduced social support from parents and family, history of drug side effects, high pill burden and fatigue, and perception of not being ill. TPT completion was enabled by combined TPT and ART refill visits, delivery of ART and TPT within the community, and continuous education and counseling from health workers. Reported barriers to TPT completion included TB and HIV-related stigma, long waiting time. Non-disclosure of HIV status by caretakers to CALHIV and fear of side effects was cited by

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health workers as a barrier to starting TPT. Facilitators of TPT initiation and completion reported by healthcare workers included patient and caretaker health education, counselling about benefits of TPT and risk of TB disease, having same appointment for TPT and ART refill to reduce patient waiting time, adolescent-friendly services, and appointment reminder phone calls.

**Conclusion** The facilitators and barriers of TPT initiation and completion among CALHIV span from individual, to health system and structural factors. Health education about benefits of TPT and risk of TB, social support, adolescent-friendly services, and joint appointments for TPT and ART refill are major facilitators of TPT initiation and completion among CALHIV in Uganda.

**Keywords** Children, Adolescents, Tuberculosis, Preventive treatment, HIV, Initiation, Completion, Barriers, Facilitators, Caretakers

## Introduction

Globally, 10.6 million people fell ill with tuberculosis (TB) in 2022, of which 12% were children below 15 years of age, and 23% reported in Africa [1]. People living with HIV (PLHIV) accounted for a disproportionate 6.7% of the TB cases and TB-HIV co-infection rates greater than 50% persist in numerous countries [1]. Out of the 1.6 million TB related deaths that occurred in 2021, 187,000 were among PLHIV, with 11% among children living with HIV [1].

Following TB exposure, PLHIV have a 20-fold increased life-time risk of progressing to TB disease, and up to 15% annual risk of TB disease, compared to the general population [2]. There is evidence that TB preventive treatment (TPT) in combination with anti-retroviral therapy (ART), reduces the risk of TB disease by up to 90% [3, 4]. During the period 2018–2021, 10.6 million PLHIV received TPT globally, which was more than the targeted 6 million PLHIV. Nevertheless, there is minimal global data reporting TPT completion rates.

Uganda is one of the 30 countries categorized as high TB and TB/HIV burden by the World Health Organization (WHO) [1], with 74,799 TB patients reported in 2022, of which 32% were HIV-co-infected, and 12% were children below 15 years of age [1]. Following three nationwide TPT uptake campaigns led by the Ugandan ministry of health, 88.8% of the eligible PLHIV received TPT [5]. In Ugandan public health facilities, only 17% PLHIV initiated TPT out of the 93% who were eligible for TPT, with only 58% completing the full TPT course [6]. Some of the documented challenges contributing to such gaps in TPT uptake among PLHIV include; hesitancy of health workers to prescribe TPT for fear of promoting drug resistance, interrupted TPT supply, patients' fear of additional pill burden and side-effects [6]. Non-completion of TPT was also associated with ART non-adherence, ART regime switch, and patient representation among adult PLHIV in rural Uganda [7]. Effective implementation of TPT, through addressing identified barriers and enhancing the facilitators of TPT [8], is key in reducing the burden of TB disease among PLHIV and bridging

the TPT uptake and completion gaps [9–11]. However, there is limited data on TPT completion especially among PLHIV who are concurrently on ART. Therefore, it is important to understand the multi-faceted barriers and facilitators of initiating and completing TPT among the PLHIV. These may be related to the different health-care system components such as; the clients or community, health policies, leadership and governance, drugs and logistics management, clinical information systems, service delivery, health workforce and financing [12]. Individual factors reported to facilitate TPT uptake and delivery among PLHIV in Tanzania include; alignment of ART and TPT visits, and TPT-related education and counseling. In South Africa, individual facilitators of TPT completion among PLHIV included; knowledge about TB and TPT, acceptance of one's HIV status, having social support in the community and at the health facility, and desire for health preservation [13]. Individual barriers to TPT uptake and delivery included; perceived or previous experience of side effects, HIV stigma, pill burden, negative cultural and religious values, misunderstanding of TPT's preventive role, financial burden of transport to the clinic and lost wages, and ineffective communication with the health workers [13–15].

Health care worker facilitators of TPT initiation among PLHIV include; comprehensive and collective planning, and supervision, presence of guidelines, TB-HIV training, positive attitude and being knowledgeable about TPT, known benefit of TPT, and effective health worker communication [8, 13, 16]. Health care worker and health system barriers to TPT delivery and uptake include; fear for isoniazid resistance due to interrupted drug supply, poor knowledge and attitude, misunderstanding about timing of TPT initiation, shortage of skilled health workers, variable TB screening practices and responsibilities, drug shortage [10], and contradicting guidelines from TB programs and HIV care programs [14, 17–19]. In South Africa, lack of fidelity to national TPT guidelines was a barrier among health workers to initiation of TPT for PLHIV [20]. Absence of parental risk perception was reported as a barrier to TPT uptake among children in

TB endemic areas [21]. Most of the documented facilitators and barriers to TPT initiation and completion are among adults, with limited reports for children, adolescents and their care takers.

Therefore, we conducted a qualitative study to explore the perceived and experienced barriers and facilitators to TPT initiation and completion among Ugandan children and adolescents living with HIV (CALHIV).

### Theoretical orientation

A growing body of literature illustrates that health outcomes are progressively influenced by the environments within which individuals thrive and less by individual behaviors [22]. We therefore adopted the social ecological model (SEM) as a theoretical framework for analysis (see Fig. 1 below). The social-ecological model (SEM) of health promotion by McLeroy and colleagues states that health behaviour and promotion are interrelated and occur around multiple levels in the individual, interpersonal, institutional, community, and policy levels [23]. This multifaceted perspective is important to understand and explicate barriers and facilitators of TPT initiation and completion among children and adolescents living with HIV, caregivers, and health care workers. The first level refers to individual factors that facilitate or inhibit a person's choices, including personal stigma, limited knowledge about the prevention treatment, financial constraints and drug characteristics. The second level is interpersonal or network influences. An individual's relationship with their closest caretakers, and family members influences their uptake and completion of preventative treatments. The third level is community perspectives, as children, caregivers and health care workers

are influenced by community-held mass awareness campaigns community drug delivery services and community misconception about prevention treatments. The fourth level refers to health system (institutional) influences, including busy, unapproachable health care workers, limited access to the right treatment and the long waits. The final level refers to structural influences including the accessibility of the information and services related to TB.

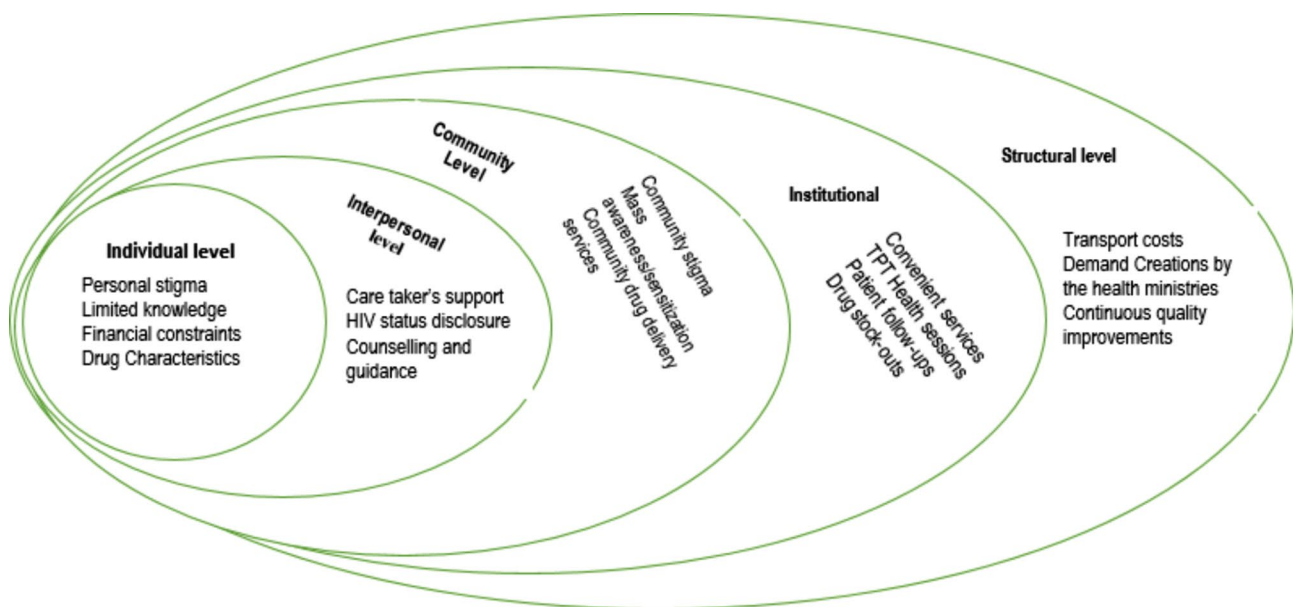
### Methods

#### Study design and data collection methods

This qualitative study was part of a prospective cohort study conducted from February 2022 to March 2023; where CALHIV and their care takers were offered to choose either facility-based or community-based initiation and delivery of TPT. This was part of the differentiated TPT delivery among CALHIV in Uganda (COMBAT TB study).

#### Study setting

The study was conducted at three high-volume paediatric and adolescent HIV treatment clinics; Baylor College of Medicine Children's Foundation-Uganda (Baylor-Uganda) center of excellence (COE) HIV clinic located in Mulago Hospital Kampala, Joint Clinical Research Center (JCRC) located in Lubowa, and the Makerere Joint AIDS Program (MJAP) ISS Clinic located on Mulago Hill in Kampala. The Baylor-Uganda clinic located about 4 km from the Kampala city center, provides comprehensive HIV care services for more than 4000 CALHIV out of more than 8000 PLHIV in care at the clinic. The JCRC Lubowa HIV clinic located in Wakiso district, 11 km



**Fig. 1** Illustration of the SEM framework showing the interrelations at various levels

from Kampala, and it provides comprehensive HIV care services to 1300 CALHIV out of 15,000 PLHIV in care. The MJAP ISS clinic located on Mulago Hill in Kampala, provides comprehensive HIV care services to 612 adolescents out of over 17,000 PLHIV in care. The three clinics run from Monday to Friday as one-stop-centers for care and research on HIV, TB and other HIV-related conditions. The HIV and TB care is provided by multi-disciplinary teams which include counselors, community health workers, peer educators, nurses, pharmacy staff, doctors and laboratory staff. The clients receive HIV prevention services, ART, TB preventive treatment and TB treatment. There is also screening and treatment of other opportunistic infections and non-communicable conditions like mental health issues, hypertension, and diabetes. The services are provided at the health facilities or within the community, based on the national HIV and TB treatment and prevention guidelines.

The CALHIV were screened for TB using the WHO-recommended TB symptom screening tool at every clinic visit. Individuals with TB symptoms completed a clinical evaluation, and TB diagnostic tests, such as Xpert MTB/RIF ultra, urine TB lipoarabinomannan (TB-LAM) for those with CD4 count <200cells/ul, and chest X-ray. Patients diagnosed with TB then start TB treatment.

Individuals who were assessed as not having TB were considered eligible for TPT, such as; PLHIV above one year of age with no evidence of TB disease, PLHIV who are close contacts of TB patients, and PLHIV who have recently completed a full course of TB treatment. The ministry of health supplied the study sites with TPT drugs; initially isoniazid taken daily for six (6) months, and later rolled-out once weekly isoniazid and rifampentine for three months. The TPT is dispensed with pyridoxine, to prevent peripheral neuropathy, a common side-effect of isoniazid. Individuals who developed mild or moderate side effects, were usually advised to continue with the TPT while the side-effects were managed. If any individuals developed severe side effects, the TPT was withheld to first manage the side effects.

Individuals who initiated TPT within the differentiated delivery approach, had follow-up done via phone calls at two weeks and four weeks after TPT initiation. Follow-up was done at 3months after TPT initiation, and thereafter every three-months at the clinic or within the community to identify and manage side-effects, screen for TB symptoms, and assess adherence to the TPT and ART.

TB screening and diagnostic tests were done for participants with TB symptoms after starting TPT. Participants diagnosed with TB disease before completion of their full TPT course had their TPT stopped and TB treatment started. Adolescents living with HIV were eligible for the study if they were aged 10–19 years, initiating TPT, and completed or did not complete the full dose of TPT.

Care takers were eligible for the study if their children aged <18years living with HIV were initiating TPT, completed or did not complete the full dose of TPT and were willing to provide written informed consent. Health care workers were eligible if they were actively involved in providing TPT and willing to provide written informed consent.

Purposive sampling was done to select eligible health workers, adolescents aged 10-19years and parents or care takers of children who were eligible to start TPT.

During selection of adolescents and care takers, selection was done to try and achieve representation from; the three clinics, with almost equal numbers of; males and females, and age categories (10-14years, 15-19years), TPT completion status (completed, did not complete, missed doses or lost to follow-up), facility-based or community-based delivery models, and ART status (initiating ART or ART-experienced).

The health care workers in this study were involved in screening the children and adolescents for TB, assessing TPT eligibility, prescribing TPT, monitoring individuals on TPT, and providing TB-HIV counseling and guidance according to the national TB and leprosy control guidelines (24). Among the health workers, efforts were made to select equal numbers of males and females, and fair representation by different cadres (nurses, clinical officers, doctors, pharmacists).

#### **Data collection procedure**

A semi-structured interview guide was used for each category to obtain in-depth descriptions and valuable insights about the barriers and facilitators to TPT initiation and completion from the three categories of participants.

During the TPT initiation visits, qualitative in-depth interviews (IDIs) were conducted face to-face by an experienced male social scientist (DN), using the piloted interview guide for the data collection process. Interviews lasted between 30 and 45 min. Field notes were also made after each data collection session. Participants were recruited through purposive sampling with the help of the study nurse (CN) at three HIV clinics between June 2022 and August 2023. The IDIs were carried out with the CALHIV, Caretakers/parents and health workers. All the IDIs were held in a conducive place that was safe, neutral and with minimal distractions for the participants and the researcher. This place was either suggested by the interviewee or preset by the interviewer at the participating HIV clinics. Data collection was conducted in a language preferred by the participant, either English or Luganda. The interviewer (DN) took time at the outset of the discussions to develop a rapport with participants, acknowledging the sensitivity of the topic and creating a safe space for them to share their thoughts

and experiences. Participants were fully informed about the purpose and objectives of the study, and they provided their informed consent to participate, indicating their understanding and agreement with the research goals and procedures. Approximately four months into the TPT study, participants were approached to participate in the second phase of IDIs for TPT completion.

**Table 1** Demographic characteristics of study participants

Variable	Health workers (HWs)	
	Female (n=4)	Males (n=6)
<b>Age</b>		
Mean (SD)	36.7 (6.95)	
<b>Training</b>		
Counsellor	0	1
Epidemiologist	0	1
Medical Doctor	0	3
Nurse	1	0
Peer educator	1	0
Pharmacy	0	1
Testing and community linkage facility	2	
<b>Primary caregivers</b>		
Variables	Caregiver	
	Phase one	Phase Two
	Male (n=1)	Females (n=9)
	Male (n=2)	Fe-males (n=8)
<b>Age</b>		
Mean (SD)	34.5 (13.42634)	
<b>Occupation</b>		
Cleaner/Charcoal seller	0	1
Dobbie/hairdresser	0	1
Farmer/Fisher monger	1	4
Not working	0	2
Tailor	0	1
Formal employment	0	0
<b>Children and Adolescents Living with HIV (CALHIV)</b>		
Variables	CALHIV	
	Phase one	Phase Two
	Male (n=3)	Females (n=7)
	Male (n=5)	Fe-males (n=5)
<b>Age</b>		
Mean (SD)	15.6 (2.07)	
<b>Education level</b>		
Primary	2	0
Secondary	1	7

During the TPT initiation visits, we conducted 30 IDIs, (N=30; 10 with HWs, 10 with CALHIV, and 10 with caretakers). At TPT completion visits, we conducted 20 IDIs, (N=20, 10 with CALHIV and 10 with Caretakers). Each IDI lasted for 30-45 min

During the analysis, we identified themes describing the perceived and experienced facilitators and barriers to TPT initiation and completion among children and adolescents living with HIV (CALHIV). These were categorized into five levels (individual, interpersonal, community, institutional and Structural) based on the SEM (Fig. 1)

### Sample size

During TPT initiation, thirty (30) IDIs were carried out with the caretakers/parents and children (N=30; 10 health workers, 10 CALHIV, and 10 Caretakers/parents). After TPT completion, interviews were conducted with 10 care takers, and 10 CALHIV. Participants were purposively sampled to represent those CALHIV who completed and those who did not complete or defaulted their TPT dose. The interview guide explored both the facilitators and the barriers for the TPT initiation and completion.

### Data management and analysis

In-depth interviews were audio recorded, transcribed verbatim, and then translated into English for a hybrid approach of inductive and deductive thematic analysis [22] by two researchers (DN and PMA) experienced in qualitative methodology. The initial deductive coding was based on the five levels of the Social Ecological Model (SEM) in Fig. 1 above, and inductive coding was used to explore other themes that were not covered by the SEM. Three transcripts were initially selected and read through for familiarization and coded manually by DN. To ensure coding consistency, the developed codes were shared with the study principal investigator PMA to facilitate collaborative thematic analyses throughout [23]. All transcripts were imported into NVivo 14 and coded using the refined codebook by DN and PMA. The transcripts were not returned to the participants. The data was organized into pre-defined key themes outlined by the levels of the SEM. A framework approach using SEM was used for data analysis [25]. Themes and sub-themes were continually reviewed and refined to capture emerging new codes. Quotes were captured to highlight thematic areas and increase our understanding of the context. The methods and results were aligned to the consolidated criteria for reporting qualitative research (CORE-Q) [26].

### Results

A total of 50 IDIs were conducted for the selected participants (health workers (N=10), adolescents (N=10), care takers (n=10) until saturation of content was achieved. Table 1 below summarises the demographic characteristics of the study participants.

#### Facilitators to initiation and completion of TPT among adolescents and children

From the IDIs, we found the following facilitators at individual level. Participants perceiving themselves as being at risk of contracting TB was a key facilitator to initiate and complete TPT. In addition, some care takers highlighted that the TPT will also help the child to have a good life without TB, but if she acquires TB and yet is already HIV positive, the child may be severally affected.

*“Apart from the fact that it will help me to prevent TB, it will help me not to get TB and am assured that I will not get TB because TB is very risky, inconvenient and I will protect others because I know I am at a very high risk. So by taking the drugs, at least I know am protecting someone in case I get it, am protecting a family member, a sibling, a sister.” Male Adolescent 15 years.*

Further analysis revealed that care takers and participants who were once diagnosed with TB and recovered narrated their agony and the experience of treating TB which they noted that they would not want to experience again. The experience they had with TB disease compelled them to initiate and complete their TPT dose.

*“Another reason why I accepted my child to start on TPT is because my child has ever suffered from TB, and given that now we have the drugs for preventing it, I had no reason to resist it. I was afraid the child might acquire it again.” Female carer of 10-year-old adolescent.*

The desire to remain free from TB emerged as a facilitator to initiating and completing TPT. The TPT was perceived as a breakthrough strategy to prevent acquisition of TB.

*“Since I had an experience of a person with TB that I told you about, I didn’t want to wait until he is affected as it did to the other one I saw. So that forced me to ensure that the dose is completed.” Female caretaker of 14-year-old adolescent.*

At the interpersonal level, support, care and encouragement from family, supervision from the caretakers also emerged as important facilitators to initiate and complete TPT. The participants remarked that receiving care and support (reminders) from immediate family encouraged them to complete their treatment.

*“Like at home, there is my mother who always reminds me to take my drugs. That helped me to always take my drugs in time.” Female Adolescent, 18 years.*

Community level facilitators included guidance and counseling, comprehensive information, mass awareness and sensitization about TPT. Participants mentioned that receiving adequate information and sensitization was helpful for their decision to initiate TPT. Participants reported that they received information from the health workers on how the child should take the medicine and how the treatment works to prevent the disease,

something that encouraged most of them to start their children on treatment.

*“The encouragement I got from doctors helped me to give treatment to my child for TB treatment which also made it easy for me to start him on TPT. I believe by the time the dose is completed the child will be okay. Doctors also sensitized us about the possible side effects of the drugs and they follow up with phone calls.” Female care taker for a 7-year old child.*

It emerged that information about the TPT made available by the health workers, with opportunities to discuss the treatment with the doctors, and making it known in the community, enabled the care givers to allow TPT to be given to their children and adolescents.

*“When people are aware, it makes the services easy to access. Many people talk about other things on TVs and radios but they don’t take about TB. We have to tell people TB is real and a killer disease. You can also inform them in case someone sees the symptoms they should be screened for TB.” Medical doctor 01.*

At the institutional and organizational level, participants preferred to have convenient services as a facilitator for the initiation and completion of the treatment. This was in terms of having TPT appointments scheduled on the same days of ART refill so that they can have all the drugs on the same appointment as this will reduce the time spent at the clinic and cost of repeat visits.

*“The other issue is integrating those TPT refills with their usual clinic visits and community services so that they can readily receive the drugs at times without even wasting much time and transport to come to the clinic.” Medical doctor 02.*

Among the healthcare providers, it emerged that many young people preferred to have the drugs taken to them so that they don’t have any excuses of not coming to the clinic for treatment.

*“Also initiating TPT delivery models that reduce the transport costs and avoid missing clinical appointments and doses. Also to make sure their drugs are delivered before they are out of stock.” Nursing officer 01.*

Besides the convenient services, health workers recognized mechanisms of following up the patients initiated

on TPT or reminding them when to take their treatment as facilitator for the completion of TPT.

*"We need to make mechanisms of follow ups when you put someone on TPT, you have to check on them to see how they are doing sometimes when you tell them to take the drug on Sunday it means they will even shift the ARVs to the same date". Epidemiologist 01.*

Health workers also cited frequent and friendly communication with children and caretakers in terms of the health talks at the clinic, calling the patients through the mobile phones and receive their feedback.

*"Another thing is when you relate with children they bring out their challenges where you share and help them out. Smoothly they can cooperate and complete the six months' TB preventive treatment". Study counsellor 01.*

*"With the care takers, it is just a matter of explaining to them. It will not be hard for them if they have understood the importance of TPT and even the challenges will be less. The information should be explained in a way which is understood." TB community linkage facilitator 01.*

At the structural level, what emerged was having national policies and good performance indicators at the health facilities that are developed to create demand for the TPT among CALHIV has a great advantage and facilitates TPT uptake.

*"Demand creation, tasking health workers. We have our weekly performance review and TPT is among the many indicators we track. Ministry of health asks us how many people are on TPT which helps the health worker to improve on performance and this will facilitate the uptake of TPT". Medical officer 01.*

Regular auditing and identifying the challenges and weaknesses at the facilitate level in relation to the prescription of the treatment emerged as a key facilitator for the uptake of TPT among CALHIV.

*"We have reached that level where we appreciate if you find your health workers are not performing well, sit down as a unit and ask yourself on the weaknesses. If you planned to start 56 participants on TPT this week what happened, open the file and do file audits. You will discover interesting things other than patients missed to come or ask the phar-*

*macist why were you not prescribing the drugs when there was even an alert". Epidemiologist 02.*

The following themes emerged as barriers to TPT initiation and completion at patient-level, structural, community and interpersonal levels.

We found the following individual-level barriers to TPT initiation and completion. One of the emerging barriers to initiate or complete their TPT was the stigma associated with taking TB or HIV drugs. The fear of being seen taking many pills on a daily basis was cited as affecting their emotional well-being and mental health.

*"Stigma will always be there and I think it's a reason why so many kids out there fear. Personally before, I didn't have any problem taking my medicine. So when the stigma started I stopped taking medicine, I stopped caring, it really caused me a lot of mental damage and trauma". Male Adolescent 18 years.*

Where there is limited privacy, taking the treatment would be difficult. Participants also mentioned that they would fail to come for their HIV clinic appointments, for fear of being identified as HIV patients or TB patients.

*"...the main challenge is the stigma of HIV which is a leading factor in the community. Some of them fail to come for their appointments because of stigma. They don't want to be identified as HIV or TB-positive". Medical officer 03.*

The fear of drug-related side effects was reported as a key barrier to starting TPT. Participants expressed their fear of taking TPT treatment for fear of side effects based on their past experiences with different drugs. At TPT completion, experience of side-effects like dizziness and nausea emerged as barriers to TPT completion.

*"It would make me feel nausea or feel like vomiting, headache and dizziness. Me I decided not to take them anymore... I even didn't tell anyone". Male adolescent, 12 years old.*

High pill burden coupled with poor drug adherence also emerged as key barriers reported by the participants, especially if the child was also on ART regimens.

*"Another issue is about the pill burden because these are people who are already on ARVs and then they are added more pills for TB so it becomes a lot for them". Nursing officer 3.*

*"The biggest barrier is adherence because it's still a challenge to even those that are HIV negative. There are clients who are not used to taking treatment*

*and if the treatment is for six months there will be a challenge of commitment to take the drugs every day.” Medical officer 03.*

Among the caretakers, it emerged that pill fatigue created by taking tablets when a person is not sick with TB, caused many adolescents to miss their doses and some did not complete, even though they reported taking the drugs when it is not true.

*“Some children fear taking drugs and time comes when the child is tired and no longer wants to take the medicine. ... the child can pretend to be taking the medicine when it is not true because the child got tired of taking the drugs.” Female Caretaker of 8-year-old child.*

*“That the medicine was a lot, and the child got tired of it, so she didn’t complete. “Sometimes she could say, “it is just for prevention, I will not take it”. The fact that the child didn’t have TB, she could not care at all.” Female caretaker of 15 years adolescent.*

Caretakers expressed the discomfort of children taking pills with a bad smell, big size, unpleasant color and poorly packaged. Participants said that a pill with no smell, small size and attractive packaging would be easier to swallow.

*“One, the smell of the medication might not be really good to the child, the pill size can be too big, you even see and say ooh! Female caretaker to 13-year-old adolescent.*

It emerged that some adolescents and their caretakers are “engaged in demanding jobs that may not allow time to collect their medication or they may forget to take it”. Community Health linkage officer 01.

Forgetting to take the additional drugs also emerged as hinderance to complete the TPT.

*“...when you work a lot and do not get time, because you are not used to it like ARVs, the busy schedule can also cause you from not taking the drugs. Male adolescent-18 years.*

*“She is so forgetful. You always have to ask her whether she has taken the medicine. If you are not around, I just know she has not taken and that’s why she didn’t complete.” Female caretaker to a 16year-old adolescent.*

At the interpersonal level, the change of caretakers and lack of support mainly from parents also emerged as key barriers to the completion of TPT.

*“Some of them like children depend on their care-takers and sometimes we experience changes of the caretakers.” Nursing officer 04.*

Among female caregivers, denial or restrictions by the husbands to come to the clinic for refills, also emerged as a barrier for TPT completion among their children

*“For those that are married, their husbands don’t allow them to come to the clinic since it was not on the program.” Female caretaker 14 years child.*

Financial constraints and lack of food contributed to delay in TPT initiation and failure to complete the treatment. Caretakers expressed concerns that certain medications require a specific diet to be effective, but they struggled to provide the necessary nutritional support, particularly for their school-aged children, which in turn impacted their ability to adhere to treatment regimens, as highlighted by one adolescent’s experience

*“Ok the major challenge I faced at school is sometimes I don’t take medicine because I have not eaten. I know the medicine is very strong and I know it will affect my stomach. It will affect me so if am to take it on an empty stomach it wouldn’t be possible. So sometimes I just don’t take it because I know it will cause me effects.” Female Adolescent 18 years.*

Failure of the caretakers to disclose HIV status to the children was cited as a barrier of children to initiate and take TPT treatment. One health worker noted that most mothers at home have never disclosed the reason why their children take these drugs daily, and when the husband is around they cannot take their drugs.

*“There is also no disclosure especially to the children. So you find when the child doesn’t take the drugs because they do not understand why they are taking the drugs.” Medical doctor 04.*

This has also been a challenge to trace TB contacts in families where the patient has never disclosed to the family members and as a result, children in these families miss the opportunity to take the TPT treatment.

*“Disclosure is the problem when families have not yet disclosed, and someone comes down with TB. It is difficult to conduct contact tracing, for example on what ground are you asking the family about TB. So it is hard.” Epidemiologist 02.*

At the community level, misconception about TPT and Community stigma associated to TB were some of



the barriers identified. Further analysis revealed that some adolescents are so inquisitive about drugs and the intended benefit of taking the drugs. However, many are confused with the different sources of information about the benefits of the drugs. In addition, they did not understand how it could work to prevent infection. For example, there was a misconception about the dangers of taking medication when you are well. Some perceived that the government would introduce these treatments as a gateway to reducing their life span.

*“Adolescents are very inquisitive. They keep questioning depending on the different sources of information they receive. So some of the questions are like, “don’t you think these are the drugs that stimulate our TB?” Most of them have those questions and I don’t know whether it’s propaganda now they keep saying “the government or the health facilities are trying to make us fall sick quickly and we even google some of these drugs kill the cells that could have protected our bodies”. This affects their TPT drug adherence.” Medical officer 02.*

Participants also reported that there was stigma related to TB disease at health facilities and in the communities where patients reside. The situation worsens especially for adolescents in schools where students fail to take their medication until their next appointment because of the stigma from their fellow peers.

*“Students may stigmatize you, which at times makes you not to take the drugs or hide it from them that you are not taking the drugs.” Female adolescent 18 years.*

*“Yes, because they disturb you, they say that one is a TB patient, and they talk a lot. This caused me to miss the refill days.” Female adolescent 14 years.*

At the institution level, the long waiting-time at the clinic emerged as a barrier to completing TPT. Participants revealed that they preferred quick access to services without having to spend long hours in queues waiting to receive the treatment.

*“It’s just embarrassing, it’s just too much. The long waiting really makes me feel like opting out. That’s the truth I can tell you.” Female care takers to a 13-year-old adolescent.*

*“I come early and leave late. That issue made it hard for me. Sometimes I tell her to go by herself but then I remember that she will not give in her complaints. Sometimes we missed coming.” Female caretaker to a 12-year-old adolescent.*

Participants were concerned about the attitude of health workers when they are seeking services. This was viewed as a major barrier because they thought if the health workers are rude to the clients, they might not find it conducive to collect their treatment. This was echoed by some health workers who shared the experience that when patients are mistreated, they fail to come back until they are followed up.

*“You may find when the person has failed to come on a clinic visit because he was mistreated by a nurse and has not been listened to. Then the person concludes by saying I will not come back.” When it comes to the next appointment, they don’t come back.” Medical officer 05.*

Health care workers forgetting to prescribe the drugs at refill visits emerged as one of the barriers to TPT completion.

*“Also to the prescribers, someone might have taken TPT like for three months and when they report back, the prescriber forgets to give the refill to add up the six months. So, a patient ends up missing the three months and restart the treatment again.” Medical officer 01.*

Health care workers also commented that health facilities may lack essential medicines, and clients are advised to buy from private pharmacies which hinders completion.

At the structural level, participants reported that if the clinic was not within easy reach, they found it a problem to pick their drug refills. This required them to travel long distances with costly transport.

*“Transport also affects us, there is a time when you have to come and get treatment but when you don’t have money and that’s why some people fail to come.” Female care giver to 12-year-old adolescent.*

## Discussion

This qualitative study explored the perceived, and experienced facilitators, and barriers to TPT initiation and completion among children and adolescents living with HIV, as reported by the Ugandan health workers, adolescents, and care takers of children.

Parental support and supervision, perceived risk of TB disease, and previous experiences of TB treatment were reported by adolescents and care takers of children as the major facilitators of TPT initiation and completion. Similar to a Kenyan study by S. Ngugi et al. [15], this study found that provision of adequate information about TPT benefits and dosing by health workers, family and

community support, and experience of treating children with TB were highlighted by care takers as facilitators that enabled their children to initiate and complete TPT. Social support is very key in determining TPT initiation and completion among CALHIV, calling for integration of psychosocial support in TPT programs.

Facilitators of TPT initiation and completion highlight the need to provide adolescent friendly services and integrated TB and HIV services to facilitate initiation and completion of TPT among adolescents living with HIV [8]. Adolescent friendly services should be accessible, acceptable, appropriate and delivered in safe and respectful environment by supportive healthcare providers (27, 28). These include promotive, preventive, curative, and referral health services (28).

The barriers to TPT initiation and completion reported by adolescents included; TB or HIV-related stigma, busy work schedules of the adolescents and care takers, reduced social support from parents and family, previous experience of side effects from other drugs, pill burden and fatigue when that are not sick, financial constraints to travel to the clinic, and lack of food to take with the medicines. The roll-out of shorter TPT regimens is very timely [9], and will most likely address concerns of pill burden and fatigue among CALHIV who are already receiving daily ART.

Although care takers identified barriers to TPT initiation and completion that were similar to those reported by the adolescents, care takers additionally reported barriers such as; pill size, burden and odour, misconception and misinformation about the benefits and duration of the TPT, long distances to the health facilities, and rude health workers. It is important to provide regular adherence support from TPT initiation to facilitate completion, and therefore the efficacious benefits of TPT.

In contrast to the study by Teklay G et al. [18], health workers did not report fear of creating isoniazid resistance as a barrier to TPT initiation among CALHIV. Barriers cited by health workers included; TB and HIV-related stigma, undisclosed HIV status to the CALHIV, misconceptions that TPT puts their life at risk, fear of side effects, missed opportunities due to forgetting by health workers, poor attitude of health workers towards the adolescents, long waiting hours, change of care takers, and lack of parental or social support. These are closely related to the contextual barriers reported by Nyarubamba R. F et al. in Tanzania [14], and Lai J et al. in Ethiopia [16]. Drug stock outs in some facilities were reported as barriers, similar to a study among health workers in Ethiopia [18].

### Limitations

The purposively selected sample is not widely representative of the CALHIV and their care takers in high

TB burden countries. Therefore, transferability of these results in other settings may vary based on; the social-ecological models used to assess patient perceptions, TB disease burden, patient/family education and support initiatives within the healthcare system. There were limited numbers of participants who did not complete TPT, limiting the depth of lived experiences about barriers to TPT completion among CALHIV. This study did not explore the perspectives of policy makers in TB care, as these are also important to guide concerted efforts to improve TPT uptake and completion among CALHIV. There was no quantitative data for triangulation with the qualitative results.

### Strengths

The in-depth interviews were conducted at TPT initiation and after TPT completion. This minimised recall bias. This enabled deeper understanding of both perceived and experienced facilitators and barriers to TPT initiation and completion among CALHIV.

### Conclusion

The facilitators and barriers of TPT initiation and completion among CALHIV are diverse, spanning from individual factors to healthcare system and structural factors. Educating patients about the benefits of TPT and the need to reduce the risk of TB, facilitates TPT initiation and completion among CALHIV. Availability of social support, adolescent-friendly services, and integration of TPT refills into ART refill visits are also major facilitators of TPT initiation and completion among CALHIV.

TB and HIV-related stigma, high pill burden of TPT in addition to ART, non-disclosure of HIV status of the children and adolescents, lack of parental support, transport difficulties, and misconceptions about TPT side effects, were the major barriers to initiation and completion among these CALHIV. Therefore, it is important to implement patient-centered TB and TPT services for CALHIV and their caretakers, so as to improve TPT initiation and completion, ultimately, reducing TB burden in this high-risk population.

### Recommendations

Provision of clear information about TPT and TB, psychosocial and adherence support, adolescent-friendly TB-HIV services, and integration of TPT delivery into ART delivery models, are promising strategies to improve the uptake and completion of TPT among children and adolescents living with HIV in high TB-HIV burden settings like Uganda. TPT completion is likely where services are offered within a family-centered approaches to enhance psychosocial support for adherence. We recommend integrating TPT delivery into existing ART

delivery approaches, at health facility and community level, to enhance uptake and completion of TPT among CALHIV.

#### Abbreviations

APN	Assisted Partner Notification
ART	Anti-retroviral therapy
ARVs	Anti-retroviral drugs
CALHIV	Children and Adolescents Living with HIV
COVID-19	Severe Acute Respiratory Syndrome due to Corona Virus-19
DSD	Differentiated Service Delivery
DSDM	Differentiated Service Delivery Models
HIV	Human Immune-deficiency Virus
3HP	3months course of Isoniazid and Rifapentine
3RH	3months course of Isoniazid and Rifampicin
ICCM	Integrated community case management
INH	Isoniazid (isonicotinylhydrazide)
IPT	Isoniazid Preventive Therapy
ITS	Interrupted time series
LTBI	Latent Tuberculosis Infection
MOH	Ministry of Health
NDA	National Drug Authority
NLTP	National Tuberculosis and Leprosy control Program
P-BC	Bacteriologically Confirmed Pulmonary Tuberculosis
P-CD	Clinically Diagnosed Pulmonary Tuberculosis
PLHIV	People Living with HIV
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
TPT	Tuberculosis Preventive Treatment
VHT	Village Health Team
WHO	World Health Organisation

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#### Author contributions

PMA conceived the original concept. The funding was secured by PMA, PJE, PNN, ARK, AK, AMM, PM. The study was designed by PMA, PJE, MSP, AG, NAS, AMM, PM. Data was curated by PMA, DN, AB, DB, MM, CB, LK and CN. The data was analysed by DN and PMA. The project was co-ordinated by PMA, DN, MM, DB, DAR, and CB. The project technical advisors and mentors were; PJE, AK, ARK, AMM, NAS, MSP, AMM, PM. The original manuscript draft and responses to all author comments were written by PMA and DN. All authors reviewed and edited the original manuscript draft before submission. PMA and DN addressed all comments, and revised the manuscript. All authors reviewed and approved the final manuscript for publication.

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#### Data availability

The data that support the findings of this study are available on request from the corresponding author Dr Pauline Mary Amuge (PMA) paulacalista@gmail.com, and the institutional representative regulatoryaffairs@baylor-uganda.org. This is to ensure that the data is shared within the provisions of the protocol approved by the Makerere University School of Medicine research and ethics committee, as it was aimed to accomplish specified study objectives.

#### Declarations

##### Ethics approval and consent to participate

Written informed consent was obtained before data collection from participants aged  $\geq 18$  years, and parents/carers of children under 18 years. Written informed assent was obtained from children aged 8 years to under 18 years. All data were stored on encrypted computers. Filed notes and signed participant-informed consent forms were kept in a locked drawer at the study site. Participants' names were not recorded anywhere during data collection. Each participant was given a unique identifying number to ensure confidentiality. The research teams did not include any identifying information that could have harmful consequences for the participants. Ethical approval was granted by the Makerere University school of medicine Research and Ethics Committee (17th June 2020, REF 2020–127), and the Uganda National Council for Science and Technology (12th November 2020; HS768ES).

##### Consent for publication

All authors reviewed and the final manuscript and consented to submission for publication.

##### Competing interests

The authors declare no competing interests.

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